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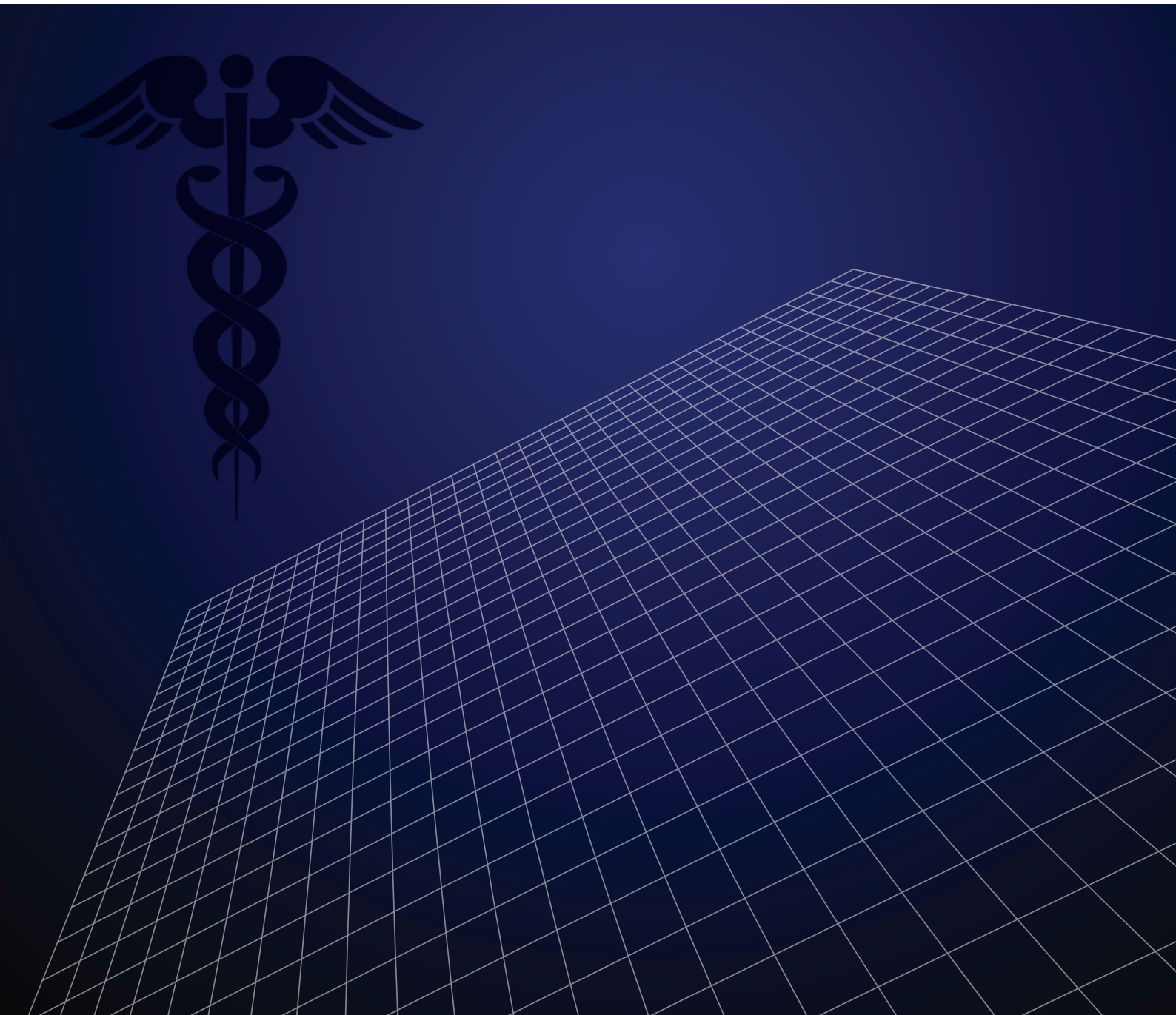

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Original Article

Prognostic significance of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, platelet/neutrophil ratio, and mean platelet volume in patients diagnosed with Hodgkin and Non-Hodgkin Lymphoma

Hodgkin ve Non-Hodgkin Lenfoma tanılı hastalarda nötrofil/lenfosit oranı, trombosit/lenfosit oranı, trombosit/nötrofil oranı ve ortalama trombosit hacminin prognostik önemi

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Abstract

Aim: We aimed to show whether easily accessible NLR, PLR, PNR and MPV values can be used as prognostic markers in lymphoma subtypes and whether they can contribute to existing prognostic scoring systems.

Material and Methods: The records of all lymphoma patients between 2005-2019 were reviewed retrospectively. NLR, PLR, PNR and MPV values at the time of diagnosis were compared with Progression-Free Survival (PFS) and Overall Survival (OS) durations.

Results: PLR and NLR values in Marginal Zone Lymphoma (MZL) and PNR and MPV values in Diffuse Large B-cell Lymphoma (DLBCL) were found to be associated with prognosis and to have a direct effect on PFS and OS. Except for these parameters, we found that lactate dehydrogenase (LDH), MPV, age, stage and histological subtype had an effect on prognosis for all patients.

Conclusion: It has been concluded that PLR and NLR can be used as prognostic factors in MZL, whereas PNR and MPV can be used as prognostic factors in DLBCL, and that these values can be used as easily accessible methods in disease prognosis scores.

Keywords: lymphoma; prognostic score; pnr; mpv; pfs; os

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Öz

Amaç: Kolay ulaşılabilir NLR, PLR, PNR ve MPV değerlerinin lenfoma alt tiplerinde prognostik belirteç olarak kullanılıp kullanılamayacağını ve mevcut prognostik skorlama sistemlerine ek katkı sağlayıp sağlayamayacağını göstermeyi amaçladık.

Gereç ve Yöntemler: 2005-2019 tarihleri arasında ki tüm lenfoma hastalarının kayıtları retrospektif olarak incelenmiştir. Tanı anında ki NLR, PLR, PNR ve MPV değerleri ile PFS ve OS süreleri karşılaştırılmıştır.

Bulgular: Marjinal zone lenfomada PLR ve NLR değerleri ve DBBHL'da da PNR ve MPV değerlerinin prognoz ile ilişkili olduğu, PFS ve OS üzerine doğrudan etkisi olduğu saptandı. Bu parametreler dışında tüm hasta grubu için LDH, MPV, yaş, evre ve histolojik alt tipin prognoz üzerinde etkili olduğunu saptadık.

Sonuçlar: Sonuç olarak PLR ve NLR Marjinal Zone lenfomada, PNR ve MPV'de DBBHL da prognostik faktör olarak kullanabilir. Hastalık prognoz skorlarında kolay ulaşılabilir yöntemler olarak yerlerini alabilirler.

Anahtar kelimeler: lenfoma; prognoz skoru, pnr; mpv; pfs; os

Introduction

Lymphomas are clinically and pathologically heterogeneous, clonal lymphoproliferative malignancies that usually originate from B cells [1]. Although various classification systems have been used to date, the World Health Organization classification of lymphoid neoplasms system, which was recently revised in 2016, is being used [2]. Known prognostic markers should be sought according to the lymphoma subtype of each patient whose diagnosis is confirmed. Prognosis scores (R-IPI, MIPI, IPS, FLIPI) developed for some common subtypes are used. The determination of prognosis helps to determine treatment management strategies such as choosing the best therapeutic treatment for the patient, predicting early relapse that may develop, and increasing stem cell transplantation plans. All these studies are also insufficient in predicting response to treatment [3]. There is a need for new easily accessible prognostic factors at this stage.

Peripheral blood leukocytosis, neutrophilia, lymphopenia and thrombocytosis may be seen in systemic inflammation. Many diseases such as cardiovascular diseases, cirrhosis and bipolar disorders have been shown to be associated with chronic inflammation [4, 5]. From this point of view, it is suggested that the values and ratios (NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, PNR: platelet-neutrophil ratio), which can be determined by fast and easily accessible full blood count, can be used as a marker of systemic inflammatory response and can be used to determine the prognosis of some diseases [6, 7]. There are many studies showing that it can be used as a prognostic marker in solid organ tumors such as breast, lung, hepatocellular, stomach, ovary and colorectal cancer [6, 8-12]. MPV (Mean Platelet Volume) is a parameter that increases in response to stress and is an indicator of platelet activation and function[13]. It has been shown to be used as a prognostic marker in endometrial cancer [14]. In addition to all these studies, there are few studies in patients with Hodgkin Lymphoma, Follicular Lymphoma and Diffuse Large B-cell Lymphoma [15-19]. In this study, we aimed to show whether NLR, PLR, PNR and MPV values can be used as prognostic markers in different lymphoma types as well as to show whether it can contribute to existing prognostic scoring systems.

Material and Methods

This study was performed retrospectively from the medical records of patients who were followed up and treated for lymphoma (HL and NHL) in Antalya Training and Research Hospital. The records of all lymphoma patients between 2005-2019 were examined (n: 539). Because of the lack of hemogram values of 21 patients at the time of diagnosis, these patients were excluded and a total of 518 patients were included to the study. Demographic characteristics, histological subtypes, B symptom, stage, laboratory results, prognosis score according to histological subtype and disease status and life status were examined at diagnosis.

This study was approved by the Antalya Research and Training Hospital Clinical Research Ethics Committee dated 28.03.2019 and No 10/4. All procedures were carried out in accordance with the 2013 Helsinki Declaration.

Statistical Analysis

Descriptive values of the obtained data were calculated as mean, SD median, minimum-maximum, number and % frequencies. The suitability of the data for normal distribution according to the groups examined was examined by Kolmogorov-Smirnov test. The relationships between the two categorical features were examined by Pearson Chi-square test or Fisher Exact

test, and changes in numerical properties were examined by independent samples t-test for normal distributed data, and Mann Whitney-U test for normal distribution. The relationship between prognosis development and ex-status and NLR, PLR, PNR and MPV measurements were examined with ROC curve and if significant correlation was found, the appropriate estimation value was found. Estimation was not calculated in non-significant relationships. OS and PFS times were compared with Log-Rank test and Kaplan Meier graph was plotted for each estimated value. The factors affecting OS and PFS durations were examined by multiple Cox regression model. SPSS 22.0 program was used in the calculations and statistical significance level was taken as P <0.05.

Results

518 lymphoma patients were included in the study. 227 of the patients were Diffuse Large B cell Lymphoma, 97 were Hodgkin Lymphoma, 68 were Follicular Lymphoma, 48 were Marginal Zone Lymphoma, 27 were Mantle Cell Lymphoma, and 51 were other Non-Hodgkin Lymphomas. The median age at the time of diagnosis was 59(18-88). 221 patients (42%) were female. The appropriate predictive value for NLR, PLR, PNR and MPV parameters in each diagnostic group and in all patients was investigated by ROC analysis. For NLR and PLR parameters, only significant results were obtained in ROC analysis in Marginal Zone Lymphoma subgroup (P=0.045 for NLR area under the curve [AUC] value: 0.690, 95% confidence interval [CI]0.526–0.854) and P=0.047 for PLR AUC value 0.688, 95% CI 0.516–0.860). There were no significant results for NLR and PLR in the other subgroups and in the whole patient group. Estimations were calculated as 1.86 for NLR and 148.95 for PLR.

For the PNR parameter, only significant predictive level was found in the DLBCL subgroup (41.64, P=0.018 AUC value 0.405, 95% CI 0.326–0.485). ROC analysis for MPV parameter revealed significant but different predictive values in the DLBCL subgroup (P=0.036 AUC value 0.584, 95% CI0.505–0.663) and in all patients group (P=0.001 AUC value 0.596, 95% CI 0.543.60.648).

Table 1 shows the comparison of demographic and laboratory results according to the predicted PNR and MPV values in the diagnosis subtypes of DLBCL patients. According to the table, gender distribution showed a significant difference in terms of PNR estimation value (P=0.027). In the group with PNR<41.65, males were found to be significantly higher. When the distribution of the stages according to PNR estimation value was examined, it was found that the rate of patients with stage 3-4 was significantly higher in the group with PNR<41.65 (P=0.003). The presence of B symptoms was significantly higher in the group with PNR<41.65 (P=0.023). The proportion of patients with low prognosis score was found to be significantly higher in the group with PNR>41.65 (P=0.001). Both age and LDH levels were significantly higher in patients with PNR<41.65 (P=0.003 and P=0.001). In contrast, the presence of Bulky lesion and hemoglobin mean values were not significantly different in patients with PNR 41.65 or higher (P=0.715 and P=0.608).

When the patients with DLBCL were examined according to the MPV estimation value, the distribution of those with normal platelet levels was found to be significantly higher in the group with PNR<10.2 (P=0.017). In addition, the frequency of patients without progression was higher in the group with MPV<10.2 or less (P=0.040). In terms of other demographic and laboratory measurements, no significant difference was found between those below and above the MPV estimation value (Table 1).

Table 2 shows the comparison of demographic and laboratory results according to the predictive values of PLR and NLR in the marginal group. When the table was examined, Bulky absence was found to be significantly more frequent in the group with a PLR estimation of less than 148.94 (P=0.003). The frequency of those with high lymphocyte levels was significantly higher in the low PLR group, whereas the frequency of those with normal platelet levels was significantly higher in the PLR group (P=0.001 and P=0.009).

It was seen that the female ratio was higher in the NLR group (P=0.009). The ratio of patients with high levels of lymphocytes was higher in the group with low NLR value (P=0.001). Absence of bone marrow involvement was higher in the group with high NLR levels (P=0.020). However, the incidence of non-progression was higher in the group with low NLR (P=0.028) and significantly higher in the group with high NLR (P=0.040). The relationship between both PLR and NLR levels with other measurements was not significant (Table 2).

The comparison of demographic and laboratory results according to MPV estimation value which is significant for evaluation in the whole patient group without differentiating according to diagnostic subtypes is given in Table 3. Significant differences in neutrophil and platelet distribution were observed among individuals below and above MPV estimation (P=0.011 and P=0.001). Accordingly, the ratio of patients with both neutrophil and platelet levels was found to be significantly higher in the MPV predictive value group 9.9 and below. It was found that there was no correlation between the high prognosis scores calculated especially for the subgroups and the MPV estimation value of the other results.

Table-1. The comparison of demographic and clinical features according to the predicted PNR and MPV values in patients with DLBCL†

Demographic and Clinical Condition		PNR≤41.65 (n=56)	PNR>41.65 (n=171)	P	MPV≤10.2 (n=177)	MPV>10.2 (n=50)	P
Gender	Female	19 (33.9)	87 (50.9)	0.027[a]	82 (46.3)	24 (48)	0.834[a]
	Male	37 (66.1)	84 (49.1)		95 (53.7)	26 (52)	
Stage	I&II	11 (19.6)	71 (41.5)	0.003[a]	67 (37.9)	15 (30)	0.307[a]
	III&IV	45 (80.34)	100 (58.5)		110 (62.1)	35 (70)	
Presence of Symptom B	Absent	12 (21.4)	65 (38)	0.023[a]	61 (34.5)	16 (32)	0.745[a]
	Present	44 (78.6)	106 (62)		116 (65.5)	34 (68)	
Presence of bulky mass	Absent	33 (58.9)	96 (56.1)	0.715[a]	101 (57.1)	28 (56)	0.893[a]
	Present	23 (41.1)	75 (43.9)		76 (42.9)	22 (44)	
Neutrophil (×103/mm3), median	<2000	4 (7.1)	16 (9.4)	0.001[a]	14 (7.9)	6 (12)	0.544[a]
	2000-7000	29 (51.8)	138 (80.7)		130 (73.4)	37 (74)	
	>7000	23 (41.1)	17 (42.5)		33 (18.6)	7(14)	
Lymphocytes (×103/mm3), median	<1200	22 (39.3)	59 (34.5)	0.026[a]	65 (37.7)	16 (32)	0.450[a]
	1200-3100	26 (46.4)	104 (60.8)		98 (55.4)	32 (64)	
	>3100	8 (14.3)	8 (4.7)		14 (7.9)	2 (4)	
Platelet (×103/mm3), median	<150	24 (42.9)	9 (5.3)	0.001[a]	21 (11.9)	12 (24)	0.017[a]
	150-450	29 (51.8)	142 (83)		134 (75.7)	37 (74)	
	>450	3 (5.4)	20 (11.7)		22 (12.4)	1 (2)	
IPI Score	0-2	22 (39.3)	114 (66.7)	0.001[a]	108 (61)	28 (56)	0.523[a]
	3-5	34 (60.7)	57 (33.3)		69 (39)	22 (44)	
Bone Marrow Involvement	Absent	17 (65.4)	91 (90.1)	0.004[b]	84 (86.6)	24 (80)	0.376[b]
	Present	9 (34.6)	10 (9.9)		13 (13.4)	6 (20)	
Progression/relapse	Absent	20 (39.2)	97 (63.8)	0.002[a]	96 (61.5)	21 (44.7)	0.040[a]
	Present	31 (60.8)	55 (36.2)		60 (38.5)	26 (55.3)	
Age median		68 (37-88)	59 (18-88)	0.003[c]	61 (18-88)	62 (27-84)	0.645[c]
Hemoglobin g/dL median		12 (5-16.1)	11.9 (4.5-16)	0.608[c]	11.8 (5-16)	12.2 (4.5-16.1)	0.775[c]
LDH IU/dL median		397.5 (117-4099)	253 (117-1483)	0.001[c]	273 (117-4216)	273 (128-1390)	0.525[c]

† Median [min-max] or frequency (%). a: Chi-Square test b: Fisher Exact test b: Mann Whitney-U test

Table-2. The comparison of demographic and clinical features according to the predicted PLR and NLR in patients with MZL †

Demographic and Clinical Condition		PLR<148.94 (n=29)	PLR≥148.94 (n=19)	P	NLR<1.85 (n=24)	NLR≥1,8571 (n=24)	P
Gender	Female	11 (37.9)	10 (52.6)	0.315a	6 (25)	15 (62.5)	0.009[a]
	Male	18 (62.1)	9 (47.4)		18 (75)	9 (37.5)	
Stage	I&II	6 (20.7)	5 (26.3)	0.732a	3 (12.5)	8 (33.3)	0.086[a]
	III&IV	23 (79.3)	14 (73.7)		21 (87.5)	16 (66.7)	
Presence of Symptom B	Absent	20 (69.0)	10 (52.6)	0.253a	16 (66.7)	14 (58.3)	0.551[a]
	Present	9 (31.0)	9 (47.4)		8 (33.3)	10 (41.7)	
Presence of bulky mass	Absent	28 (96.6)	11 (61.1)	0.003b	22 (91.7)	17 (73.9)	0.137[b]
	Present	1 (3.4)	7 (38.9)		2 (8.3)	6 (26.1)	
Neutrophil (×103/mm3), median	<2000	5 (17.2)	0 (0)	0.147a	5 (20.8)	0 (0)	0.057[a]
	Normal	19 (65.5)	16 (84.2)		15 (62.5)	20 (83.3)	
	>7000	5 (17.2)	3 (15.8)		4 (16.7)	4 (16.7)	
Lymphocytes (×103/mm3), median	<1200	3 (10.3)	10 (52.6)	0.001a	2 (8.3)	11 (45.8)	0.001[a]
	Normal	10 (34.5)	9 (47.4)		7 (29.2)	12 (50)	
	>3100	16 (55.2)	0 (0)		15 (62.5)	1 (4.2)	
Platelet (×103/mm3), median	<150000	13 (44.8)	2 (10.5)	0.009a	10 (41.7)	5 (20.8)	0.282[a]
	Normal	16 (55.2)	14 (73.7)		13 (54.2)	17 (70.8)	
	>450000	0 (0)	3 (15.8)		1 (4.2)	2 (8.3)	
Progression/relapse	Absent	11 (64.7)	4 (30.8)	0.065a	10 (71.4)	5 (31.3)	0.028[a]
	Present	6 (35.3)	9 (69.2)		4 (28.6)	11 (68.8)	
Age median		61 (20-84)	69 (38-78)	0.082c	61 (18-88)	62 (27-84)	0.274[c]
Hemoglobin g/dL median		11.8 (5-15.7)	9.6 (7.5-15.8)	0.343c	11.8 (5-16)	12.2 (4.5-16.1)	0.040[c]
LDH IU/dL median		196 (140-285)	207 [9-466]	0.696c	273 (117-4216)	273 (128-1390)	0.89[3c]

† Median [min-max] or frequency (%). a: Chi-square test b: Fisher Exact test c: Mann Whitney-U test

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Table 3. The comparison of MPV estimation with demographic and laboratory data in all lymphoma patients †

		MPV≤9.9 (n=364)	MPV>9.9 (n=154)	p
Gender	Female	152 (41.8)	69 (44.8)	0.522[a]
	Male	212 (58.2)	85 (28.6)	
Lymphoma Subtypes	DLBCL	165 (45.3)	62 (40.3)	0.057[a]
	FL	41 (11.3)	27(17.5)	
	HL	73 (20.1)	24 (15.6)	
	MZL	35 (9.6)	13 (8.4)	
	MCL	21 (5.8)	6(3.9)	
	Others	49 (13.4)	20 (12.9)	
Stage	I&II	106 (29.4)	47 (31.3)	0.671[a]
	III&IV	254 (70.6)	103 (68.7)	
Presence of Symptom B	Absent	155 (43.1)	66 (44)	0.845[a]
	Present	205 (56.9)	84 (56)	
Presence of bulky mass	Absent	243 (67.1)	101 (67.3)	0.964[a]
	Present	119 (32.9)	49 (32.7)	
Neutrophil (×103/mm3), median	<2000	24 (6.6)	19 (12.3)	0.011[a]
	Normal	257 (70.6)	114 (74)	
	>7000	83 (22.8)	21 (13.6)	
Lymphocytes (×103/mm3), median	<1200	127 (34.9)	40 (26)	0.072[a]
	Normal	193 (53.0)	87 (56.5)	
	>3100	44 (12.1)	27 (17.5)	
Platelet (×103/mm3), median	<150000	45 (12.4)	35 (22.7)	0.001[a]
	Normal	278 (76.4)	113 (73.4)	
	>450000	41 (11.3)	6 (3.9)	
Prognosis Score	Low	186 (62)	74 (62.2)	0.972[a]
	High	114 (38)	45 (37.8)	
Progression/relapse	Absent	188 (61.6)	68 (51.9)	0.058[a]
	Present	117 (38.4)	63 (48.1)	
Age median		58.5 (18-88)	61 (19-87)	0.953[b]
Hemoglobin g/dL median		11.85 (5-17.2)	12.1 (3.7-16.1)	0.324[b]
LDH IU/dL median		244.5 (93-4216)	241.5 (107-1390)	0.285[b]

† Median [min-max] or frequency (%). a: Chi-square test b: Mann Whitney-U test

When the results of PFS and OS duration according to PNR estimation value determined by ROC analysis for DLBCL patients were examined, PFS and OS were found to be significantly longer in those above the predictive value (P=0.001&P=0.001). Kaplan Meier graphs are given in Figure 1A and 1B.

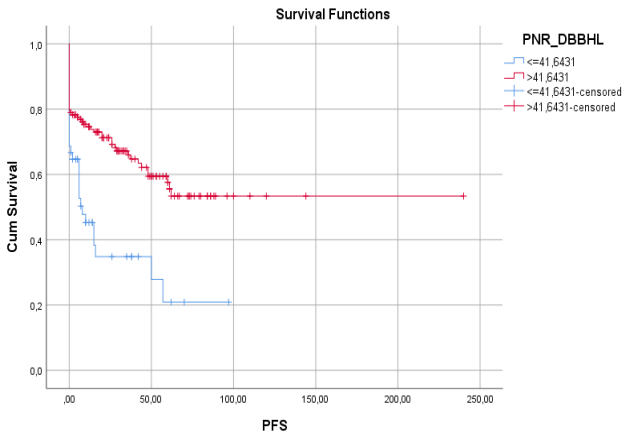

Figure-1A. PFS analysis according to PNR estimation in DLBCL

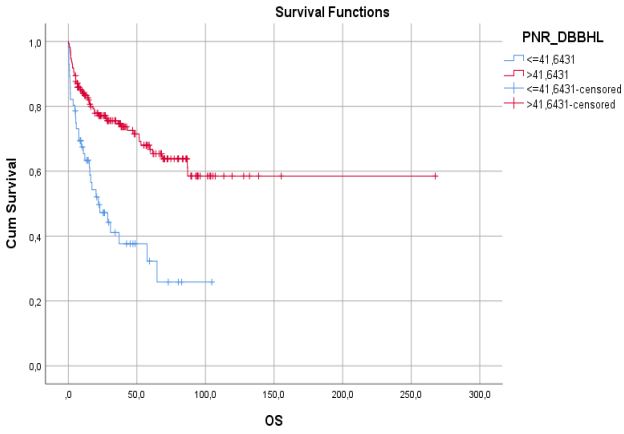

Figure-1B. OS analysis according to PNR estimation in DLBCL

When the results of PFS and OS duration according to MPV estimation value determined by ROC analysis for DLBCL patients were examined, there was no significant difference in PFS between MPV>10.2 and <10.2 (P=0.196), whereas OS was significantly shorter in patients with MPV>10.2 (P=0.048). Kaplan Meier graphs are given in Figure 2A and 2B.

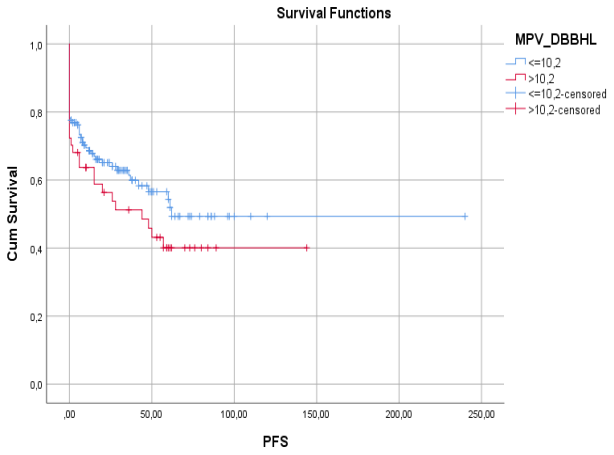

Figure-2A. PFS analysis according to MPV estimation in DLBCL

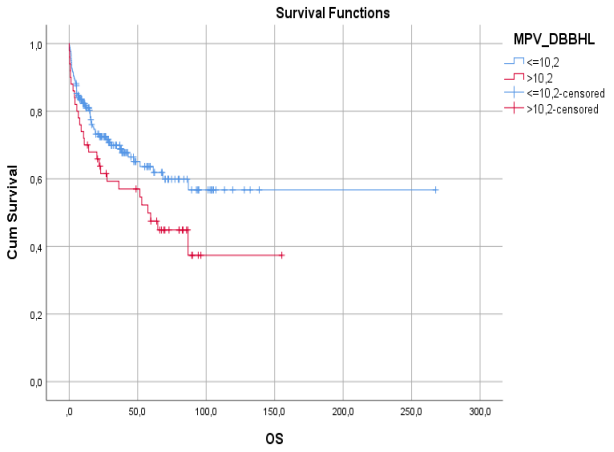

Figure-2B. OS analysis according to MPV estimation in DLBCL

When the diagnoses were evaluated separately, the predictive values of NLR and PLR were obtained only for the MZL subgroup. NLR and PLR ratio were classified according to this value and PFS and OS durations were compared. When the results were examined, no significant difference was found in terms of PFS for NLR>1.86 and <1.86 (P=0.174). On the other hand, OS was found to be significantly shorter in patients <1.86 (P=0.049). There was no significant difference in PLR in terms of> 148.95 and <148.95 PFS (P=0.432). But it was found that OS was significantly longer in subjects who had a value below the estimation (P=0.045). Kaplan Meier graphs are given in Figure 3A, 3B, 4A and 4B.

All patients were classified according to the ROC curve and the predictive value of MPV and compared for PFS and OS durations. It was determined that there was no significant difference in terms of PFS and OS duration in subjects with MPV values below and above 9.9 (P=0.362&P=0.070).

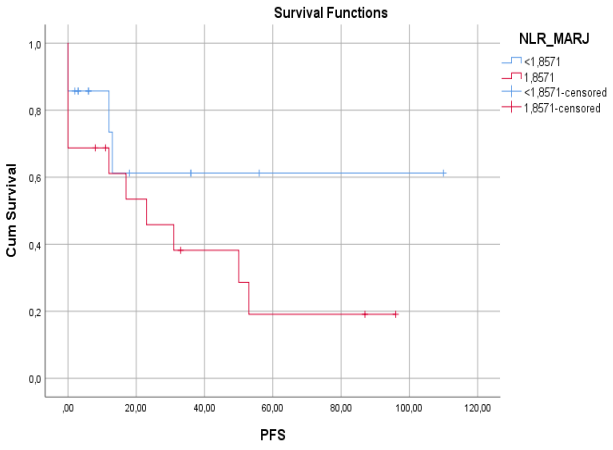

Figure-3A. PFS analysis according to NLR estimation in marginal zone lymphoma

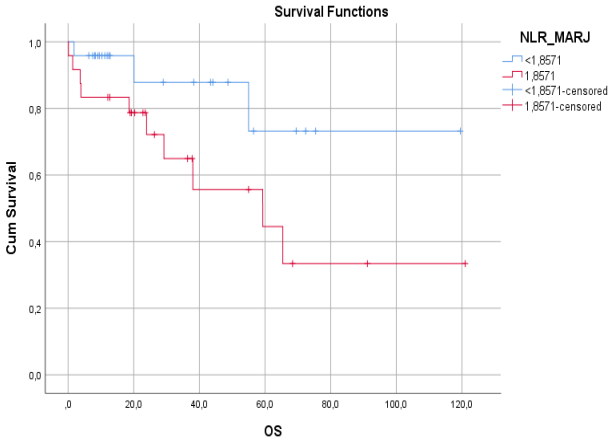

Figure-3B. PFS analysis according to NLR estimation in marginal zone lymphoma

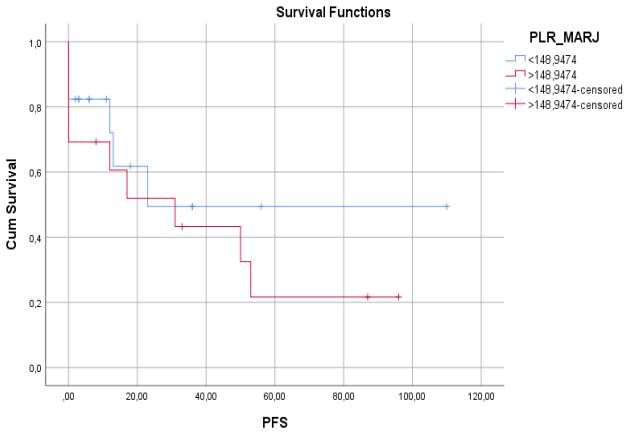

Figure-4A PFS analysis according to PLR estimation in marginal zone lymphoma

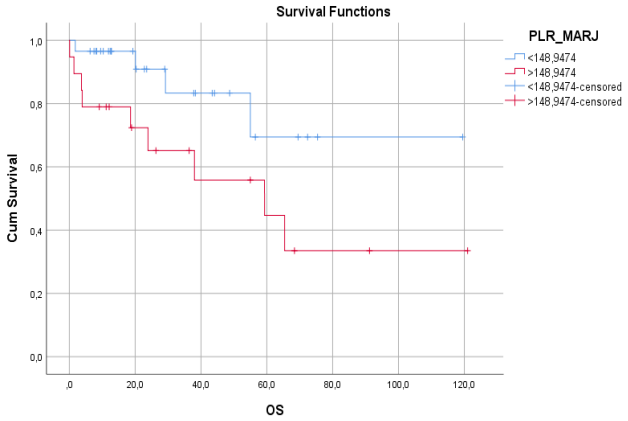

Figure-4B OS analysis according to PLR estimation in marginal zone lymphoma

The effects of each of the factors such as gender, age, disease subtype, stage, symptom b, hemoglobin, platelet, lymphocyte, MPV, LDH, and bulky lesion presence were examined individually and uncorrected hazard ratio values were found. Factors without significant effect in these analyzes were not included in the multivariate Cox regression model. Others were modeled together to obtain corrected hazard ratio values. When the results were examined, it was observed that the risk of death increased 1.052 times significantly as age increased 1 year (p = 0.001). The risk of death was found to be 0.519 times lower in patients with follicular diagnosis than those with DLBCL (P=0.030). It was seen that the risk of death increased by 2,331 times compared to those with stage level 3-4 (P=0.001). When LDH level increased by 1 unit, it was found that the prognosis development increased by 1,001 times (P=0.001). When MPV level increased by 1 unit, the risk of death increased by 1,138 times (P=0.030). Apart from these factors, the presence or absence of symptom B does not have a different effect on survival. Again, it was seen that increase or decrease in hemoglobin, platelet and lymphocyte levels did not significantly affect survival.

Discussion

This study is the first in the literature because it evaluates all lymphoma patients and subtypes separately and also investigates parameters such as NLR, PLR, PNR and MPV in a single study. There are various prognosis scores (R-IPI, MIPI, IPS, FLIPI) used in lymphoma subtypes. Prognosis scores consist of parameters such as age, hemoglobin level, stage and LDH level. When evaluated comparatively with OS and PFS, we found that the parameters we studied may be part of prognosis scores in some subtypes.

Inflammation is known to play a role in the development of many cancers and has an impact on disease progression, angiogenesis and treatment resistance [20-22]. The result of this is that inflammation affects OS in patients. Neutrophils are important markers of inflammatory response. They increase in response to inflammation in cancer. While platelets increase with neutrophils, there is a suppression of lymphocytes responsible for immune response [23]. It was thought that NLR can be used as a prognostic marker from this relationship and many studies have been conducted. Studies other than solid organ tumors for the effect of NLR on PFS and OS are usually of the subtypes of DLBCL [16, 19, 24]. The effect of NLR on MZL has never been studied. In our study, we found that having NLR>1.86 significantly shortened OS although not associated with PFS. Although not in lymphoma patients, Kelkitli et al. showed that the relationship between NLR height and decreased PFS and OS in MM patients [25]. The prognostic value of NLR was also investigated in many solid organ tumors and positive results were obtained [8-10]. In our study, we found that NLR was insufficient to show PFS and OS in patients with other subtypes except MZL. There are different results in this regard in the literature. Wang et al. found that NLR elevation was not associated with PFS, but was associated with OS in patients with DLBCL [19]. In studies conducted by Ho et al. including DLBCL studies and Romano et al. including HL studies, they showed that NLR was unrelated to PFS and OS[24, 26]. The results of these two studies are parallel to our study.

Studies on PLR are not as common as NLR. In our study, we found that having PLR>148.95 significantly shortened OS even though it was not only associated with PFS in MZL. Seo et al. found a significant relationship with PFS in their study with MZL, but there was no data about OS in this study [27]. Reddy et al. found significant results between 2-year PFS and PLR in HL patients and no information was given about OS [18]. In addition to these studies, Ni et al. found that PLR had a significant relationship with PFS in DLBCL, but not with OS [28].

In our study, in the analysis for PNR, PFS and OS were seem to be significantly shorter in those with PNR<41.64 in the DLBCL subtype. Platelets and neutrophils are cells that are expected to increase in inflammation. The prognostic significance of the rates of increase in this rate was investigated. However, it should be kept in mind that the disease may be thrombocytopenia due to bone marrow involvement. It is known that bone marrow involvement in lymphoma patients is considered to be stage-4 and is associated with poor prognosis. In our study, bone marrow involvement was found to be significantly higher

in the group with PNR<41.64 (P=0.004). There are no studies related to prognosis associated with PNR in the literature. Mercier and Voutsadakis found PNLR to be significantly associated with PFS and OS in their study of colorectal cancer [29]. Choi et al. found that thrombocytopenia is associated with low PFS and OS in peripheral T cell lymphoma [30]. In our study, platelet levels of those with PNR<41.64 were found to be significantly lower than those with PNR> 41.64.

MPV value increases in response to stress [13]. The increase in stress has suggested us that it can be used as a prognostic marker in newly diagnosed lymphomas. In our study, we found OS to be significantly shorter in patients with DLBCL with MPV>10.2. We could not find any relationship between PFS and MPV. When all patients were evaluated as a whole, no significant correlation was found between the predictive value for MPV and PFS and OS. However, when we look at 5-year survival, it is seen that 1 unit increase in MPV value was found to cause 1,138-fold increase in mortality risk. In a study by Zhou et al., it was found that MPV was associated with OS in parallel with our study in patients with DLBCL diagnosis [18]. Rupa-Matysek et al. showed that VTE also increased due to the increase in MPV, but OS regressed significantly [31].

The weakness of the study is that it is monocentric and includes very few patients, especially subtypes such as CNS lymphoma and T-cell lymphoma. Multinational and multicenter simultaneous study will have more meaningful results. In addition, there is no common predictive value for the parameters we investigate. Each retrospective study has its own value and it is very difficult to standardize them. A recent study showed that values such as NLR and PLR may vary according to age [32]. This makes it difficult to determine a common value for all patients.

Conclusion

It has been concluded that PLR and NLR can be used as prognostic factors in MZL, whereas PNR and MPV can be used as prognostic factors in DLBCL, and that these values can be used as easily accessible methods in disease prognosis scores.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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Orijinal Makale

Anesteziyoloji ve reanimasyon yoğun bakım ünitesinde yatan hastalarda gelişen kateter ilişkili üriner sistem infeksiyonlarının irdelenmesi

Investigation of catheter-related urinary tract infections in intensive care unit patients of anesthesiology and reanimation

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ÖZ

Amaç: Bu çalışmanın amacı, Ankara Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon yoğun bakım ünitesinde yatan hastalarda gelişen kateter ilişkili üriner sistem infeksiyonlarının hızlarının ve infeksiyon etkenlerinin retrospektif değerlendirilmesidir.

Gereç ve Yöntemler: Çalışmaya, 1 Ocak 2018-31 Aralık 2019 tarihleri arasında Anesteziyoloji ve Reanimasyon yoğun bakım ünitesi (ARYBÜ)'nde yatan ve kateter ilişkili üriner sistem infeksiyonu tanısı konulan hastalar dahil edildi. Hasta verileri enfeksiyon kontrol hemşirelerinin günlük vizitleri ve enfeksiyon hastalıklarının günlük konsültasyon kayıtlarından ve Ulusal Hastane Enfeksiyonları Sürveyans Ağı İNFLİNE programı verilerinden, laboratuvar verileri ise Mikrobiyoloji laboratuarından elde edildi. Hastaların demografik verileri, üriner kateterle ilişkili enfeksiyonları, enfeksiyon etkenleri, hastalardaki komorbid durumların varlığı kaydedildi.

Bulgular: Anesteziyoloji ve Reanimasyon yoğun bakım ünitesinde iki yıllık sürede 17910 hasta gününde 1243 hasta takip edilmişti. Hastaların üriner kateter günü 17470 gün idi. Çalışmanın yapıldığı dönemde toplam 85 hastaya 116 Kİ-ÜSİ tanısı konuldu. Üriner kateter kullanım oranı 0.97, kateterle ilişkili üriner sistem infeksiyonu hızı (Kİ-ÜSİ) ise 6.63 olarak saptandı. 2019 yılı Sağlık Bakanlığı Eğitim ve Araştırma Hastaneleri ARYBÜ'lerinin sürveyans verileri ile karşılaştırıldığında; hastanemizin ARYBÜ üriner kateter kullanım oranının %25 persentil ile uyumlu olduğu, Kİ-ÜSE hızının ise %90 persentilin üzerinde olduğu saptandı.Hastaların 47 (% 55)'si kadın, 38 (%45)'i erkek, yaş median değeri 66 idi. Hastaların tümünde üriner kateter mevcuttu. Hastalarda görülen komorbid hastalıklar; 44 (%51.8) hastada nörolojik hastalık (serebrovasküler olay, demans vb.), 40 (%47.1) hastada hipertansiyon, 28 (%32.9) hastada diyabetes mellitus, 20 (%23.5) hastada KOAH ve iki (%2.4) hastada kronik böbrek hastalığı olarak belirlendi. Hastaların 72 (%84.7)'si entübe idi ve 19 (%22.4)'unda dekübit ülseri mevcuttu. Kİ-ÜSİ etkenlerinin dağılımı incelendiğinde 27 (%31.8) hastada birden fazla etkenin izole edildiği görüldü. Üriner sistem etkenleri 18 (%21.2) hastada Klebsiella türleri (spp.), 10 (%11.8) hastada Escherichia coli, dokuz (%10.6) hastada Enterococcus spp.,sekiz (%9.4) hastada Pseudomonas spp., yedi (%8.2) hastada Proteus spp., dört (%4.7) hastada Acinetobacter spp., bir (%1.2) hastada Staphylococcus aureus ve bir (%1.2) hastada Enterobacter spp. olarak belirlendi. Kİ-ÜSİ saptanan 85 hastanın 19'unda kan kültüründe de aynı etken izole edildi. Kan kültüründen en sık izole edilen etkenler sırasıyla; altı olguda birden fazla etken, yedi Klebsiella spp., iki E. coli ve iki Enterococcus spp., bir Acinetobacter spp., bir Proteus spp. olarak belirlendi.

Sonuç: Yoğun bakım ünitelerinde kateter ilişkili üriner sistem infeksiyonu oranlarının azaltılması için üriner kateter takılması endikasyonlarının iyi belirlenmesi, gereklilik ortadan kalktığında kateterin çekilmesi ve enfeksiyon kontrol önlemlerine dikkat edilmesi uygun bir yaklaşım olacaktır. Yoğun bakım ünitesinde yatan hastalarda hastane infeksiyonu etkenlerinin belirlenmesi, ampirik tedavide yol gösterici olacağından mortalite ve morbidite oranlarının azaltılmasına da katkı sağlayacaktır.

Anahtar kelimeler: yoğun bakım ünitesi; kateter ilişkili üriner sistem infeksiyonu; risk faktörleri

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ABSTRACT

Aim: The aim of this study is to retrospectively evaluate the rates and infectious factors of healthcare-associated urinary tract infections in patients with Ankara Training and Research Hospital, Anesthesia and Reanimation intensive care unit.

Material and Methods: Patients hospitalized in the Anesthesia and Reanimation intensive care unit (ICU) between January 1, 2018 and December 31, 2019 and diagnosed with healthcare-related urinary tract infection were included in the study. Patient data were obtained from the daily visits of infection control nurses and daily consultation records of infectious diseases, while laboratory data were obtained from the Microbiology laboratory. The rate of infection associated with urinary catheter, distribution of infectious agents, and presence of comorbid conditions in patients were recorded.

Results: Totaly 1243 patients were followed up for 17,910 patient days in the Anesthesia and Reanimation intensive care unit for two years .The urinary catheter day of the patients was 17470 days. A total of 85 patients were diagnosed with 116 urinary catheter-related urinary tract infections. Forty- seven of the patients (55%) were female, 38 (45%) were male, age median value was 66.During the period of the study, it was found that the rate of urinary catheter use was 0.97, and the rate of catheter-related urinary tract infection (CI-UTI) was 6.63.When the rate of urinary catheter use in the Anesthesia and Reanimation intensive care unit in our hospital is compared with the 2019 Ministry of Health Education and Research Hospitals Anesthesia ICU surveillance data; it was found that the rate of urinary catheter use was consistent with the 25th percentile (0.97), and the rate of CI-UTI was above the 90th percentile (3.8).The most common comorbid diseases in patients were at least one neurological disease (cerebrovascular event, dementia, etc.) in 44 (51.8%) patients, hypertension in 40 (47.1%), diabetes mellitus in 28 (32.9%), chronic obstructive pulmonary diseases in 20 (23.5%) patients and 2.4% of the patients were identified as chronic kidney disease. All patients had urinary catheters. 72 (84.7%) of the patients were intubated and 19 (22.4%) had decubitus ulcers.Distribution of agents causing urinary tract infection; multiple agents in 27 (31.8) patients, Klebsiella species (spp.) in 18 (21.2%) patients, E.coli in 10 (11.8%) patients, Enterococcus spp. in nine (10.6%) patients, Pseudomonas spp in eight (9.4%) patients, Proteus spp. in seven (8.2%) patients, Acinetobacter spp. in four (4.7%) patients, Staphylococcus aureus in one (1.2%) patient, Enterobacter spp. in one (1.2%) patient were determined.In 19 of 85 patients with urinary system infection, the agent was also isolated from the blood culture. The most common factors isolated from blood culture are; 36.8% Klebsiella spp., 31.6% multiple agents, 10.5% E.coli and 10.5% Enterococcus spp. was determined.

Conclusion: As a result, it would be an appropriate approach to determine the indications for urinary catheter insertion well and withdraw the catheter when the necessity is eliminated in order to reduce the urinary system infection rates associated with healthcare in the ICU. Determining the factors of nosocomial infection in patients hospitalized in the intensive care unit will contribute to the reduction of mortality and morbidity rates as it will be a guide in empirical treatment.

Keywords: intensive care unit; catheter-related urinary tract infection; risk factors

Giriş

Yoğun bakım üniteleri (YBÜ), hastanelerde sağlık bakımıyla ilişkili infeksiyonların en sık görüldüğü üniteler olup, bu ünitelerde görülen infeksiyonlar önemli bir mortalite ve morbidite nedenidir.[1] Yoğun bakım ünitesinde infeksiyon oranları, invazif aletlerin kullanılması, yatış süresinin uzaması, altta yatan hastalıkların çeşitliliği ve yoğun bakımın özelliklerinden dolayı yüksektir.[2] YBÜ'ler hastanedeki tüm yatakların en fazla %10'unu oluşturmasına karşın YBÜ'lerde gelişen enfeksiyonlar, tüm hastane enfeksiyonlarının yaklaşık %20-25'ini oluşturmaktadır.[3] Hastanelere ve bölümlere göre değişmekle birlikte en sık görülen sağlık bakımı ile ilişkili infeksiyonlar üriner sistem infeksiyonları (ÜSİ) olup, tüm sağlık bakımı ile ilişkili infeksiyonların %36'sını oluşturur. Kateterle ilişkili üriner sistem enfeksiyonu (Kİ-ÜSE) üriner sistem infeksiyonlarının %80'ini oluşturur.[4] Bu çalışmada, Ankara Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon yoğun bakım ünitesinde (ARYBÜ) yatan hastalarda gelişen kateter ile ilişkili üriner sistem infeksiyonlarının hızlarının ve infeksiyon etkenlerinin, retrospektif olarak değerlendirilmesi amaçlandı.

Gereç ve Yöntemler

Çalışmada, 1 Ocak 2018-31 Aralık 2019 tarihleri arasında ARYBÜ'de yatan ve Kİ-ÜSE tanısı konulan hastalar dahil edildi. Hasta verileri enfeksiyon kontrol hemşirelerinin günlük vizitleri, enfeksiyon hastalıklarının günlük konsültasyon kayıtları ve Ulusal Hastane Enfeksiyonları Sürveyans Ağı İNFLİNE programı verilerinden, laboratuvar verileri ise Mikrobiyoloji laboratuarından elde edildi. Hastaların demografik verileri, kateterle ilişkili üriner infeksiyonları, infeksiyon etkenleri ve komorbid durumların varlığı kaydedildi. Üriner kateter kullanım oranı ve Kİ-ÜSE hızı aşağıdaki formüller ile hesaplandı.

Üriner kateter kullanım oranı= Üriner kateter günü / Hasta günü

Kateterle ilişkili üriner sistem infeksiyonu hızı = Kateterle ilişkili üriner sistem infeksiyonu sayısı/ üriner kateter günüX1000

Çalışmanın verileri Excel programına girildi ve istatistiksel analizler SPSS programı ile yapıldı. Çalışma için Ankara Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurul'undan 20/08/2020 tarihinde E-20 sayı numaralı onay alındı. Hastalara aydınlatılmış onam belgesi imzalatıldı.

Bulgular

ARYBÜ'de iki yıllık sürede 17910 hasta gününde 1243 hasta takip edilmişti. Hastaların üriner kateter günü 17470 gün idi. Çalışmanın yapıldığı dönemde toplam 85 hastaya 116 Kİ-ÜSE tanısı konuldu. Üriner kateter kullanım oranı 0.97, kateterle ilişkili üriner sistem infeksiyonu hızı (Kİ-ÜSE) ise 6.63 olarak saptandı. 2019 yılı Sağlık Bakanlığı Eğitim ve Araştırma Hastaneleri ARYBÜ'lerinin sürveyans verileri ile karşılaştırıldığında; ARYBÜ üriner kateter kullanım oranının %25 persentil ile uyumlu olduğu, Kİ-ÜSE hızının ise %90 persentilin üzerinde olduğu saptandı.

Çalışma süresince ARYBÜ'de yatan hasta sayısı, hasta günü, üriner kateter günü, ÜSİ sayısı, üriner kateter kullanım oranı ve Kİ-ÜSİ oranı Tablo 1'de verildi.

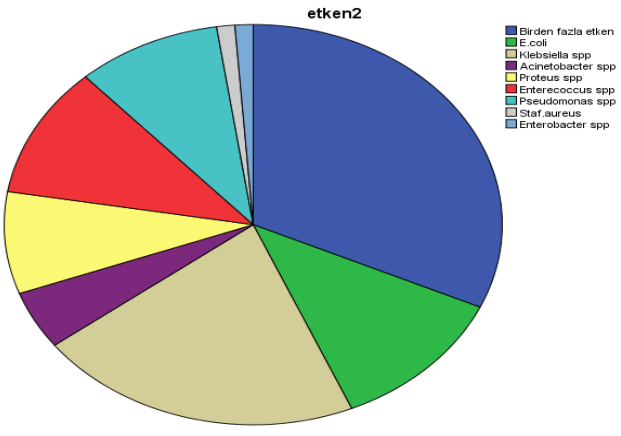
Tablo 1: Hastaların üriner kateter günü, ÜSİ sayısı, üriner kateter kullanım oranı ve Kİ-ÜSİ oranı

ARYBÜ	Hasta sayısı	Hasta günü	Üriner kateter günü	Üriner sistem enfeksiyonu	Üriner kateter kullanım oranı	Kİ-ÜSE
	1243	17910	17470	116	0.97	6.63

Toplam 85 hastanın 47'si kadın (%55.3), 38'i (%44.7) erkek hasta idi. Hastaların median yaşı 66 olarak belirlendi. Hastaların tümünün üriner kateteri vardı. Hastaların ilk Kİ-ÜSİ atakları baz alınarak risk faktörleri ve etkenler belirlendi.

Hastaların 44 (%52)'ünde nörolojik hastalık, 40 (%47)'ında hipertansiyon, 28 (%33)'inde diyabetes mellitus, 20 (%23.5)'sinde KOAH, iki (%2.4)'sinde kronik böbrek hastalığı mevcuttu. Hastaların 72 (%84.7)'si entübe idi, 19 (%22.4)'unda dekübit ülseri mevcuttu.

Üriner sistem infeksiyonu etkenlerinin dağılımı incelendiğinde; 27 (31.8) hastada birden fazla etken olduğu görüldü. 18 (%21.2) hastada Klebsiella spp., 10 (%11.8) hastada E. coli, dokuz (%10.6) hastada Enterococcus spp., sekiz (%9.4) hastada Pseudomonas spp., yedi (%8.2) hastada Proteus spp., dört (%4.7) hastada Acinetobacter spp., bir (%1.2) hastada Staphylococcus aureus,bir (%1.2) hastada Enterobacter spp. etken olarak izole edildi. İdrar kültüründen izole edilen etkenlerin dağılımları Şekil 1'de gösterildi.



Şekil 1. Üriner sistem infeksiyonu olan hastalarda kültürden izole edilen etkenlerin dağılımları

Üriner sistem infeksiyonu olan 85 hastanın 19 (%22.4)'unda kan kültüründen de aynı etken izole edildi. Kan kültüründen en sık izole edilen etkenler sırasıyla; %36.8 Klebsiella spp., % 31.6 birden fazla etken, %10.5 E.coli ve %10.5 Enterococcus spp. olarak belirlendi. Üriner sistem infeksiyonuna sekonder bakteriyemi gelişen 19 hastanın 13'ü (%47) kadın, altı'sı (%38) ise erkekti.

Kan kültüründen izole edilen etkenlerin dağılımı Tablo 2'de gösterildi.

Tablo 2. İdrar kültürü ile birlikte kan kültüründe üreme saptanan 19 hastada etkenlerin dağılımı

Etkenler	Sayı	(%)
Birden fazla etken (E.coli, Klebsiella spp., Acinetobacter spp., Pseudomonas spp., Proteus spp. vb.)	6	31.6
Klebsiella spp.	7	36.8
E.coli	2	10.5
Enterococcus spp.	2	10.5
Acinetobacter spp.	1	5.3
Proteus spp.	1	5.3
Toplam	19	100

Tartışma

YBÜ'de görülen sağlık bakımıyla ilişkili infeksiyon türleri (kateter ilişkili üriner sistem, ventilatör ilişkili pnömoni, kateter ilişkili kan dolaşımı vb.) ve oranlarının hastaneler ve YBÜ'ler arasında farklılıklar gösterdiği bildirilmektedir. Pnömoniler, üriner sistem infeksiyonları ve kan dolaşımı infeksiyonları nozokomiyal infeksiyonların yaklaşık %68-77'sini oluşturmaktadır.[1,6,7]

Kİ-ÜSE, artan morbidite ve mortalite ile ilişkilidir ve sekonder kan dolaşımı infeksiyonlarının en yaygın nedenidir. Kİ-ÜSE gelişimi için risk faktörleri arasında uzun süreli kateterizasyon, kadın cinsiyet, ileri yaş ve diyabet yer almaktadır.[8]

Kalıcı idrar sondası yerleştirilmesinin kanıta dayalı olmadığı veya uygunsuz olduğu, bu durumun hasta bakım yükünü ve maliyeti önemli oranda artırdığı, hastada rahatsızlığa ve aktivitelerinde kısıtlamalara neden olduğu bildirilmektedir. En iyi uygulama kılavuzları, personelin aktif katılımını eğitim ve izleme ile birleştiren çok yönlü müdahalelerin, tek bir müdahaleye odaklananlara göre uygulama değişikliği sağlamada daha etkili olduğunu göstermiştir. Kİ-ÜSİ, üriner sistem infeksiyonlarının çoğunu temsil eder, tüm hastanede yatan hastalarda ÜSİ'lerin yaklaşık %67'sini, YBÜ'lerde yatan hastalarda ise %97'sini oluşturur. Hastanede yatan hastaların %12 ila %16'sına kısa süreli kalıcı üriner kateter takılmaktadır ve bu kateterlerin çoğunun uygunsuz takıldığı tespit edilmiştir (5). Kİ-ÜSİ riski, kateterizasyon süresi ile önemli ölçüde artar. Bu durum, önemli oranda bakım yüküne, hastane maliyetlerinde artışa, hastada rahatsızlığa, ağrı ve aktivite kısıtlamaları gibi istenmeyen durumlara neden olur . Yapılan bir çalışmada, 48 saatten uzun süre hastanede yatarak tedavi gören hastaların %1.7'sinin ÜSİ geçirdiği ve hastanede kalış sürelerinin uzamasına (ortalama 4 gün) neden olduğu bildirilmiştir.[5,9]

Bir meta-analiz çalışmasında, Kİ-ÜSE için risk faktörlerinin kadın cinsiyet, kateterizasyon süresinin uzun olması, hastalarda diabetes mellitus varlığı, daha önce kateterizasyon uygulanması, hastanede ve YBÜ'de daha uzun süre yatış olduğu bildirilmiştir. Ek olarak, Kİ-ÜSİ'lerin mortalitede artışa neden olduğu rapor edilmiştir.[10]

Çalışmamızda da Kİ-ÜSİ hastaları arasında kadın cinsiyet daha fazla idi. Hastaların %33'ünde diyabetes mellitus mevcuttu. Diğer en sık görülen komorbid hastalıklar ise hipertansiyon, nörolojik hastalık ve KOAH idi.

Yoğun bakım ünitelerinde sağlık bakımıyla ilişkili infeksiyon etkeni mikroorganizmalar da hastaneler ve YBÜ'leri arasında farklılıklar gösterir. Deniz ve ark. [6] Anestezi yoğun bakım ünitesinde üriner sistem infeksiyonlarından en sık izole edilen etkenleri sırasıyla; Pseudomonas aureginosa, Acinetobacter baumannii ve Escherichia coli olarak bildirmişlerdir.

Sunduğumuz çalışmada, üriner sistem infeksiyonu etkenlerinin dağılımı sıklık sırasına göre; 27 hastada birden fazla etken, 18 hastada Klebsiella türleri (spp.), 10 hastada E.coli, dokuz hastada Enterococcus spp.,sekiz hastada Pseudomonas spp., yedi hastada Proteus spp., dört hastada Acinetobacter spp., bir hastada Staphylococcus aureus, bir hastada Enterobacter spp. olarak belirlendi.

Öncül ve ark. [11] yoğun bakım ünitesinde gelişen infeksiyonların 42'sini (%28,4) primer bakteremi veya santral venöz kateter ilişkili kan dolaşımı infeksiyonu (SVK-KDİ), 40'ını (%27) ventilatör ilişkili pnömoni (VİP) veya trakeobronşit, 22'sini (%14,9) pnömoni veya pnömoni dışı alt solunum yolu infeksiyonu, 38'ini (%25,7) üriner sistem infeksiyonu (ÜSİ), altı'sını (%4,1) yumuşak doku enfeksiyonu olarak bildirmişlerdir. Üriner sistem enfeksiyonlarında etkenlerin dağılımını %31,6 Pseudomonas spp., %31,6 Candida spp., %14,6 E. coli olarak bildirmişlerdir. Komorbid hastalıklar açısından tüm infeksiyon gelişen hastalarda en sık görülen altta yatan hastalığın %57,7 oranıyla serebrovasküler hastalık (SVH) olduğu, diyabetin yumuşak doku enfeksiyonu olan hastalarda daha fazla görüldüğü rapor etmişlerdir.

Dizbay ve ark. [12] Anestezi Reanimasyon ve Nöroloji yoğun bakım ünitesinde yaptıkları çalışmada üriner istem infeksiyonlarında en sık izole edilen mikroorganizmaları Pseudomonas, Acinetobacter ve E.coli olarak bildirmişlerdir.

Yapılan çok merkezli bir çalışmada YBÜ'lerde en sık görülen hastane kaynaklı infeksiyonlar; pnömoniler (%40), üriner sistem infeksiyonları (%20,5) ve yara yeri infeksiyonu (%13) olarak bildirilmiştir.[5,6] Deniz ve ark. [6] yeniden yapılandırılan Anestezi reanimasyon ünitesinde yapılandırma öncesi ve yapılandırma sonrası pnömoni oranlarını %32,7-14,6; üriner sistem infeksiyonu oranlarını %18,7-10,4; kateter infeksiyonu oranlarını %12-11; ve yara yeri infeksiyonunu oranlarını %4,7-4,7 olarak bildirmişlerdir.

Kateterle ilişkili bakteriürisi olan yatan her 27 hastanın birinde sekonder bakteriyemi geliştiği rapor edilmiştir.[13] Sistematik bir değerlendirmede, hastanede yatan üriner kateterle ilişkili bakteriürisi olan erkek hastalarda bakteriyemi gelişme riskinin kadın hastalardan daha yüksek olduğu bildirilmiştir. Bu nedenle, yüksek riskli hastalarda zorunlu olmadıkça üriner kateter takılmasından kaçınılması önerilmektedir.[14]

Sunduğumuz çalışmada üriner sistem infeksiyonu olan 85 hastanın 19'unda kan kültüründen de etken izole edildi, bakteriyemi mevcuttu. Kan kültüründen en sık izole edilen etkenler sırasıyla ; %36.8 Klebsiella spp., % 31.6 birden fazla etken, %10.5 E.coli ve %10.5 Enterococcus spp. olarak belirlendi. Üriner sistem infeksiyonuna sekonder bakteriyemi gelişen 19 hastanın 13'ü (%47) kadın, altı'sı (%38) ise erkekti. Sunduğumuz çalışmada literatürden farklı olarak kadınlarda Kİ-ÜSİ'ye sekonder bakteriyemi oranı erkeklerden daha fazla saptandı.

Çalışmamızda ARYBÜ'de üriner kateter kullanım oranı 0.97, Kİ-ÜSİ hızı ise 6.63 olarak belirlendi. Bu oran ülkemizdeki diğer eğitim ve araştırma hastanelerinin 2019 sürveyans verileri ile karşılaştırıldığında; ARYBÜ'deki üriner kateter kullanım oranının 25. persentil ile uyumlu olduğu, Kİ-ÜSE hızının ise 90. persentilin üzerinde olduğu saptandı.[15]

Sonuç

YBÜ'de sağlık bakımıyla ilişkili üriner sistem infeksiyon oranlarının azaltılması için üriner kateter takılması endikasyonlarının iyi belirlenmesi, gereklilik ortadan kalktığında kateterin çekilmesi ve enfeksiyon kontrol önlemlerine dikkat edilmesi uygun bir yaklaşım olacaktır. Yoğun bakım ünitesinde yatan hastalarda hastane infeksiyonu etkenlerinin belirlenmesinin, ampirik tedavide yol gösterici olacağı ve mortalite ve morbidite oranlarının azaltılmasına da katkı sağlayacağı görüşündeyiz.

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Original Article

Anti-adhesion activity and physicochemical features of the surgical silk sutures coated with Liquidambar orientalis styrax

Liquidambar orientalis styrax ile kaplanan cerrahi ipek sütürlerin anti-adezyon aktivitesi ve fizikokimyasal özellikleri

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Abstract

Aim: The present study was aimed to characterize the surgical silk sutures coated with Styrax liquidus, Turkish sweetgum balsam obtained from Liquidambar orientalis, and to investigate their anti-adhesion capacity against oral pathogenic microorganisms.

Material and Methods: Fourier Transform Infrared Spectroscopy (FTIR) was applied to determine the chemical composition of the Liquidambar orientalis styrax (LOS)-coated sutures. Thermogravimetric Analysis (TGA) was performed to compare the thermal stability of the LOS-coated sutures. Scanning Electron Microscopy (SEM) was used to evaluate the morphological structure of the sutures. Anti-adhesion activity of the LOS-coated sutures was investigated against common oral pathogenic microorganisms.

Results: FTIR spectrum and SEM images revealed out that LOS was succesfully coated onto the silk sutures. TGA analysis showed that LOS coating moderately affected the thermal stability of the silk sutures. According to the anti-adhesion activity analysis, the highest activity was observed against S. aureus, a gram positive bacteria.

Conclusion: Coating the surgical silk sutures with LOS might be useful to prevent the surgical site infections in oral surgery.

Keywords: anti-adhesion; characterization; Liquidambar orientalis; styrax; suture

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Öz

Amaç: Bu çalışmada, Liquidambar orientalis'ten elde edilen Türk sığla balsamı olan Styrax liquidus ile kaplanmış cerrahi ipek sütürlerin karakterize edilmesi ve oral patojenik mikroorganizmalara karşı anti-adezyon kapasitelerinin araştırılması amaçlandı.

Gereç ve Yöntemler: Liquidambar orientalis styrax (LOS) kaplı sütürlerin kimyasal bileşimini belirlemek için Fourier Transform Kızılötesi Spektroskopisi (FTIR) uygulandı. LOS kaplı sütürlerin termal stabilitesini karşılaştırmak için Termogravimetrik Analiz (TGA) yapıldı. Sütürlerin morfolojik yapısını değerlendirmek için Taramalı Elektron Mikroskopisi (SEM) kullanıldı. LOS kaplı sütürlerin anti-adezyon aktivitesi, yaygın oral patojenik mikroorganizmalara karşı araştırıldı.

Bulgular: FTIR spektrumu ve SEM görüntüleri LOS'un ipek sütürlere başarılı bir şekilde kaplandığını ortaya koydu. TGA analizi, LOS kaplamanın ipek sütürlerin termal stabilitesini orta derecede etkilediğini gösterdi. Anti-adezyon aktivite analizine göre, en yüksek aktivitenin gram pozitif bakteri olan S. aureus'a karşı olduğu gözlendi.

Sonuç: Cerrahi ipek sütürlerin LOS ile kaplanması, oral cerrahide cerrahi bölge enfeksiyonlarını önlemek için yararlı olabilmektedir.

Anahtar kelimeler: anti-adezyon; karakterizasyon; Liquidambar orientalis; styrax; sütür

Introduction

Surgical site infections (SSIs) represent a major complication which occurs after surgical procedures [1, 2]. The reported rates of SSIs vary from 2% to 5%, accounting for 20% of all-health care-associated infections [1]. SSIs lead to longer hospital stays and greater health-care costs as well as substantial morbidity and mortality [3]. In case of infection, further surgical interventions may be required followed by a decrease in patient quality of life and work productivity [3, 4].

SSIs have a multifactorial nature. Bacterial colonization of the suture is one of the most important factors in the development of SSIs [1]. As a foreign body, suture materials may act as a potential surface for bacteria bioadherence and lead to microbial colonization on the incision site. The biofilm is established by the colonization and proliferation of microorganisms [2]. Once the biofilm is formed, the antibiotic treatment is often ineffective [3].

Silk has been widely used as a suture material due to its excellent internal performance. It is easy to use and provides a safe knot [5]. However silk sutures tend to cause a more intense and prolonged inflammatory response [6]. The braided nature of the silk suture facilitates bacterial accumulation, thereby increasing the risk of infection [5].

Several studies have demonstrated that developing silk sutures with good antibacterial properties is essential in order to avoid the suture being a risk factor for SSIs [5, 7]. Baygar et al. used silver nanoparticles (AgNPs) to coat the silk sutures [8]. Bide et al. reported the antimicrobial properties of silk sutures immobilized with ciprofloxacin [9]. Viju and Thilagavathi have studied the chitosan-based antimicrobial sutures [10].

The use of medicinal plants for the treatment of various infectious diseases has been known since ancient times. Medicinal plants are essential herbal products which represent an important source of biologically active compounds. The antimicrobial compounds of these plants prevent bacterial proliferation by mechanisms different from the commonly used antimicrobial agents. Therefore medicinal plants have a significant therapeutic value [11].

Liquidambar orientalis is a herbaceous plant which is known to have medicinal and cosmetic properties [12]. Liquidambar orientalis Mill tree is commonly known as “Sığla ağacı” or “Günlük ağacı” in Turkey. This species has locally distributed in the South-western coastal district of Turkey [13]. In the mediterranian region, it is commonly used in phytotherapy for treatment of various diseases including ulcer, stomach ache, mouth diseases, burn, wounds, cuts, whooping cough and skin diseases [14]. This herbaceous plant has good antiseptic properties [15]. The antimicrobial properties of the ethanolic extract of the leaves of Liquidambar orientalis have been previously studied [16, 17]. Styrax liquidus, locally named as “sığala or sığla yağı” is a resinous exudate obtained from the wounded trunk of Liquidambar orientalis Miller from Altingiaceae family (Hamamelidaceae) [18]. The balsam is not a natural part of the tree but is produced as a result of the stimulus from wounds in the bark. The outer bark is

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bruised, and then the inner bark becomes saturated with this pathological exudation. The outer bark is removed and the inner is boiled in water, the storax is skimmed off the surface as it rises, then afterward the boiled bark is pressed [15, 19]. Resin produced by injuring tree is a good antiseptic and has also been used as a topical parasiticide for the treatment of some skin diseases [20].

In the present study surgical silk sutures were coated with Liquidambar orientalis styrax (Styrax liquidus) using dip slurry technique. Coated sutures were characterized using Fourier Transform Infrared Spectroscopy (FTIR) and thermogravimetric analysis (TGA). Coated sutures were also investigated morphologically by Scanning Electron Microscopy (SEM). Antiadhesion activity was evaluated against oral pathogenic bacteria Candida albicans, Enterococcus faecalis, Staphylococcus aureus and Streptococcus mutans.

Material and Methods

LOS coating of the sutures

Liquidambar orientalis styrax used within the present study was obtained from a local company from Koycegiz Province, Mugla, Turkey and extracted with ethanol (1:10) then evaporated after filtration. Nonabsorbable 3.0 silk sutures (Dogsan, Turkey) silk sutures were dipped in LOS for 2 min, and dryed for 24h [8, 21].

Characterization of the LOS-coated sutures

Morphological and microanalytical characterization

FTIR Spectroscopy

FTIR spectrum of the LOS-coated sutures was obtained by FTIR (Thermo Scientific Nicolet iS10-ATR, USA) and compared. The spectra were recorded in the wavelength interval of 4000 and 400 cm^{-1}.

Thermogravimetric analysis (TGA)

Thermogravimetric analysis of non-coated and LOS-coated sutures were performed on a TGA instrument (Perkin Elmer TGA 4000, Perkin Elmer, Waltham, MA). Samples were heated from 30°C to 900°C at a rate of 10°C min^{-1} under a nitrogen flow rate of 20 mL min^{-1}.

Scanning Electron Microscopy (SEM)

Surface morphology of the LOS-coated sutures were evaluated using a JSM 7600F Field Emmission Scanning Electron Microscope (JEOL, Japan) and compared with the non-coated group. Non-coated and LOS-coated sutures were coated with gold before examining with SEM and monitorized under 15 kV accelaration voltage.

Anti-adhesion activity

Anti-adhesion activity of the LOS-coated silk sutures was determined against oral pathogenic bacteria obtained from American Type Culture Collection (ATCC); Staphylococcus aureus ATCC 25923, Enterococcus faecalis ATCC 29212, Candida albicans ATCC 10231 and Streptococcus mutans ATCC 25575. Suture fragments (1 cm) were incubated in inoculated broth media (Sabouroud Dextrose Broth for C. albicans, Mueller Hinton Broth for S. aureus and Brain Heart Infusion Broth for E. faecalis and S. mutans) under appropriate temperature for 24-48 h (37°C for S. aureus and E. faecalis, 30°C for C. albicans and 37°C, 5% CO2 for S.mutans). After incubation periods, suture fragments were discarded and ultrasonicated in fresh broth mediums for 5 minutes. Ultrasonicated broths were incubated at appropriate periods again. Afterwards, the absorbances of the broth mediums were recorded at 540 nm using a UV-Vis spectrophotometer (Multiskan GO UV/Vis Microplate Spectrophotometer, Thermo-Fisher Scientific, USA) and the inhibition percentages were calculated.

Results

FTIR spectrum of the LOS-coated silk sutures is given at Figure 1. The peaks were obtained at 3277 cm^{-1}, 2939 cm^{-1}, 2160 cm^{-1}, 2027 cm-1, 1704 cm-1, 1633 cm-1, 1512 cm-1, 1448 cm-1, 1379 cm^{-1}, 1309 cm^{-1}, 1262 cm^{-1}, 1163 cm^{-1}, 1068 cm^{-1}, 971 cm^{-1}, 862 cm^{-1}, 765 cm^{-1} and 687 cm^{-1}.

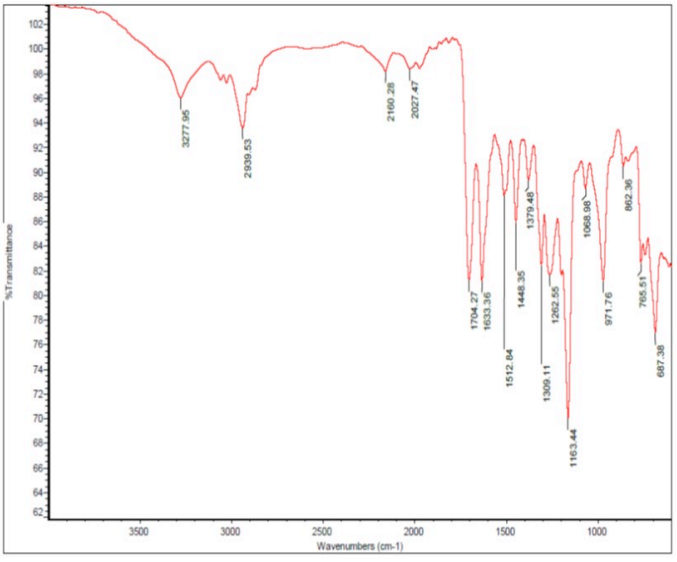

Figure 1. FTIR spectrum of the LOS-coated silk sutures.

TGA result of the LOS-coated suture is given at Figure 2. According to the TGA result, the initial decomposition stage which was marked at 0-100 °C was due to evaporation of water.

The second stage started at 225-260 °C. At 900°C, a total mass change of 85.79% was observed with a residual mass of 14.20%.

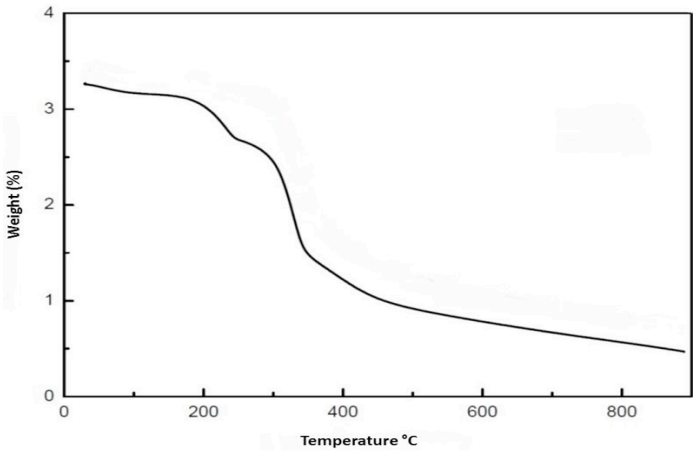

Figure 2. TGA spectrum of LOS-coated silk sutures.

The SEM micrographs of the non-coated and LOS-coated sutures are given at Figure 3. SEM images displayed that the diameter of the control group (non-coated) suture fragment was measured as 296 µm while the diamater of the LOS-coated suture fragment was 304 µm. The SEM images indicated the succesful coating process of the styrax onto the suture surface.

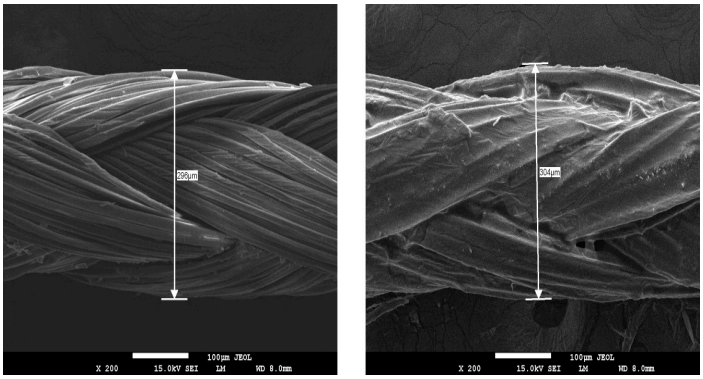

Figure 3. SEM images of the non-coated (left) and LOS-coated (right) silk sutures.

Anti-adhesion analysis indicated that, there was a 20.87% decrease in the biofilm amount onto the LOS-coated sutures (Table 1). There was not a significant inhibiton value for other microorganisms.

Table 1. Anti-adhesion activity of LOS-coated sutures

Microorganism	Inhibition %
S. mutans	4.66
E. faecalis	2.17
S. aureus	20.87
C. albicans	-

Discussion

Surgical silk sutures were coated with Liquidambar orientalis styrax and their anti-adhesion properties were characterized in the present study. Silk is commonly used as a suture material in oral surgery and accepted as a comparison standard for the assessment of suture properties [22]. Therefore, silk suture has been selected for this study. Similar to the SEM images, the FTIR spectrum of the LOS-coated sutures also indicated that the sutures were coated with LOS completely. The peak at 3277 cm^{-1} could be related to –OH group vibrations. The bands at 2939 cm^{-1}, 1448 cm^{-1}, 1379 cm^{-1} and 1309 cm^{-1} could be due to the C-H stretching vibration. The band at 1704 cm^{-1} could be probably related to the ketones. The bands between 687 cm^{-1} and 1262 cm^{-1} could be due to the steroidal or triterpenic structure [23]. According to the thermal decomposition stages, LOS-coating of the sutures moderately affected the thermal stability of the silk sutures. Elakkiya et al. (2014) reported that the weight loss was due to thermal decomposition of the antiparallel β-sheet structure of fibroin which forms the structural core of silk [24].

Surgical site infection remains one of the most common complications among surgical patients, which causes a significant amount of morbidity and increases medical costs [25]. In the presence of contamination, the sutures may act as a source of bacterial colonization and contributes to the development of surgical site infection [26]. The formation and growing of the bacterial biofilm on the surface of surgical sutures has been widely reported as an important causative factor for the SSIs [10, 25]. The oral cavity poses a high infectious potential due to the moist and vascularized environment [27, 28]. Multifilamentous and braided silk sutures cause a significant inflammatory reaction due to the bacterial adhesion in oral mucosa [28]. The suture related infections in the oral mucosa appear to be linked with the amount of contamination during the placement of sutures [27]. Therefore several studies have focused on the development of antimicrobial coated silk sutures. Janiga et al. (2012) employed the synergistic drug combination of levofloxacin-tinidazole to coat the silk suture [29]. They reported a good antibacterial activity and persistence against both Gram-positive and negative organisms. Baygar et al.(2019) used silver nanoparticles (AgNPs) obtained via a green synthesis approach [8]. The authors demonstrated a strong antimicrobial and antibiofilm capacity for AgNP-coated silk sutures. Pethile et al.(2014) concluded that coating

silk sutures with a combination of poly(ε-caprolactone) (PCL) and sulfamethoxazole trimethroprim (SMZ) has a suitable antibacterial efficacy [5].

Liquidambar orientalis styrax, which is used traditionally to treat peptic ulcer disease by the inhabitants in the south-western Turkey, is a balsam obtained from the barks of Liquidambar orientalis tree [30]. Due to their potent antimicrobial activities, plant-derived secondary metabolites are known to be critical in the treatment of various diseases [31, 32]. Sağdıç et al. (2005) reported that the ethanolic extract of L. orientalis storax (styrax) had strong antibacterial activity against B. subtilis, E. coli, P. aeruginosa, S. aureus [15]. Within the present study, LOS-coated sutures had potent anti-adhesion activity against S. aureus, S. mutans and E. coli while there were no anti-adhesion activity against C. albicans strain. The major constituents of the L. orientalis styrax are reported as terpinen-4-ol, α-terpinol, sabinene and -terpinene along with cinnamyl cinnamete, phenylpropyl cinnamete, cinnamaldehyde, cinnamyl alcohol, ethyl cinnamate, methyl cinnamate and cinnamyl acetate [33-36].

The use of antimicrobially coated sutures presents a beneficial approach to deal with suture-associated infections [37]. By the year 2002, the Food and Drug Administration (FDA) approved the first antimicrobial surgical suture coated with triclosan which is a biocide that exhibits broad-spectrum activity against both gram-positive and gram-negative bacteria [38]. Since the introduction of triclosan-coated sutures, several studies have shown its efficacy for decreasing the rate of SSIs in various surgical operations [39-42]. However contradictory results have also been demonstrated and reported no change in terms of infection rates with the use of triclosan-coated sutures [43-45] In a current study, Tabrizi et al.(2019) compared the rate of SSI with the use of polyglactin 910 and polyglactin 910 coated with triclosan sutures in dental implant surgery. The authors found no significant difference between two groups and concluded that triclosan coated sutures had no influence for decreasing the incidence of SSIs in dental implant surgery[43].

Recently absorbable sutures coated with chlorhexidine have been developed and introduced as a commercial product into the markets. Studies on clorhexidine coated sutures have shown good antibacterial results and chlorhexidine was proposed as a promising agent for the prevention of SSIs [25, 46]. The antibacterial drug octenidine has also been investigated as a coating agent. The authors reported high antimicrobial efficacy and biocompatibility [37].

Based on the previous findings, the present study was designed to obtain an efficient surgical suture with potent antiadhesion activity. The results indicated that LOS-coated silk sutures may be beneficial for preventing SSIs following oral surgery operations.

Conclusion

The present study was conducted to characterize the surgical silk sutures coated with Liquidambar orientalis styrax and to display their antiadhesive potentials against oral pathogenic microorganisms. Sutures coated with LOS were found to have moderate antiadhesion activity. The results of the study figured out that, the strong biological activites of L. orientalis styrax may enhance the surface features of the sutures in respect to their antimicrobial and anti-adhesion capacities. The further studies are required to investigate the biomedical use of the LOS-coated sutures for dental applications and their clinical potential.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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Original Article

Management of incidental dermatofibrosarcoma protuberans: A single center 5-year experience

Insidental olarak saptanan dermatofibrosarkom protuberans tedavisi: Tek merkez 5 yıllık deneyimlerimiz

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Abstract

Aim: Dermatofibrosarcoma protuberans (DFSP) is a rare skin tumor. The diagnosis is challenging because it is usually hard to differ DFSP from other skin lesions. Distant metastasis is rare, but local recurrence is common.The aim of this study is to review the treatment algorithms in DFSPs that are detected incidentally and to increase awareness about this rare tumor.

Material and Methods: 17 patients who underwent excision of epidermal lesions which were considered to be benign and were diagnosed with DFSP, at department of general surgery between 2012 and 2017, were analyzed.

Result: A total of 17 patients were analyzed retrospectively. No recurrence was detected in any of ourpatients.

Conclusion: Awareness of this rare entity is important for diagnosis and management of the disease.

Keywords: dermatofibrosarcoma protuberans; mesenchymal tumor; mohs micrographic surgery (MMS)

Öz

Amaç: Dermatofibrosarkoma protuberans (DFSP) nadir görülen bir deri tümörüdür. Teşhis zordur çünkü DFSP'yi diğer deri lezyonlarından ayırmak genellikle zordur. Uzak metastaz nadirdir ancak lokal nüks yaygındır. Bu çalışmanın amacı incidental olarak saptanan DFSP'lerde tedavi algoritmalarını gözden geçirmek ve bu nadir tümör hakkında farkındalığı artırmaktır.

Gereç ve Yöntemler: 2012-2017 yılları arasında genel cerrahi kliniğinde benign olduğu düşünülenerek eksizyonu yapılan ve DFSP tanısı alan 17 hasta retrospektif olarak incelendi.

Bulgular: Toplam 17 hasta geriye dönük olarak analiz edildi. Hastalarımızın hiçbirinde nüks saptanmadı.

Sonuç: Bu nadir antitenin farkında olunması hastalığın tanı ve tedavisi için önemlidir.

Anahtar kelimeler: dermatofibrosarkom protuberans; mezenkimal tümör; mohs mikroskopik cerrahi (MMS)

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Introduction

Dermatofibrosarcoma protuberans (DFSP) is a very rare mesenchymal skin tumor. In the latest World Health Organization (WHO) 2013 classification, these tumors were classified as moderately malignant myofibroblastic tumors [1]. Although it was first described by Darier and Ferrand, the no men clature was made by Hoffman [2].

It constitutes less than 1% of all malignancies and approximately 1% of all soft tissue sarcomas. The incidence is between 0.8 and 4.5 permillion [3-7]. Although congenital cases have been reported, they usually occur in the 3rd decade [8-10]. Although it may have a nodular appearance, such as slow-growing hypertrophic scars, it can also occur without any symptoms, such as soft tissue sarcomas. Hematogenous or lymphatic spread is very rare in DFSPs. Despite showing only local growth; it has an aggressive behavior all patterns that progress to the dermis, subcutaneous tissue, and finally to muscles as finger-like extensions. There is no difference between races, but pigmented DFSP, also known as Bednar tumor, is more common in the black race [11]. Although the difference between the genders is not provento be significant, there are different studies showing that women or men are slightly more common [8,12].

Approximately 10-15% of cases can turn into spindle cell carcinoma similar to adult fibrosarcoma. Such cases are associated with increased mitotic activity and loss of CD34 expression. In tumors that develop fibrosarcomatous transformation, the local recurrence rate is similar to ordinary dermatofibrosarcoma, but distant metastasis is observed in approximately 13% of these patients [13].

Diagnosis is madeby skin biopsy in cases which have been suspected before; however, since the early clinical symptoms of DFSP are nonspecific, diagnosis is difficult. Therefore, it is also frequently encountered in excisions of skin lesions which were considered to be benign.

Standart treatment is surgical excision. Mohs surgery or wide local excision may be preferred. The most challenging part of the management is to achieve local control. Because DFSP originates from the dermis, it invades the collagen bundles and deep connective tissue radially, and therefore it is very difficult to obtain a clean surgical border. Local recurrence has been reported in approximately 50% of studies [14].

In this study, our aim is to review the treatment algorithms in DFSPs that are detected incidentally and to increase awareness about this rare tumor.

Material and Methods

Our study began with the approval of the ethical committee of our institute. Between 2012 and 2017, patients who underwent mass excision and were diagnosed with DFSP in our center were evaluated retrospectively. Patients previously diagnosed with dermatofibrosarcoma and had re-excision, and those diagnosed with biopsy before excision, were excluded from the study. Patients were compared in terms of age, gender, tumor localization, surgical margin status, re-excision status, surgical margin status after re-excision, immunohistochemical markers, mitotic activity in 10 hpf, Ki67 proliferation index, follow-up times, whether they received radiotherapy and complications related to radiotherapy. All patients were called for clinical control and the presence of recurrence was investigated. Distance larger than 0.1 cm was considered as clean surgical margin. Statistical analysis was performed using SPSS v22 statistical program. This study was carried out in accordance with the Declaration of Helsinki and was approved by the local ethics committee and informed consents were taken from all participants.

Results

Between 2012-2017, 17 patients who had mass excision and were diagnosed as dermatofibrosarcoma protuberans incidentally were evaluated retrospectively. The clinicopathological features of the patients are shown in Table 1. When the gender distribution was analyzed, it was determined that 9 of 17 patients were male and 8 were female. The average age at the time of diagnosis was 43.88 (21-72). The tumor was on the back in 5 patients (29.4%), on the forearm in 4 patients (23.5%), on the anterior chest wall in 3 patients (17.6%), on the shoulder in 3 patients (17.6%), and on the leg in 2 patients (11.8%). Surgical margin positivity was detected in 12 patients (70.6%) after the first resection. Clean surgical margins were obtained in 5 patients (29.4%) after the first resection. Re-excision was performed in 12 patients with surgical margin positivity. However, 8 of these 12 patients (66.6%) were found to have clean surgical margins, while 4 patients (33.3%) were not able to achieve clean surgical margins. The treatment was completed with radiotherapy in 4 patients who had positive margins after re-excision. Radiation-induced dermatitis was observed in 2 patients receiving radiotherapy, while no complications occurred in other patients. While CD34 was positive in all patients, we have detected Factor 13A in 6 patients (35.3%), p53 in 2 patients (11.8%), CD99 in 2 patients (11.8%), and vimentin in

2 patients (11.8%) (Table 2). The mitotic activity in 10 hpf and Ki 67 proliferation index did not pass the homogeneity test. The median value for the number of mitosis was 4.00, and the median value for the Ki 67 proliferation index was 7.00. Clinically and radiologically, no recurrence was observed in any of the patients called for control in October 2019. Radiological recurrence control was done by ultrasonography. Our average follow-up time was 23.9 months. This study was approved by the local ethics committee, all procedures were carried out in accordance with the 2013 Helsinki Declaration and informed constents were taken from all participants.

Table 1.

Statistics	Age	Mitosis	Ki 67	Following time
Mean	43,88	4,71	10,12	24,59
Median	43,00	4,00	7,00	17,00
Std. Deviation	13,656	4,469	16,035	15,879
Minimum	21	1	1	6
Maximum	72	20	70	61

Discussion

Dermatofibrosarcoma protuberans (DFSP) is a very rare mesenchymal skin tumor. Although it has been reported that it is slightly more common in women in some studies, it has been shown in many studies that it is seen in both sexes equally as well as in our study [4]. It may appear nodular, such as a slowly growing hypertrophic scar, or appear without any symptoms, like soft tissue sarcomas. In addition, atrophic plaque or morphea-like appearance may cause delay in diagnosis [15]. Although its dimensions vary during diagnosis, it can be detected in sizes ranging from 0.5 cm to 12 cm [4]. Many morphological variants have been defined, and the pigment variant is called the "Bednar Tumor" [16]. It usually shows only local growth but has an aggressive growing pattern such as giving finger like extensions into the dermis, subcutaneous tissue and finally muscle tissue [8]. In 60% of cases, tumor cells extend parallel to the epidermis [8,9].

Table 2.

		Count	Row N %	Column N %	Table N %
Gender	Male	9	100,0%	52,9%	52,9%
	Female	8	100,0%	47,1%	47,1%
Localization	Dorsum	5	100,0%	29,4%	29,4%
	Chest	3	100,0%	17,6%	17,6%
	Shoulder	3	100,0%	17,6%	17,6%
	Leg	2	100,0%	11,8%	11,8%
	Forearm	4	100,0%	23,5%	23,5%
Surgical Margins (SM)	Negative	5	100,0%	29,4%	29,4%
	Positive	12	100,0%	70,6%	70,6%
Re-excision	No	5	100,0%	29,4%	29,4%
	Yes	12	100,0%	70,6%	70,6%
SM After Re-excision	Negative	8	100,0%	66,6%	66,6%
	Positive	4	100,0%	33,3%	33,3%
Radiation Therapy	No	13	100,0%	76,5%	76,5%
	Yes	4	100,0%	23,5%	23,5%
CD34	Negative	0	0,0%	0,0%	0,0%
	Positive	17	100,0%	100,0%	100,0%
Factor 13A	Negtive	11	100,0%	64,7%	64,7%
	Positive	6	100,0%	35,3%	35,3%
p53	Negative	15	100,0%	88,2%	88,2%
	Positive	2	100,0%	11,8%	11,8%
CD99	Negative	15	100,0%	88,2%	88,2%
	Positive	2	100,0%	11,8%	11,8%
Vimentin	Negative	15	100,0%	88,2%	88,2%
	Positive	2	100,0%	11,8%	11,8%
Recurrence	No	17	100,0%	100,0%	100,0%
	Yes	0	0,0%	0,0%	0,0%
Complication	No	15	100,0%	88,2%	88,2%
	Yes	2	100,0%	11,8%	11,8%

In the early stages, DFSPs can be mixed with lipomas, epidermalcysts, keloid tissue or nodular fasciitis [17]. In advanced disease, pyogenic granuloma, Kaposi's sarcoma and other soft tissue sarcomas should also be considered. There are also studies showing that it can develop in traumatized tissues or scars that have under gone multiple surgical procedures [18]. Hematogenous or lymphatic spread is very rare in DFSPs [17]. DFSP is microscopically characterized by diffuse infiltration of dermis and subcutaneous tissue. The tumor grows among fibrous septi and infiltrates adipose tissue, creating the typical honeycomb look. The atypia is minimal and mitotic rate is low [15]. Increased mitotic activity, necrosis and fibrosarcomatous changes; are indicators of aggressive behavior and poor prognosis [19].

Immunohistochemically, vimentin, CD34, apolipoprotein D, nestin and sometimes EMA can be detected in tumorcells. Mostly, desmin, S100 protein, stromelysin III, tenascin and keratin are negative. Infibrosarcomatous DFSPs, CD 34 loss and increased TP53 expression can be demonstrated [19,20].

Genetically, DFSP is characterized by a COL1A1- PDGFB gene fusion in most cases. The promoter and variable portions of the collagen 1A1 (COL1A1) gene are combined with exon 2 of the platelet-derived growth factor beta (PDGFB) gene, causing irregular regulation of PDGFB protein [21,22]. At the chromosome level, gene fusion is caused by the exchange of substances between the chromosome bands 17q21 (COL1A1) and 22q13 (PDGFB). This exchange can be seen as balanced or unbalanced t (17; 22) or as one or more super numerary ring chromosomes [14,23,24]. These ring chromosomes, which may contain many copies of fusion genes or other parts of the arms of 17q and 22 q chromosomes, are more common in elderlypatients [25]. The other form is more common in children [26,27]. In rare cases, fusion of PDGFB with other chromosomal regions has been demonstrated. COL6A3-PDGFB fusion was demonstrated in the DFSP of the breast. This fusion, like COL1A1-PDGFB fusion, activates the PDGFB receptor [28,29].

Intreatment, excision of the skin and subcutaneous tissue with distant surgical margins is recommended [30]. If there is muscle or bone invasion; resection of these tissues are also recommended to obtain negative surgical margins [31]. There currence rate is related to the width of the resection [32]. In some studies, recurrence rates have been shown to be under 5% in those with a clean margin of 5 cm or more [31]. Mohs surgery, also known as Mohs micrographic surgery (MMS), is the name of the method in which the tumor is gradually removed into thin layers and examined. This process continues until there are not any tumor cells in the samples taken. It can be done in one session as an out patient procedure. Reasonable tissue excision ,which is the basic principle of MMS, reduces scar tissue an deliminates the need for future surgical or medical treatment [33,34]. The average lesion length at the time of diagnosis ranges from 4.4 cm to 4.9 cm in different studies. The average wound area is 21.7 cm2 in Mohs surgery and 63.4 cm2 in wide local excision [35-37].

Imantinib mesylate is an oral tyrosine kinase inhibitor. It can be used in adults for recurrent, unresectable and metastatic disease. It prevents the binding of ATP to the PDGF-beta receptor, a tyrosine kinase, by competitive inhibition. This; slows kinase activity, limits tumor growth and provides apoptosis. Patients with t (17; 22) translocation respond better to imatinib and therefore this translocation should be investigated prior to treatment. This translocation can be detected by the FISH (fluorescent in situhybridization) or reverse transcription polymerase chain reaction (RT-PCR)methods. Imatinib has side effects such as indigestion, edema, fatigue, anemia, and skin rash. Most of the patients which have translocation respond well to imatinib mesylatetherapy. In studies, the response to imatinib treatment is about 65%. The duration of treatment is variable. Some sources recommend 6 months of treatment, but this can be extended if needed. Alternatively, radiotherapy can be used in unresectable or recurrent tumors. In addition, adjuvant radiotherapy can reduce the risk of local recurrence [38-39]. Radiotherapy combined with surgery should be considered in the presence of a positive or inadequate surgical margin, in cases of recurrence, or if extensive surgical excision will have unacceptable cosmetic or functional out comes [40,41].

One of the limitations of our study is the absence of translocation testing. Chemotherapy had not been tried in any of our patients, but successful results had been achieved with radiotherapy.

The number of patients in our study is 17. Since this is a relatively small group, more studies on incidental cases will be a guide for what lesions should be suspected.

Conclusion

Performing a biopsy before excision in patients with a skin lesion and suspection of dermatofibrosarcoma protuberance is important in order to achieve clean surgical margins and to prevent re-excision. In this way, chemotherapy and radiotherapy treatments that may need to be given additionally can be prevented. Therefore, increasing our awareness about

DFSP will increase the success in local control, which is the most challenging part in the treatment of this disease.

Declaration of conflict of interest

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Original Article

Changes in the frequency of thyroid cancer and distribution of some subtypes in our region; Retrospective analysis of 4917 thyroidectomies

Bölgemizde tiroid kanseri sıklığında ve bazı alt tiplerin dağılımında gözlenen değişimler; 4917 tiroidektominin retrospektif analizi

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Abstract

Aim: The aim of this descriptive study is to determine the frequency of thyroid cancer (TC) and evaluate the changing rates of histopathological types, age and sex distribution of thyroid tumours in our region.

Material and Methods: A total of 4917 patients who underwent thyroidectomy for different indications between May 2010 and May 2019 were included in this retrospective study. Patients' age, sex, selected surgical method and postoperative final pathology results were recorded. All data were evaluated using statistical analyses.

Results: Of the 4917 patients, 922 were male (18.8%) and 3995 were female (81.2%). The mean age was 48.3 ± 12.3 (17-84) years. Among all cases 27.1% (1335) of them were malignant and 2.6 % (125) of them were well-differentiated tumours of uncertain malignant potential. The 1335 cases diagnosed with a malignant thyroid tumour had a mean age of 44.7±11.6 years and a female-to-male ratio of 4,3. Of these, 94.9% of them had papillary thyroid carcinoma (PTC), 1.72% had follicular thyroid carcinoma (FTC), 2.32% had medullary thyroid carcinoma (MTC), and 0.45% had anaplastic thyroid carcinoma. Of the cases with PTC, 62.66% of them had microcarcinoma.

Conclusion: Papillary thyroid microcarcinoma (PTMC) frequency increases especially in the younger and female population in our region, FTC frequency decreases significantly and MTC is the second most common type of TCs after papillary cancers. In all TCs, the 59.47% PTMC share (mostly detected incidentally, 83.7%) appears to be the result of pathologists examining more tissue blocks and histological sampling over time.

Keywords: epidemiology; pathology; thyroid cancer; thyroidectomy

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Öz

Amaç: Bu tanımlayıcı çalışmanın amacı, bölgemizdeki tiroid kanseri (TK) sıklığını belirlemek ve histopatolojik tiplerin değişen oranlarını, tiroid tümörlerinin yaş ve cinsiyet dağılımını değerlendirmektir.

Gereç ve Yöntemler: Mayıs 2010 ile Mayıs 2019 tarihlerinde arasında farklı endikasyonlarla tiroidektomi uygulanan 4917 hasta bu retrospektif çalışmaya dahil edildi. Hastaların yaşı, cinsiyeti, seçilen cerrahi yöntem ve postoperatif nihai patoloji sonuçları kaydedildi. Tüm veriler istatistiksel analizler kullanılarak değerlendirildi.

Bulgular: Dörtbindokuzyüzonyedi hastanın 922'si erkek (% 18,8) ve 3995'i kadın (% 81,2) idi. Yaş ortalaması 48,3 ± 12,3 (17-84) idi. Tüm vakaların % 27,1'i (1335) malign,% 2,6'sı (125) malignite potansiyeli belirsiz iyi diferansiye tümördü. Malign tiroid tümörü tanısı konan 1335 olgunun yaş ortalaması 44,7 ± 11,6 yıl, kadın / erkek oranı 4,3 idi. Bunların % 94,9'unda papiller tiroid karsinomu (PTK), % 1,72'sinde foliküler tiroid karsinomu (FTK), % 2,32'sinde medüller tiroid karsinomu (MTK), ve % 0,45'inde anaplastik tiroid karsinomu vardı. PTK olan olguların% 62,66'sında mikrokarsinom vardı.

Sonuç: Bölgemizde özellikle genç ve kadın popülasyonda papiller tiroid mikrokarsinom (PTMK) sıklığı artmakta, FTK sıklığı önemli ölçüde azalmaktadır ve MTK, papiller kanserlerden sonra ikinci en sık görülen TK tipidir. Tüm TK'lerinde, % 59,47 PTMK payı (çoğunlukla tesadüfen saptanmıştır, % 83,7), zaman içinde patologların daha fazla doku bloğunu incelemesi ve histolojik örnekleme yapmasının bir sonucu gibi görünmektedir.

Anahtar kelimeler: epidemiyoloji; patoloji; tiroid kanseri; tiroidektomi

Introduction

Thyroid cancer (TC) is the commonest endocrine system malignancy and its incidence has increased significantly in the last 4 decades [1]. TC is the sixth most common cancer in women in the USA and 52070 new cases occurred in both sexes in 2019. TC is still responsible for 0.3 % of cancer-related deaths, and has an incidence of 3.4 % among all cancers [2]. The reasons for this increase are still controversial. But the advances in imaging techniques for the detection of TC, which allows biopsy of even the smallest nodules, is thought to be main reason. However, it is noteworthy that in many countries of the world, this increase, which is mainly observed in microcancers, is not reflected in the mortality rates caused by TC [3].

More than 95% of all TCs are differentiated TCs originating from the thyroid follicular epithelial and includes papillary, follicular and Hürthle cell TCs. Papillary thyroid cancer (PTC) is the most common subtype and has the best prognosis. Follicular thyroid cancer (FTC), Hürthle cell cancer (HCC), and undifferentiated thyroid cancers are high-risk subtypes and tend to distant metastases. Medullary thyroid cancer (MTC) originating from parafollicular C cells constitutes 1-2% of all TCs. In a quarter of patients, MTC may be a component of multiple endocrine neoplasias (MEN) syndromes [4]. Anaplastic thyroid cancer (ATC) in the undifferentiated group is very rare, and its incidence is less than 1%. Patients often present with a rapidly growing neck mass, often accompanied by lymph nodes (LNs), with hoarseness, dysphagia and dyspnea. It may originate from differentiated cancers, as well as de nova. The prognosis of ATC, where distant metastases such as lung, bone and brain are common, is very poor [5]. Primary thyroid lymphoma (PTL) constitutes 1-5% of all thyroid malignancies and only 2% of extranodal lymphomas. Chronic lymphocytic thyroiditis and Hashimoto's thyroiditis are thought to be the cause of 90% of cases [6]. Well-differentiated tumour of uncertain malignant potential (WDT-UMP) are among the follicular tumours of the thyroid, which encapsulate and do not fully meet the criteria of malignancy, but exhibit suspicious structural and cytological features. Although all these tumour subtypes have unique behavioral characteristics, treatment of thyroid tumours (TTs) is usually surgical and the surgical method to be selected according to the type and stage of the tumour may vary from lobectomy to extended neck dissections.

This descriptive study aims to determine the frequency of TC and evaluate the changing rates of histopathological types, age and sex distribution of TTs in our region, by examining the patients who underwent thyroidectomy for a period of 9 years.

Material and Methods

A total of 4917 patients who underwent thyroidectomy for different indications between May 2010 and May 2019 at the Breast and Endocrine Surgery Clinic of Ankara

Numune Training and Research Hospital were included in this retrospective study. Patients' age, sex, selected surgical method and postoperative final pathology results were recorded. Informed consent was obtained from patients at the time of enrolment in the registry. Local ethics board approval was obtained for this study on December 24, 2019 (Number of ethics committee approval: E1-19-201). This study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

The Statistical package for social science (SPSS 20.0 software, IL-Chicago-USA) standard version was used for data analysis. Descriptive analyses were presented as number/percentage for categorical variables, and mean± standard deviation (SD), percentages, minimum and maximum values for continuous variables. One-way analysis of variance (ANOVA) was used to compare continuous variables. The difference between the ratios was compared using Pearson Chi-square test. In the calculations, $p < 0.05$ was considered statistically significant.

Results

Of the 4917 patients included in the study, 922 were male (18.8%) and 3995 were female (81.2%). The mean age of all patients was 48.3 ± 12.3 (17-84) years. Bilateral total thyroidectomy was performed in 4257 (86.58%) patients, total lobectomy in 324 (6.59%) patients and complementary thyroidectomy in 269 (5.47%) patients. The number of substernal and intrathoracic goitre cases performed by sternotomy or thoracotomy was 39 (0.79%). The selected surgical methods in patients operated for different indications are summarized in Table 1. When the final pathologies of the patients were examined, it was found that 70.3% (3457) of the patients were benign and multinodular goiter was in the first place with 1982 patients (40.31%), lymphocytic thyroiditis was seen in 522 patients (10.61%), nodular goiter was observed in 353 patients (7.19%) and Hashimoto thyroiditis was seen in 245 patients (4.98%). The histopathological results of 4917 patients who underwent thyroidectomy are presented in Table 2. Among all TTs; 15.06% (259) of the tumours were benign, 77.66% (1335) of them were malignant and 7.28% (125) of them were TTs with uncertain malignancy potential (Table 3). The most common malignant diagnosis was papillary thyroid microcarcinoma (PTMC) with 16.14% (n = 794), while PTC was seen in 9.61% (n = 473). When PTCs were detected with fine needle aspiration cytology before surgery (469 patients, 97.05%), the vast majority of the PTMCs (665 patients, 83.7%) were diagnosed incidentally. MTC was identified in 31(0.63%) patients, FTC in 23 (0.46%), ATC in 6 (0.12%) and lymphoma in only 3 (0.06%) patients. The detailed age and sex distribution of the cases are presented in Tables 3 and 4.

Table 1. Selected Surgical Methods in Patients Included in the Study

Operation method	n	%
Bilateral total thyroidectomy	4257	86.58
Total lobectomy	324	6.59
Complementary thyroidectomy	269	5.47
Substernal-intrathoracic	39	0.79
One side total, opposite side subtotal thyroidectomy	16	0.32
Subtotal lobectomy	9	0.18
Bilateral subtotal thyroidectomy	3	0.06
Central neck dissection	378	7.68
Lateral neck dissection	108	2.19
Total number of patients	4917	100

Table 2. Histopathological Results of 4917 Thyroidectomy Cases

Pathological diagnosis	n	%
MNG	1982	40.31
PTMC	794	16.15
LT	522	10.61
PTC	473	9.63
NG	353	7.19
HT	245	4.98
FA	176	3.58
WDT-UMP	125	2.55
HCA	83	1.68
TDG	96	1.95
MTC	31	0.63
FTC	23	0.46
ATC	6	0.12
HCC	5	0.10
PTL	3	0.06
Total	4917	100

Abbreviations: MNG, Multinodular goiter; PTMC, Papillary thyroid microcarcinoma; LT, Lymphocytic thyroiditis; PTC, Papillary thyroid carcinoma; NG, Nodular goiter; HT, Hashimoto's thyroiditis; FA, Follicular adenoma; WDT-UMP, Well- differentiated tumour of uncertain malignant potential; HCA, Hürthle cell adenoma; TDG, Toxic diffuse goiter; MTC, Medullary thyroid carcinoma; FTC, Follicular thyroid carcinoma; ATC, Anaplastic thyroid carcinoma; HCC, Hürthle cell carcinoma; PTL, Primary thyroid lymphoma.

Table 3. Age and sex characteristics of benign and malignant thyroid tumours

	Number of cases n (%)	Age mean ± ss (min-max)	p(age)	Female n (%)	Male n (%)	p(sex)
Benign (FA, HCA)	259 (15.06)	36.9.1±12.6 (18-72)	0.048	202 (78)	57 (22)	0.001
Malignant (PTMC, PTC, FTC, MTC, ATC, HCC,PTL)	1335 (77.66)	44.7±11.6 (17-84)		1084 (81.2)	251 (18.8)	
WDT-UMP	125 (7.28)	42.4±9.2 (28-61)		92 (73.6)	33 (26.4)	
Total	1719 (100)	43.8±13.2 (17-84)		1378 (80.2)	341 (19.8)	

Abbreviations: FA, Follicular adenoma; HCA, Hürthle cell adenoma; PTMC, Papillary thyroid microcarcinoma; PTC, Papillary thyroid carcinoma; FTC, Follicular thyroid carcinoma; MTC, Medullary thyroid carcinoma; ATC, Anaplastic thyroid carcinoma; HCC, Hürthle cell carcinoma; PTL, Primary thyroid lymphoma; WDT-UMP, Well- differentiated tumour of uncertain malignant potential.

Table 4. Distribution of malignant thyroid tumours by age and sex characteristics

Tumour type	Number of cases n (%)	Age (yıl)	p(age)	Female (F)	Male (E)	F/M	p(sex)
PTMC	794 (% 59.47)	43.8±11.7 (20-79)	0.032	659	135	4.8	<0.001
PTC	473 (% 35.43)	45.1±13.2 (17-81)		366	107	3.4	0.039
FTC	23 (% 1.72)	44.2±15.3 (21-67)		21	2	10.5	0.034
MTC	31 (% 2.32)	49.4±16.8 (22-69)		19	12	1.5	0.168
ATC	6 (% 0.45)	69.2±7.8 (58-84)		0	6	0	-
HCC	5 (% 0.38)	44.0±10.2 (38-63)		4	1	4	0.428
PTL	3 (% 0.23)	58.0±26.1 (39-76)		1	2	0.5	0.588
Total	1335 (%100)	44.7±11.6 (17-84)		1070	265	4.0	<0.001

Abbreviations: PTMC, Papillary thyroid microcarcinoma; PTC, Papillary thyroid carcinoma; FTC, Follicular thyroid carcinoma; MTC, Medullary thyroid carcinoma; ATC, Anaplastic thyroid carcinoma; HCC, Hürthle cell carcinoma; PTL, Primary thyroid lymphoma.

Discussion

In our country, the incidence of TC has increased by 14% in recent years. It is still the second most common cancer in women after breast cancer, and it is among the first fifteen in men [7]. In our study, which aims to show the changing trends of TC in our region; 1335 (27.1%) of 4917 patients were diagnosed with TC. In a 2008 study of 1632 thyroidectomy specimens from Turkey, the rate of malignant cases was reported to be 16% [8]. Compared with this study, the difference between TC rates, reflecting the same population over a 10-year period, is striking. Similarly, a study from Spain reporting a significant increase in the proportion of TC, which increased from 16.7% in 1978 to 43% in 2001 [9]. Another remarkable issue in TC is gender inequality. In a review of 2016 combining many important studies, TC is reported to be approximately 3 times more common in women than men [10]. In our study, the mean age of thyroid malignancies was 44.7 ± 11.6 years and the female/male (F/M) ratio was 4.3. We found that the female gender was slightly more dominant than the literature.

PTC, which constitutes more than 80% of TCs, is observed 3 times more in women and the average age at first diagnosis is between 40-50 [11]. In the current study, we examined PTMC and PTC as two different subtypes and we found their ratio among all TCs to be 94.9% in total. While the mean age for PTMC and PTC was 43.8 ± 11.7 and 45.1 ± 13.2, respectively, F/M ratios were 4.8 and 3.42. Compared to PTC, it can be said that PTMC is a little more common in young people and women. The predominance of PTMC to make up 59.47% of all thyroid malignancies may be a response to the overall increase in the incidence of TCs.

Contrary to decreases in mortality from TC, in recent years, the incidence of this neoplasm has increased in many countries around the world [2]. Considering that there is no defined change in the known risk factors for TC in our region, it is not wrong to explain this increase in TC incidence (predominantly PTMC) by overdiagnosis and treatment. It is reported in many studies that there is an increase in the detection of micropapillary lesions as a result of increased diagnostic imaging and ultrasound-guided needle biopsies, increased thyroid surgery rates and further cross-sectional examination of histopathological specimens [12, 13]. In this way, thyroid lesions are over-treated and at the same time, other subtype lesions, which may have a worse prognosis, are treated without further growth. All these processes are likely to be associated with an increased incidence of TC and decreased mortality.

Follicular adenoma (FA) and FTCs are defined as follicular neoplasms of the thyroid gland and are seen in 5 to 1 ratio in surgical specimens [14]. FTCs, which constitute 5-10% of TCs, are 3 times more common in women and peak at the 5th decade [11]. In our series, the mean age of the FTC was 44.2 ± 15.3, while the F/M ratio was found to be 10,5. More interestingly, the FA/FTC ratio was 176/23 [7,6] in this study, which was higher than the literature and the incidence of FTC in all TCs was 1.72%. These results show that the female predominance in FTC is increased, but its incidence among TCs is significantly decreased. There may be three reasons for this decline. Firstly, It is a known fact that FTC develops more in patients with iodine deficiency, and PTC predominates in those given excess dietary iodine [14]. As a result of the iodization of household salt, which was started in 1994 and made compulsory in 2000, in Turkey [15]; It can be thought that there has been a significant increase in the frequency of PTC and a relative decrease in FTC over the years. Secondly, a more accurate diagnosis of the follicular variant of papillary cancer and Hürtle cell cancer may also have been effective in this decrease. And finally, the evolution of FAs to FTCs caused by oncogenic mutations. Approximately 20% of patients with FA may develop FTC as a result of N-RAS and K-RAS mutations [14]. Early treatment of these patients with FA by lobectomy or total thyroidectomy may end this transformation before it begins. Similarly, in 2008, Netea-maier et al. emphasized the decrease in other TC subtypes such as FTC and ATC, despite the increase in the incidence of PTC in their study involving 5080 patients [16].

In our study, MTC had a share of 2.32% among all TCs and became the second most common subtype after PTC. Although it can be seen at any age, the mean age for MTC in this study was 49.4 ± 16.8 years, and no significant gender superiority was detected. And ATC, the worst type of TC was 0.45%. The ages of the patients ranged from 58 to 84 years (mean: 69.2 ± 7.8) and all 6 patients were male. In a study of 635 cases reported from our country, Erten et al. detected PTC in 93.2%, FTC in 3.3%, MTC in 2.2% and ATC in 0.6% of TCs [17]. These findings support our study in terms of the decrease in the incidence of FTC and ATC. HCC is another rare type of well-differentiated TC, which accounts for approximately 5% of TC diagnoses. In our series, the HCC rate was 0,38%. Four of 5 patients with HCC were female and the mean age was 44 years. The decreasing percentage of subtypes (such as FTC, HCC and ATC) with poor prognosis, as a result of an increase in the incidence of TC thought to be caused by over-detection may explain this decline. Another hypothesis may be that; As a result of over-treatment of millimetric nodules detected, possible subtypes originating from these nodules disappear before they are formed.

In our study, the diagnosis of PTL was 0.23% of all TCs. Unlike other lymphomas, PTL is a rare entity that accounts for 1% to %5 of all thyroid malignancies, frequently seen in older women and is 2-6 times more common in women [6]. Of the 3 patients, 2 were male and the mean age was 58 years. There was no significant difference between the sexes due to the small number of patients.

The strong sides of this study can be expressed as follows. We reviewed 4917 thyroidectomy cases as one of the most important reference hospitals in our country. While 1/4 of our patients were from Ankara, 3/4 were from local hospitals in other parts of the country. Therefore, the current study, which summarized the data of 1335 TC cases that we encountered in a 9-year period, is also important in terms of reflecting the general characteristics of TC cases in the whole country. A limitation to our study is retrospective nature and has a limited number of variables that did not allow us to compare the risk factors of TCs, such as radiation exposure, family history or dietary factors.

Data collected from 2010 to 2019 showed that more patients who had undergone thyroidectomy had benign thyroid disease (70.3%). But an increased cancer rate (27.1%) is remarkable compared to previous years. This study shows that PTMC frequency increases especially in the younger and female population in our region, FTC frequency decreases significantly and MTC is the second most common type of TCs after papillary cancers. In all TCs, although the share of TMPCs is 59.47%, the vast majority (83.7%) were detected incidentally. This seems to be the result of pathologists examining more tissue blocks over time and an increase in direct histological sampling.

Conclusion

This study confirms an increase in the incidence of TC in our region in recent years. This increase is largely due to an increase in the diagnosis of the PTMCs detected incidentally in the thyroid glands removed for benign thyroid diseases. However, further studies are needed to determine if this increase in the incidence of TC is due to overdiagnosis and detailed cross-sectional examination of histopathological specimens or an increase in TC risk factors.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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Original Article

Effects of modified ultrafiltration on postoperative hepatic and renal function of pediatric patients with congenital cyanotic/non-cyanotic heart defect who underwent open heart surgery: Retrospective study

Açık kalp cerrahisi uygulanan siyanoti/non-siyanotik konjenital kalp hastalıklarında modifiye ultrafiltrasyonun postoperatif karaciğer ve böbrek fonksiyonları üzerine etkisi: Retrsopektif çalışma

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Abstract

Aim: Increased total body water and capillary permeabilty in pediatric cardiopulmonary bypass can cause organ disfunction. Modified ulltrafiltration is developed to decrease total body water and attenuate organ disfunction. The purpose of this study, is to investigate retrospective effects of modified ultrafiltration on postoperative hepatic and renal functions of pediatric patients with congenital cyanotic/noncyanotic heart defect who underwent open heart surgery.

Material and methods: In this study, we assessed 93 children who underwent pediatric cardiac surgery with cardiopulmonary bypass from January 2009 to August 2011.Patients were divided into two groups. Group 1 (n=62) patients, to whom modified ultrafiltration was performed, compared with 31control patients (group 2). Patients who had redo cardiac surgery, preoperative organ disfunction, autoimmune disease, genetic disorders, shunt and emergency operations were excluded. Pre and postoperative biochemical parameters, postoperative urinary output, chest tube drenaige, diüretic usage, blood and blood product transfusion, dialysis requirement and mortality were compared.

Results: Age, weight, body surface area, congenital defect type and number, preoperative and intraoperative blood samples measurement, cross clamp time, cardiopulmonary bypass time were similar between 2 groups (p>0,05). The percant increase in creatinine level was statistically significant between the two groups, when these changes were re-evaluated according to the body surface area by univariate analysis(p<0,05). Percent increase in total plasma protein level was also statistically significant between the groups (p<0,05) (6,5% in group 1 and -5,5% in group 2). Percent increase in plasma albumin level was -18,2% in group 1, and -13,4% in group 2. When these changes were re-evaluated according to the body surface area by univariate analysis, a significant statistical difference was detected. (p<0,05). While two patients required dialysis in group 1, dialysis was performed in 4 patients in group 2. There was no statistical difference between the groups in terms of dialysis needed(p<0,05). There was no difference between the groups in terms of mortality (p>0,05)

Conclusion: Hemodynamic, pulmonary, hematologic and immunologic effects of modified ultrafiltration are well known. Although our study group was not big enough to get a conclusion, we believe that modified ultrafiltration can be an effective method in preservation of renal and hepatic function of the patients who underwent total reconstructive congenital heart surgery.

Keywords: modified ultrafiltration; cardiopulmonary bypass; pediatric open heart surgery

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Öz

Amaç: Pediatrik kardiyopulmoner baypas total vücut sıvında ve damar geçirgenliğinde artmaya neden olur. Dokular aralarına sızan bu sıvı organ fonksiyonlarında bozulmalara neden olmaktadır. Modifiye ultrafiltrasyon çocuklarda kardiyopulmoner baypasa bağlı oluşan toplam vücut sıvı artışının neden olduğu organ fonksiyon bozukluklarını önlemek amacıyla geliştirilmiştir. Bu çalışmada amacımız konjenital kalp hastalığı nedeni ile kardiyopulmoner baypas kullanılarak opere edilen siyanotik ve siyanotik olmayan çocuklarda MUF kullanımının karaciğer ve böbrek fonksiyonları üzerine etkisiniaraştırmaktı.

Gereç ve Yöntemler: Ocak 2009 ile ağustos 2011 yılları arasında Ankara Üniversitesi Tıp Fakültesi Kalp ve damar cerrahisi kliniğinde opere edilen modifiye ultrafiltrasyon kullanılan (grup 1) n:63, kullanılmayan (grup 2) n:31 toplam 93 hasta çalışmaya dahil edildi. Daha önceden bilinen operasyon ve organ fonksiyon bozukluğu olan, acil şartlarda operasyona alınan, sistemik ve otoimmün hastalığı olan ve kompleks kardiyak anomali nedeni ile parsiyel düzeltme yapılan hastalar çalışmaya dahil edilmedi. Organ fonksiyonlarının değerlendirilmesi amacıyla operasyon öncesinde ve sonrasında kan örnekleri alındı. Hastalar operasyon sonrası ilk 8 ve 24.saat idrar miktarı, drenaj miktarı, diüretik kullanımı, inotrop kullanımı, kan ve kan ürünü kullanımı, diyaliz ihtiyacı ve mortalite açısından retrospektif olarak incelendi.

Bulgular: Preoperatif verileri ve operasyon verileri açısından gruplar benzerdi. Grup 1 için kreatinin düzeyinin operasyon sonrasında yüzde değişim oranı %56,5, grup 2 için %25,8 olarak hesaplandı. Vücut yüzey alanına göre univaryant analizde anlamlı olarak bulundu. (p:0,031<0,05) Total protein değerlerinin operasyon sonrası değişim yüzdesi (-)%6,5, grup 2 için (-)%5,5 olarak hesaplandı. Bu sonuçlar istatistiksel olarak anlamlı bulundu. (p:0,04<0,05) Albümin düzeylerindeki yüzde değişim oranı açısından grup1 (-)%18,2, grup 2 için (-)%13,4 olarak hesaplandı. Bu değişimler vücut yüzey alanına göre yeniden univaryant analiz ile değerlendirildiğinde anlamlı istatsitiksel fark saptandı (p=0,05). Grup 1 için dializ ihtiyacı olan hasta sayısı 2, Grup 2 için 4 hasta olarak bulundu. Bu sonuç istatistiksel olarak anlamlı bulundu (p=0,05). Mortalite grup1 için 4 hasta, grup 2 için 1 hasta olarak bulundu. Mortalite açısından gruplar arasında anlamlı istatistiksel fark hesaplanmadı (p>0,05).

Sonuç: Pediatrik açık kalp cerrahisinde modifiye ultrafiltrasyonun kullanımının böbrek yetmezliği gelişimini azalttığı ve karaciğer fonksiyonlarını koruduğunu düşünmekteyiz.

Anahtar kelimeler: modifiye ultrafiltrasyon; kardiyopulmoner baypas; pediatrik açık kalp cerrahisi

Introduction

In cardiopulmonary bypass, the body's defense cells and proteins are activated as a result of contact of blood with non-epithelial surfaces. This condition, called systemic inflammatory response syndrome (SIRS), is one of the mechanisms responsible for the undesirable effects of CPB.[1]

After the surface contact, the complement system is activated. Inflammatory mediators join the circulation. These mediators affect vascular endothelial permeability, heart function, intestinal fluid amount, coagulation system and end organ functions.[2]

Unlike adult patients, pediatric patients undergoing open heart surgery via cardiopulmonary bypass are more susceptible to both excessive body fluid increase due to high prime volume and systemic inflammatory response, because of incomplete maturation of organs and tissues. Various ultrafitration strategies developed to reduce cytokines and fluid load have also been used for pediatric patients.[3] Zero balanced modified ultrafiltration(MUF) is one of these strategies. It has been claimed that modified Ultrafiltration, developed to reduce excess fluid in the body, helps to remove inflammatory cytokines from the circulation and reduces the effects of some mediators by filtering them.[4]

Like many other organs, impaired liver function is common after CPB. High transaminases, hyperbilirubinemia, decrease in coagulation factors, prolongation of coagulation parameters and increase in bleeding can be detected. Total body protein may be reduced, making it difficult to retain body fluid in the intravascular space. it can also cause hepatorenal syndrome. Depending on the inability to remove toxic agents, toxic ileus may develop as well as central nervous system changes. even hepatic coma may develop.[5] Due to all these factors, mortality and morbidity increase.[6] As claimed in some studies, liver functions can be preserved and the incidence of hyperbilirubinemia can decrease with the use of MUF.[7] MUF can also assure a significant difference in the amount of chest tube drainage and in the development of hepatic coma and hepatorenal syndrome.[8]

Hemoconcentration provided by modified ultrafiltration has

positive effects on the clotting system. In a study conducted by Chew et al.[9], It was found that the use of blood and blood product and chest tube drainage significantly decreased in patients undergoing MUF compared to the CUF and control group. In the same study, fibrinogen, factor VII (FVII) levels were increased, while platelet count, factor IX (FIX) and factor X (FX) levels did not change.

MUF targets a higher hematocrit (Hct) value than before CPB. In this way, it provides hemoconcentration of blood and increases in total body protein and albumin levels.[10] Children underdeveloped kidney function can be preserved. Studies have been claimed to prevent impaired kidney function even if it does not improve kidney function significantly.

Material and Methods

This study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Ankara University Faculty of Medicine, Ankara, Turkey.

In this study, between January 2009 and August 2011 at Ankara University Faculty of Medicine Cardiovascular Surgery Cebeci Heart Center, the data of patients with cyanotic and non-cyanotic heart disease and operated under cardiopulmonary bypass were collected. In order to investigate the effect of using zero-balanced MUF on kidney and liver functions, Patients were divided into two groups. 62 patients who were operated after routine use of the technique in the first group (group 1) and 31 patients who were operated before the routine use in the second group (group 2) were included. The data of 93 patients were collected and analyzed retrospectively. Patients with a body weight between 3 and 30 kg and without any previous known systemic autoimmune, genetic, kidney and liver diseases, who were not used total circulatory arrest technique, who were not performed emergency / urgent surgery, who did not have heart failure and who did not have shunt surgery were included in the study.

All patients were hospitalized one week before the operation and evaluated by the pediatric cardiology specialist and pediatric infection diseases specialist. Dental diseases were consulted in terms of focal infection focus. 1 day before the operation, all rutine blood sample tests were reevaluated.

Cardiopulmonary bypass was established in all patients by aortobicaval cannulation with median sternotomy. Mild to moderate (28-32^{o}C) hypothermia was achieved during cardiopulmonary bypass. After cardiopulmonary bypass was terminated, the previously integrated MUF cycle has been activated and filtration was performed. Care was taken to maintain stable hemodynamics during the procedure. The hematocrit value was increased to 35% -40% levels. After the MUF process, decanulation was done. The bleeding control was completed and the sternum was closed with steel wires and transferred to the cardiovascular surgery intensive care unit. All surgical procedures were performed by the same surgical team.

Blood samples were collected from all patients in the early postoperative period (immediately after the operation and 8 hours after the operation) and at the 24th hour.

In our study, BUN, creatinine, total protein and albumin values were collected from the blood samples that were collected in the preoperative, postoperative 8th and 24th hour to evaluate kidney function. In addition, the total amount of fluid delivered to the patient, total urinary output and chest tube drainage, as well as the need for furosemide, duration of hospitalization and intensive care unit stay and the amount of blood and blood products were recorded. The need for hemodialysis and / or peritoneal dialysis was also noted.

Evaluation of liver function was made by preoperative, postoperative early (8th hour) and postoperative 24th hours value of AST, ALT, GGT, ALP, LDH, TOTAL PROTEIN, ALBUMIN, TOTAL / DIRECT BILIRUBIN, INR, APTT values. In addition, the amount of chest tube drainage and blood and blood product usages were also collected during intensive care follow-ups.

Statistical Analysis

SPSS 17.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum - maximum where necessary). Chi-square test statistics were used to compare categorical measurements between groups. In the comparison of continuous measurements between groups, T test (Student T Test) was used in independent groups, and Mann Whitney U test was used if assumptions were not provided. Spearman Correlation test statistics were used to compare continuous variables between groups. Due to limited sample size, intensive care unit's datas were recalculated according to body mass index by univariate analysis. Statistical significance level was taken as 0.05 in all test.

Results

In our study, the number of patients is an important limiting factor. In some critical data, a mathematical difference was detected, but no statistical significance was found. Also there is not enough data to be used to evaluate the systemic inflammatory response, In addition, the fact that the deterioration in the basic biochemical parameters showing end organ damage is mathematically less.

The diagnosis and operation data of the patients are presented in Table 1 below.

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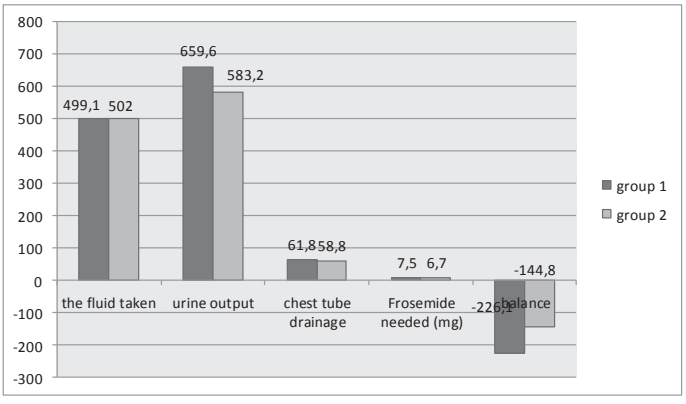
Table 1. Patient Diagnoses and Operations by Groups				
Diagnosis	Operation	Group:1	Group:2	Total
ASD	ASD closure	10	11	21
ASD, PDA	ASD closure, PDA ligation	1	0	1
VSD	VSD closure	20	6	26
VSD, PDA	VSD closure, PDA ligation	1	1	2
VSD, PS	VSD closure, with transanüler patch	1	0	1
ASD,VSD	ASD clusure, VSD closure	3	3	6
AVSD	Closure with Modified single patch technique	8	6	14
AVSD, PDA	Closure with Modified single patch technique, PDA ligation	1	1	2
TOF	Total correction	12	2	14
SUBAORTIC MEMBRAN	Closure with Modified single patch technique	4	1	5
COR TRİATRİATUM	Membran excision	1	0	1
Total		62	31	93

ASD, atrial septal defect; VSD, ventriculer septal defect; PDA, patent ductus arteriosus; PS, pulmonery stenosis; AVSD, atrioventriculer septal defect; TOF, Tetralogy of Fallot

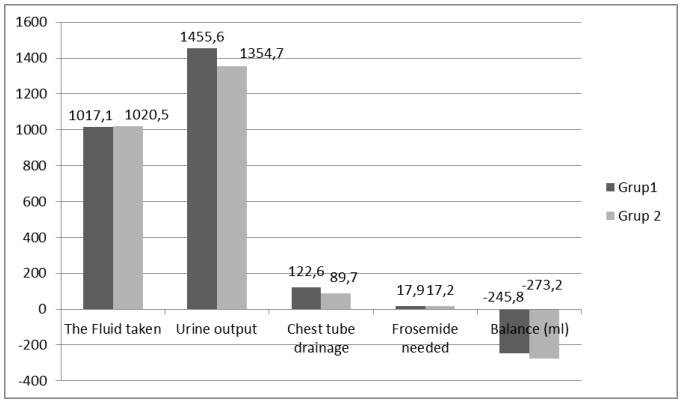
The demographic data and preoperative blood sample results of the study groups are presented in Table 2 below. There was no statistical difference between the groups(p> 0.05).

There was no statistically significant difference between the study groups in terms of intraoperative data. (p> 0.05) (Table 3)

İntensive care unit datas were collected and presented in graph 1 for first 8 hours and graph 2 for first 24 hours.



Graphic 1. First 8 hours of ICU data



Graphic 2. First 24 hours ICU data

Table 2. Demographic data			
Gender(M/F)	Group:1 (n:62)	Group:2 (n:31)	P value
	28/34(%45-55)	19/12(%62,1-37,9)	0,552
	(mean)	(mean)	
Age (ay)	49,5	38,5	0,420
Weight (kg)	14,5	12,4	0,425
Body surface area (kg/m^2)	0,59	0,54	0,554
BLOOD SAMPLES			
BUN (mg/dl)	11,4	11,0	0,546
CRE (mg/dl)	0,59	0,8	0,193
SODIUM	138,4	139,7	0,783
POTASSIUM	4,01	4,2	0,806
TOTAL BODY PROTEIN (g/dl)	6,62	6,8	0,195
ALBUMIN (g//dl)	5,73	4,6	0,078
TOTAL BILIRUBIN (mg/dl)	0,61	0,6	0,352
DIRECT BILIRUBIN (mg/dl)	0,14	0,2	0,816
ALT (U/L)	21,5	31,1	0,708
AST (U/L)	46,3	40,2	0,841
GGT (U/L)	14,7	22,9	0,535
LDH (U/L)	372,8	441,6	0,443
ALP (U/L)	158,6	194,4	0,204
BLEEDING PROFILE			
APTT (second)	31,9	31,7	0,473
INR	1,13	1,09	0,232
INFLAMMATORY MEDIATOR CRP (mg/L)	2,2	3,0	0,725

BSA, Body surface area; BUN, blood ürine nitrogen; CRE, creatinin; ALT, alanin aminotransferase; AST, aspartat aminotransferase; GGT, gama glutamyl transferase; LDH, lactat dehydrogenase; ALP, alcaline phosphatase; APTT, actived prothrombin time; CRP, C- reactive protein.

The groups were compared in terms of ICU data and it is presented in Table-4 and Table-5 below. Percent changes between postoperative values were evaluated. Due to the limited number of samples, intensive care data were recalculated by univariate analysis according to body mass index (p(BSA)).

Table 3. Intraoperative Data

Intraoperative data	Group:1	Group:2	P value
CPB time (min)	117,0	99,1	0,131
Cross Clamping time (min)	74,9	66,4	0,129
Hemoglobulin (g/dl)			
Before CPB	9,5	9,7	0,543
During CPB	7,8	7,8	0,485
After CPB	8,0	7,9	0,623
Hematocrit (%)			
Before CPB	28,5	36,6	0,106
During CPB	23,4	32,7	0,134
After CPB	23,9	23,9	0,615

CPB: Cardiopulmonary bypass,

The use of fresh frozen plasma was found 219.1 ± 147.5ml for group 1. Group 2 was 167.7 ± 111.0ml. There was no statistically significant difference between the groups in the values examined with the Mann Whitney U test (P> 0.05)(Table 4). However, univariate analysis was performed to calculate the use of fresh frozen plasma proportioned to the patient's BSA. Fresh frozen plasma use was higher in group 1 and it was statistically significant (p: 0.011<0.05) (Table 4).

Dialysis requirement was 2 patients for group 1. 4 patients were found for group2. There was a statistically significant difference between the groups (p: 0.058). In group 2, the number of patients in need of dialysis was higher (p = 0.05) (Table 4).

The percent change of creatinine was calculated as 56.5% for group 1. Group 2 was 25.8%. There was no difference in statistical tests using Mann Whitney U and chi-square test. (p> 0.05) But there was a significant difference in univariate analysis acording to BSA. It was observed that the recalculated percent change of creatine was higher in Group 1. (p: 0.031<0.05) (Table 5).

The percent change of total protein level was calculated as -6.5% in group 1, -5.5% in group 2. There was statistically significant difference was found between the groups. (p<0.05).(Table 5).

Percent change of plasma albumin level after operation was found to be -18.2% in group 1. This change rate for Group 2 was calculated as -13.4%. There was no statistically significant difference between the groups. (P> 0.05). However, according to BSA, a statistically significant difference was found in recalculated percentage change rate in univariate analysis. (p = 0.05) It was observed that the decrease in Group 1 was higher (Table 5).

Table 4. ICU Data

ICU data	Group:1	Group:2	p value	p (BSA) (univariate analysis)
Lenght of stay in ICU (hour)	63,0	56,5	0,971	
Fluid taken (ml)				
8 hours	499,1	502,0	0,789	
24hours	1017,2	1020,5	0,987	
Chest Tube Drainage (ml)				
8 hours	61,8	58,8	0,335	
24hours	122,6	89,7	0,453	
Urine Output (ml)				
8 hours	659,6	583,2	0,393	
24hours	1455,6	1354,6	0,854	
Frosemide needed (mg)				
8 hours	7,4	6,7	0,849	
24 hours	17,9	17,2	0,363	
Balance (ml)				
8 hours	-226,1	-144,9	0,189	
24hours	-245,8	-273,2	0,883	
Inotropic drug				
Dopamine	41	20	0,877	
Dobutamine	22	8	0,347	
Adrenalin	18	8	0,744	
Noradrenalin	2	0	0,551	
Milrinon	19	14	0,168	
NTG	5	2	1,000	
Blood product usage(ml)				
Packed RBC	218,3	208,9	0,740	-0,940
FFF	219,1	167,7	0,123	0,011*
PLATELET CONCENTRATE	97,6	96,7	0,584	0,873
Dialysis neened	2	4	0,058*	
Exitus	4	1	0,662	

RBC, red boold cell; FFF, fresh Frozen Plasma; .

Table 5. Postoperative blood samples' results

Percentage change (%)	Group:1	Group:2	P (percentage change)	P (BSA) (univariate analysis)
BUN	80,6	79,6	0,496	
KRE	56,5	25,8	0,138	0,031*
SODIUM	11,5	13,7	0,328	
POTASIUM	23,3	27,0	0,643	
TOTAL PROTEIN	-6,5	-5,5*	0,040*	0,416
ALBUMIN	-18,2	-13,4	0,194	0,056*
TOTAL BILIRUBINE	179,7	119,0	0,313	0,105
DIREKT BILIRUBINE	110,5	182,1	0,792	0,304
ALT	25,0	22,6	0,058	0,282
AST	190,0	315,0	0,149	0,103
GGT	45,3	47,7	0,694	
LDH	126,6	180,8	0,600	
ALP	-42,1	-57,1	0,098	
APTT	-4,7	-1,6	0,555	
INR	26,8	8,3	0,458	
CRP	277,8	185,8	0,224	

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Discussion

It is a technique that has been demonstrated by various studies that modified ultrafiltration has positive effects on heart and lung function, coagulation and inflammatory system. It has been found to reduce end organ damage. For this reason, many centers perform pediatric cardiac surgery have added MUF to their operation techniques and use them widely. Although the incidence of complications of CPB decreases in pediatric patients after the use of MUF becomes widespread, it still appears as an important and serious problem.

Today, the use of CPB is absolutely necessary in the corrective surgery of complex congenital heart diseases. Besides its advantages such as providing an immobile and bloodless working area, complications that can be seen due to the development of systemic inflammatory response syndrome (SIRS), coagulation system disorders, multiple organ failure are its major disadvantages.[2]

In children, hypothermia, hemodilution, and prolonged CPB increase the amount of fluid that escapes the interstitial space. As a result, total body fluid rises by 11-18%. Modified ultrafiltration reduces this amount of fluid by up to 4%.[11]

It has been determined that with the modified ultrafiltration, inflammatory mediators of a size that can pass through the pores of the filter can be removed from the blood, thereby reducing the systemic inflammatory response.[12] Due to the randomized and non-randomized results regarding this issue, there have been many controversial publications. Hiramatsu et al. Showed that ET-1 levels decreased in patients undergoing MUF.[13] Wang et al. argue that IL-8 and ET-1 levels decrease and TNF-α level does not change.[14] Pearl et al. Found that MUF did not change the TXB2 and LTB4 levels after KPB.[15] Chew et al. Showed that there is no change in TNF-α, IL1-beta, IL-ra, C3d and C4d levels.[9] In our study, there was no data regarding the inflammatory cytokine values and no evaluation could be made. However, there was no significant decrease in the MUF group in terms of CRP values ($p > 0.05$).

Kidney functions are not fully developed in children under 3 years old and under 10 kg, Glomerular filtration rate is low, bicarbonate re-absorption is insufficient, and urinary concentration is very low. Kidneys' ability to remove the increased acid and liquid load is low .[16]

Excessive use of blood products poses an additional burden on the kidneys in the postoperative period. In contrast, increasing the amount of hematocrit and oxygen in blood helps to maintain renal cortex functions. Activation of the renin angiotensin system and Vasospasm are reduced. Oxygen delivery to tissues increases and the workload of the kidneys decreases.[17]

In our study, it was observed that the creatinine value increased statistically significant in group 1 patients in contrast to expectations in blood samples made to evaluate the change in kidney function ($p < 0.05$). This adverse effect can be explained by high hemoconcentration and relative hypovolemia. A statistically significant decrease in the need for postoperative dialysis in group 1 indicates that although creatinine is elevated, kidney function is preserved ($p < 0.05$). Likewise, the difference in the amount of fluid given to the patients within 8 and 24 hours and the improvement of creatinine values afterwards supports hypovolemia.

In our study, no statistically significant difference was found in terms of BUN, urine output, balance, and furosemide use. In the group without modified ultrafiltration, the amount of urine was higher in the first 24 hours. Osmotic pressure of the blood decreases as some of the fluid escaping to the interstitial space is taken back during the operation by the modified ultrafiltration. Accordingly, the first 8 and 24 hours urine output may decrease in patients undergoing modified ultrafiltration. On the contrary, the increase in urine output seen at the end of the first 24 hours in patients without ultrafiltration may be related to the transfer of fluid that escapes to the interstitial space during the CPB to the intravascular area during intensive care follow-ups. There is no difference between groups in the first 8 hours in terms of furosemide use. however, more furosemides were used in the group with MUF in 24 hours. this may be associated with both decreased fluid in the intravascular area and forced diuresis.

There was no statistically significant difference between the study groups in terms of the need for dialysis ($p > 0.05$). The need for dialysis was numerically higher in group patients without ultrafiltration. This result may indicate that some of the inflammatory cytokines and excess fluid collected in the interstitial area are removed and kidney function is preserved in patients with MUF. This result also supports that the rise in KRE may be due to relative hypovolemia rather than renal damage.

Increased total body fluid-induced liver congestion in children can lad to a reduction of liver-induced clotting factors (fibrinogen, prothrombin, Factor V, VII, IX, and X) and toxic radicals released after ischemia reperfusion injury.[18] The decrease in the synthesis of plasma proteins, which have important functions, may increase liver damage by causing excess fluid to escape into the tissue

spaces[2] Consequently, bleeding disorder and chest tube drainage may increase.[3] Also development of hepatorenal syndrome, low cardiac output, ileus, ascites can be seen. Although the frequency of these complications decreases after the use of modified ultrafiltration has become widespread, it is still an important and serious problem.[10]

In our study, there was no statistically significant difference between the patient groups in terms of liver transaminase levels, but there was more increase in the group without MUF. This result supports the view that liver function and end organ damage are reduced in patients who underwent MUF stated in the study by Elliot et al.[19]

When plasma protein changes were examined, it was seen that total plasma protein levels decreased more in the MUF group. The decrease in the total protein values in the MUF group independent of the albumin may be due to the filtration of the immunoglobulins. In addition, although there is no statistically significant difference between the groups in terms of FFF use in the postoperative period, the increased presence of the MUF can be explained by the loss of immunoglobulin.

When evaluated in terms of chest tube drainage, the first 8 hours in the MUF group was lower. This finding Naik et al. matches the results of his work. The meaningless statistical analysis can be explained by the fact that the patient groups do not contain a sufficient number of patients.

Edema in the heart is reduced by modified ultrafiltration. In 1993, Elliot et al. In 1998, Rivera et al.[20] showed that MUF decreased heart size, increased systemic vascular resistance, increased systolic blood pressure, decresed heart rate, so increased cardiac index and decreased inotropic support needs.[21,22] In contrast, Mauerman et al. Showed that MUF was not effective on the development of atrial fibrillation in adult patients.[23] Naik et al. Measured his heart rate, blood pressure, right and left atrial pressures, pulmonary artery pressure, and cardiac output before and after MUF, there was no change in left atrial pressure, decrease in heart rate, increase in systolic pressure and cardiac index without change in systemic vascular resistance.[24] It has been determined. In the same study, it was reported that heart sizes decreased significantly after MUF. Hodges et al. confirmed the increase in cardiac index and systolic pressure after MUF.[25] In this study, it was determined that there was no effect of decreasing plasma fentanyl level after MUF on arterial pressure change. Davies et al. determined that the increase in systolic arterial pressure was due to the improvement in intrinsic left ventricular systolic functions. Post-diastolic width and post-diastole pressure decrease after modified ultrafiltration have been associated with an increase in left ventricular compliance due to reduced myocardial edema.[20] No data to confirm these findings were found in our study. it was seen that the need for inotropic support decreased significantly in patients undergoing MUF, but no statistical difference was found due to insufficient number of patients (Table 4). It is seen that the use of Milrinon is higher in group 2.

Hemoconcentration provided by modified ultrafiltration has positive effects on the coagulation system. In the study conducted by Chew et al., It was found that the use of blood and blood products and chest tube drainage decreased compared to the CUF and control group in patients with MUF. In the same study, it was stated that modified ultrafiltration also influences the coagulation factors.[26] fibrinogen, factor VII (FVII) level increased, platelet, factor IX (FIX) and factor X (FX) levels were shown to be unchanged.[27]

Coagulopathy is a well-defined problem after cardiopulmonary bypass. Ootaki et al. Reported an increase in Hct, platelet, total plasma protein and albumin values in patients with MUF. Fibrinogen, prothrombin, and FVII levels were higher, but showed no change in FIX and FX.[28] In our study, no significant difference was found in terms of hematocrit and platelet counts. Total plasma proteins were lower in group 1. The decrease in total protein without decreasing albumin can be explained by loss of globulin due to filtration ($p<0.05$). Adequate data for statistical analysis could not be obtained regarding fibrinogen and coagulation factors.

Hemostasis mechanism changes after cardiopulmonary bypass is the most important factor responsible for post-operative blood loss and blood product use. In studies conducted by Naik, Bando, Gurbuz and Draaisma, they were found that the use of blood and chest tube drainage decreased significantly in patients with MUF.[29] In our study, no mathematical and statistical difference was found between the groups in terms of blood use. This has been linked to insufficient number of patients included in the study.

Conclusion

Since our study was planned as a retrospective study, the data that could ensure the effectiveness of MUF could not be reached sufficiently. therefore MUF appears to be effective in maintaining kidney and liver function, although there is insufficient data available. İn to the future, more randomized controlled prospective studies are needed.

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Declaration of conflict of interest

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Original Article

Knowledge and implication about oral antineoplastics drugs use of cancer patients

Kanser hastalarının oral antineoplastik ilaç kullanımına ilişkin bilgi ve uygulamaları

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Abstract

Aim: Study was conducted as descriptive to evaluate information and practice about oral antineoplastics drug used of cancer patients.

Material and Methods: There research sample consists of 100 people who use oral antineoplastic drugs in Ankara Numune and Ankara Yıldırım Beyazıt Education and Research Hospital Oncology wards. Patient conversation form and evaluation of drug information form, which was developed by the investigator according to literature, was used as a data obtaining an instrument. In the evaluation of data percentage and chi-square tests was used.

Results: Average age of the person that participates in surveying is 51.5±7,1. We observed that 48% of participants use capecitabine as oral antineoplastic, and 51% of participants have cure number between 0-3. 93% of participant that they informed about medicine by the doctor when prescribed, and 50% by the nurse at the outpatient clinic. It is observed71% of participants stake medicine not in time. As the reason for this case, forget fullness is on the top with a 51% rate. It is observed male more successful than female for taking medicine in time ($p<0.05$) and the rate of taking medicine in time is increasing with education level ($p<0.05$). Besides, we observed that the rate of taking medicine in time is lower for participants that informed verbally than informed verbal and written.

Conclusion: This study suggests that individuals have a low educational level successful in drug-taking at the same hour and the long period of drug-taking decrease this success. Female take assistance drug use more than male and taking assistance increases while the educational level decrease in both genders.

Keywords: cancer; cancer treatment; drug; oral chemotherapy

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ÖZ

Amaç: Araştırma, kanser hastalarının oral antineoplastik ilaç kullanımına ilişkin bilgi ve uygulamalarını değerlendirmek amacıyla kesitsel çalışma olarak yapılmıştır.

Gereç ve Yöntemler: Araştırmanın örneklemini Ankara Numune Eğitim ve Araştırma Hastanesi ile Ankara Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi Onkoloji polikliniklerinde, oral antineoplastik ilaç kullanan 100 kişi oluşturmuştur. Veri toplama aracı olarak literatür bilgisinden yararlanılarak araştırmacı tarafından hazırlanan "Hasta Görüşme Formu" ve "İlaca İlişkin Bilgilerini Değerlendirme Formu" kullanılmıştır. Verilerin değerlendirilmesinde ki-kare testi kullanılmıştır.

Bulgular: Araştırmaya katılan bireylerin yaş ortalaması 51.5±7,1 'dir. Bireylerin %48'inin oral antineoplastik ilaç olarak kapesitabin kullandığı, %51'inin kür sayısının 0-3 aralığında olduğu görülmektedir. Hastaların %93'ü ilaç ile ilgili bilgileri poliklinikte ilaç yazılması esnasında doktor tarafından, %50 si ayaktan kemoterapi alma ünitesinde hemşire tarafından sözlü eğitim şeklinde almaktadır. Bireylerin %71'inin ilacı aynı saatte almadıklarını ifade ettikleri görülmüştür. İlacı aynı saatte almama nedenleri arasında %51 oranı ile unutkanlık ilk sırada yer almaktadır. Erkeklerin kadınlara göre aynı saatte ilaç alma konusunda daha başarılı olduğu ($p<0.05$) ve eğitim düzeyi artıkça aynı saatte ilaç kullanma durumlarının arttığı görülmektedir ($p<0.05$). Bunun yanında sadece sözel olarak bilgi alanların, hem sözel hem yazılı bilgi alanlara göre 'aynı saatte ilaç kullanma' oranlarının daha düşük olduğu görülmektedir ($p<0.05$).

Sonuç: Eğitim seviyesi düşük olan kişilerin aynı saatte ilaç kullanma konusunda başarısız olduğu ve hastanın kür sayıları arttıkça aynı saatte ilaç kullanmada başarılarının azaldığı belirlenmiştir. Kadınların erkeklere göre ilaç kullanımında daha fazla yardım aldığı ve tüm bireylerde eğitim seviyesi düştükçe ilaç kullanımında yardım almanın arttığı belirlenmiştir. Ayrıca bireylerin yaşı arttıkça ilaç almayı daha çok unuttukları belirlenmiştir.

Anahtar kelimeler: İlaç; kanser; kanser tedavi; oral kemoterapi

Introduction

Cancer is one of the leading health problems of our age for many reasons such as increased life expectancy, developments in diagnosis and treatment methods. The frequency of cancer increases by 1-2% per year in almost every country worldwide [1]. In parallel with this increase in cancer incidence, treatment methods and options are increasing day by day. One of these treatment methods is the oral administration of antineoplastic drugs. The number of oral antineoplastic drugs and their importance in an application is increasing every day [2, 3].

Administration of oral antineoplastic agents provides several advantages to patients. These advantages; application shortening, increased independence, non-invasive, decrease the burden of the patient and increase the quality of life [4,5]. Despite these advantages, it is a disadvantage that patients do not comply with the principles such as correct dosage, right time, correct storage, proper retrieval. Drug compliance; with medical advice, patient behaviour and lifestyle is defined as incompatible and discontinuity of drug, wrong dosage, misuse of drugs at the wrong time is considered applications. Non-compliance with drug therapy in cancer patients may lead to the development of drug resistance, low response to treatment, the progression of disease and death [5,6]. For patients to take optimal advantage of oral antineoplastic drug therapies, it is essential that they take their medication as recommended and correct. Patient education has great importance in terms of increasing patient safety, optimal dose and compliance with the treatment plan. Nurses working in the oncology outpatient clinic should educate the patient and the family. Thanks to drug training, ensuring the continuation of treatment is beneficial in preventing or early detection of problems at home [7, 8].

In the literature, the adaptation of the patients receiving oral antineoplastic medication, the factors affecting their adaptation and the use of drugs were evaluated, nursing care for the problems and applications planned [6,9,10]. In our country, the studies evaluating the knowledge and applications of the patients taking oral antineoplastic drugs on drug use could not reach. Therefore, there is a need to evaluate the knowledge and applications of cancer patients using oral antineoplastic drugs. This study aimed to evaluate the knowledge and applications of cancer patients receiving oral antineoplastic drugs.

Material and Methods

Setting and Sample

The study was carried out cross-sectional studies in order to evaluate the knowledge and applications of cancer patients on the use of oral antineoplastic drugs. Due to insufficient data on the number of people using oral antineoplastic drugs, an exact number could not determine, and sample selection based on "duration. According to this study, people who used oral antineoplastic drugs in Oncology outpatient clinics of Ankara Numune Training and Research Hospital and Ankara Yıldırım Beyazıt Training and Research Hospital between March 1, 2009, and June 1, 2009, in 3 months formed the sample. Repetitive applications excluded in the study, and 110 patients reached during this period. 2 out of 110 patient died before the meeting, and eight patient could not interview because they were out of town. Eighteen years - 65 years of age, cncer patients, at least one cure oral antineoplastic drug, who can communicate quickly, who agreed to participate in the study completed with 100 people.

Instruments

The research data collected by the researcher using "Patient Interview Form" and "Drug Information Evaluation Form" prepared by the literature[4-10].

Data Collection Procedure

Support was obtained from the policlinic nurse and doctor to find patients using oral antineoplastic agents. Besides, we followed up and reached to the patients through the secretariat of the polyclinic. The researcher interviewed the patients in the relaxation room, which was a quiet area. Interviews with each patient took 20-25 minutes.

Ethical consideration

The application permission obtained from the General Directorate of Treatment Services of the Ministry of Health, and "LUT 08 / 68-31" has been obtained from Hacettepe University Ethics Committee. The participants were informed about the study. Then, both individuals permitted in both verbal and written form.

Statistical Analysis

SPSS 13 program used in the statistical analysis of the data. Descriptive data were shown as numbers and percentages. The relationship between the knowledge-application and the independent variables analyzed by chi-square significance test.

Results

The mean, standard deviation of the ages of the participants was 51.5 ± 7.1. Of these participants, 53% of the patients were female, 53% of them were primary and lower education, 49% of them were homemakers, and 68% of them lived with their spouse and children. 31% of patients are metastatic breast cancer, and 60% of patients receive oral antineoplastic treatment alone. 48% of patients use capecitabine, and 51% of the patients had cure number 0-3 (Table 1).

Table 1. Demographic and Clinical Data of the Participants

Features		n	%
Age X±SS: 51.5±7,1	39- 47	12	12
	48-56	45	45
	57-65	43	43
Gender	Female	53	53
	Male	47	47
Diagnosis of the disease	Breast Cancer	31	31
	Colon Cancer	26	26
	Leukemia	15	15
	Ovarian Cancer	9	9
	Melanoma	9	9
	Brain cancer	8	8
	Rectum Cancer	2	2
Oral Chemotherapy drug	Capecitabine	48	48
	Temozolomide	17	17
	Tegafur-uracil	11	11
	Cyclophosphamide	9	9
	Tiguanin	8	8
	Mercaptopurine	7	7
Cure	0-3 Cure	51	51
	4-7 Cure	47	47
	8-11 Cure	2	2
Total		100	100

95% of the individuals experienced nausea and vomiting related to the antineoplastic drug, and 95% did not record the onset, severity, and duration of the side effect when the drug-related side effect developed. The drug uses medication outside. 100% of these drugs is antiemetic, and 95% is antacid. 93% of the patients received information about the drug by the doctor, and 50% of the patients received verbal training by the nurse. Individuals stated that 71% did not take the drug at the same time. For reasons of not taking the drug at the same time, forgetfulness (51%) is in the first place. 58% of the patients said that when they remembered their oral antineoplastic drug, they forget to take the medication. (Table 2). 21% of individuals use oral antineoplastic drugs (with a doctor's recommendation (68%), with their request (31%) have left.

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Table 2. Status of drug use by individuals			
Features		n	%
Same Time/ Everyday	Yes	29	29
	No	71	71
Causes not to use the drug as recommended	Forgetfulness	51	51
	Neglect	44	44
	Side effects of the drug	14	14
Drug withdrawal cases during cure	Yes	21	21
	No	79	79
Causes of drug withdrawal *(n=21)	Doctor with proposal	15	68,2
	With own request	6	31,8
When the drug is forgotten to take*(n=51)	I get when I remember	30	58,8
	I get two at the next dose	14	27,5
	Continue my normal dose schedule	7	13,7
* The question was given more than one answer, Percentages over "n"			

81% of the patients stated that they received help with oral antineoplastic drug use. The patients mostly received help from their children (59.8%) and about drug time (44.4%). When the information of individuals about the drug examined; 93% of patients know how many times a day the drug will be used, 90% of patients know how often to go to control, and 75% of patients know the expected side effects of the drug. On the other hand, only 1% of patients know how to manage the expected side effects of the drug, and Only 3% of the patients know what to do when the drug vomited.

In our study, men are more successful than women at the same time ($p<0.05$), and the use of drugs increased at the same time as the education level of the patients increased ($p<0.05$). This study suggests the patients who received only verbal information had lower rates of drug use at the same time' than those who received oral and written information ($p<0.05$). In the statistical analysis, no significant difference found between age and number of cures and usage at the same time ($p>0.05$). As the level of education in the patients decreased, getting help in the use of drugs increased. Besides, participations who receive oral information about drug use receive more help in drug use ($p<0.05$), and the age of the individual's increases and the women have forgotten to take more drugs. Also, patients receiving oral information about drug use seem to have forgotten to take more drugs ($p<0.05$)(Table3).

Table 3. According to age, gender, educational status, number of cures and the way of taking information at the same time taking medication, taking medication use and taking medication						
Feature	Same Time/ Everyday		Getting help		Forgetfulness	
Age	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n(%)
39-47	5(17,2)	7(9,8)	6(7,4)	6(31,6)	-	12 (24,5)
48-56	13(44,8)	32(45)	39 (48,1)	6(31,6)	22 (43,1)	23(47)
57-65	11(37,9)	32(45)	36(44,1)	7(36,8)	29(56,9)	14(28,5)
Test value	p:0.063/X2: 7.394		p:0,082/ X2:2,488		p:0,001/ X2:7,248	
Gender	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n(%)
Female	12(41,3)	41(57,7)	44(54,3)	9(47,3)	45(88,2)	8(16,3)
Male	17(58,6)	30 (42,2)	37 (45,6)	10 (52,6)	6(17,8)	41(83,7)
Test value	p:0,001/ X2:4.04		p:0,061/ X2:5,870		p:0,003/ X25,482	
Educational status	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n(%)
Primary school	12(41,3)	41(57,7)	47(58)	6 (31,5)	23 (45)	30 (61,2)
Middle School	10(34,4)	26(36,3)	30(37)	6 (31,5)	20 (39,3)	16(32,7)
High school	7 (24,1)	4(5,6)	4(4,9)	7 (36,8)	8 (15,7)	3 (6,1)
Test value	p:0,002/ X2:4.209		p:0.000/ X2: 5,744		p:0.067/ X2:4.592	
Informed about drug	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n(%)
Verbal	19 (65,5)	52 (73,2)	69 (85,2)	2 (10,6)	45 (88,2)	26 (53)
Verbal-written	10 (34,4)	19 (26,7)	12 (14,8)	17 (89,4)	6 (11,8)	23 (47)
Test value	p:0,044/ X2:5.286		p:0,002/ X2: 4,764		p:0,000/ X2:3,499	
Cure	Yes n (%)	No n (%)			Yes n (%)	No n(%)
0-3 cure	18 (62)	33 (46,4)			22 (43,1)	29(59,2)
4-7 cure	10 (34,4)	37 (52,1)			28 (54,9)	19 (38,8)
8-14 cure	1 (3,4)	1 (1,4)			1(2)	1 (2)
Test value	p: 0,073/ X2:5,286				p:0.094/ X2:7,333	
Chi-square test						

Discussion

Most of the individuals who participated in the study used antiemetic and antacid besides oral antineoplastic drug. It is also noteworthy that patients do not know about drug interaction. In the studies recommended that oral antineoplastic drugs be taken 2 hours before or after antacid intake [11-12]. Nausea and vomiting were the most common side effects, and individuals had a lack of knowledge in managing nausea and vomiting. More recently, studies showed counselling on issues such as how long the oral antineoplastic drug should repeat after vomited and how to remove waste [12,13].

Decker et al. in his study with oral antineoplastic drug cancer patients, statistically significant relationship found between symptom management and drug compliance [14]. Similarly, in a study of the factors affecting the compliance of oral chemotherapy drugs in patients with colon cancer, it was found that the symptoms affected drug compliance [15]. Most of the individuals in our study does not record the onset, severity, and duration of the related side effects. When literature is reviewed, it recommends that individuals record this information and inform the medical team [4,5,9,12,16].

Most of the patients received drug training verbally. Studies have shown that oral administration of drug education is insufficient. Thus, drug education should support by many methods such as written material, electronic follow-up system at home, reminders, message tracking, telephone consultancy and follow-up [5,6,8,17].

In our study, very few of the patients used the name of the oral antineoplastic drug correctly. Moreover, most of the patients have identified their medicine only with colour, shape, and box. At the same time, most of the patients expressed their medication as mgr but not as tablet number. As is known, oral antineoplastic drugs have many forms in different milligrams. Therefore, it should include in the follow-up of drug doses in drug education. According to studies that the drug use guidelines contain mgr does the information of the drugs [10,12,13].

In contrast to our study; Marques et al. (2008) reported that 86.9% of the individuals know the name and dose of the drug correctly. We think that this situation originates most of the patients have a high education level (80.4%)[18]. On the other hand, caregivers of cancer patients have been experiencing difficulties in knowing the side effects of treatment, symptom control, the sources they can refer to, mgr drugs [19,20].

This study suggests that most of the patients received help from their relatives about drug time, cure program and drug dose. Similarly, in the literature, it is seen that cancer patients receive help from caregivers on many issues such as drug use [21,22]. In our study, patients who received both verbal and written information were more successful in using drugs at the same time ($p<0.05$). Studies have shown that drug education train with written and visual materials and the patient needs to use the right medication [7,12]. In this study, the rate of drug forgets increases as individuals' ages increase ($p<0.05$). Similarly, in many studies, it was found that the most common behaviour of drug use was seen in the elderly group [23,24].

Unlike our study, Marques et al. found that the rate of forgetting of individuals was 6.6%. The reason for the difference in the study may think to be that most of the individuals were graduated from university (80.4%) [18]. When the patients forget their drugs, most of the patients often take the drug when recalled or take two drugs at the next dose. Chan et al. found that 38.8% of the patients in the study with 126 cancer patients jumped the drug when they forgot to take the drug, 46.6% of them took two at the next dose time. [25].

Conclusion

Individuals who participated in the study had side effects due to oral antineoplastic drug and Patients experience difficulty in recording, monitoring and managing side effects. Patients have comorbidity and polypharmacy.

Suggestions

• According to the education, age, and duration of drug use of cancer patients using oral antineoplastic drugs, drug training should be given by using written and visual materials.

• In oncology outpatient clinics and outpatient chemotherapy units, regular drug education should train to the patients, and the patients should monitor when they come to each control.

Study Limitations

The most important limitation of the study is that the drug use ınformatıon base on the patient declaration. Besides, there are several potential problems related to reliability because the patient does may include a self-reporting response bias or may have been not reported correctly.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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Original Article

The relationship between serum endocan levels with the presence of contrast-induced nephropathy in patients undergoing coronary angiography

Koroner anjiyografi uygulanan hastalarda serum endokan düzeyleri ile kontrast kaynaklı nefropati varlığı arasındaki ilişki

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Abstract

Aim: Contrast-induced nephropathy (CIN) is associated high mortality and morbidity risks in the patients undergoing coronary angiography (CAG).Endocan, a new endothelial dysfunction biomarker, could be a potential immunoinflammatory biomarker for CIN.We investigated the possible association between serum endocan levels and CIN in the patients undergoing CAG.

Material and Methods: We prospectively enrolled 92 patients undergoing CAG.For each patient, serum endocan levels were assessed at hospital admission before CAG.Contrast-induced nephropathy was defined as an increase in serum creatinine 25% or 0.5 mg/dl from baseline in the first 48 - 72 hours.

Results: Overall, 32 cases (34.8%) of CIN were diagnosed.There were no significant differences between the two groups (CIN and without-CIN) in demographic data and general risk factors. 38 patients (41%) were performed percutaneous coronary intervention. Patients with CIN had higher serum endocan levels (3.68 ng/dl;IQR, 0.78-17.3 vs 1.81 ng/dl;IQR, 0.19-17.4, p:0,002) than patients without CIN. Additionaly; basal glomerular filtration rate, contrast volume, serum endocan level and left ventricle ejection fraction were detected as independent risk factors of CIN (p= 0.014, B:0.94, CI: 0.89-0.98, p= 0.024, B:2.55, CI:1.13-5.77, p= 0.026, B:2.45, CI:1.11-5.42, p= 0.044, B:0.91, CI:0.83-1.43, respectively).

Conclusion: In patients undergoing CAG, high serum endocan levels could be associated with an increased risk for CIN.

Keywords: endocan; contrast-induced nephropathy; endothelial dysfunction.

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ÖZ

Amaç: Kontrast kaynaklı nefropati (KİN), koroner anjiyografi (KAG) uygulanan hastalarda yüksek mortalite ve morbidite ile ilişkilidir. Yeni bir endotelyal disfonksiyon biyomarkeri olan Endocan, KİN için potansiyel bir immünoenflamatuar biyobelirteç olabilir. KAG uygulanan hastalarda, serum endokan düzeyleri ile KİN arasındaki olası ilişkinin araştırılması amaçlandı.

Gereç ve Yöntemler: KAG yapılan 92 hasta çalışmaya alındı. KAG öncesinde, hastane başvurusunda her hastanın serum endokan düzeyleri değerlendirildi. Kontrast kaynaklı nefropati, maruziyetten 48-72 saat sonrasındaki kreatinin düzeyinin başlangıç serum kreatinin düzeyine göre % 25 veya 0.5 mg / dl artış olması olarak tanımlandı.

Bulgular: Toplam 32 hastada (%34.8) KİN saptandı. KİN olan ve olmayan 2 grup arasında demografik veriler ve genel risk faktörleri açısından anlamlı fark saptanmadı.38 hastaya (%41) perkutanöz koroner girişim yapıldı. KİN saptanan hastalarda serum endokan düzeyleri (3.68 ng/dl;IQR, 0.78-17.3 karşı 1.81 ng/dl;IQR, 0.19-17.4, p: 0,002) KİN olmayan hastalara göre daha yüksek bulundu. Ek olarak; bazal glomerüler filtrasyon hızı, kontrast volümü, serum endokan ve sol ventrikül ejeksiyon fraksiyonu KİN için bağımsız risk faktörü olarak saptandı (p= 0.014, B: 0.94, CI: 0.89-0.98, p= 0.024, B: 2.55, CI: 1.13-5.77, p= 0.026, B: 2.45, CI: 1.11-5.42, p= 0.044, B: 0.91, CI: 0.83-1.43, sırasıyla).

Sonuç: KAG yapılan hastalarda, yüksek serum endokan seviyeleri KİN oluşma riski ile ilişkili olabilir.

Anahtar kelimeler: endokan; kontrast ilişkili nefropati; endotelyal disfonksiyon.

Introduction

It was known that coronary angiography (CAG) and percutaneous coronary intervention reduce ischemic complications and improves survival in patients with coronary artery disease (CAD). However, contrast agents used for performing cardiovascular interventions are potential risks for contrast-induced nephropathy (CIN). CIN could cause renal dysfunction, longer hospital stay, increased cardiovascular events and mortality [1]. So many factors such as hypovolemia, contrast volume, some drugs (diuretics etc.) and baseline glomerular filtration rate (GFR) may contribute to the development of CIN [2]. Because of these, identifying the risk of CIN is important in patients performed CAG.

First study about Endocan was in 1996 [3]. It was cloned from human umbilical vein endothelial cell cDNA library. Endocan is a proteoglycan and produced from vascular endothelial cells (ECs) and plays as a regulator role in vascular proliferation, migration and adhesion processes [4]. Endocan has shown as a novel mediator for ECs dysfunction and inflammation in the previous studies [5,6]. Additionally, it was found to associate with cardiovascular diseases [7,8], cancer [9], sepsis [10], chronic kidney disease [11,12] and acute rejection of renal transplantation [5].

Oxidative stress, endothelial dysfunction, and apoptosis were described as pathophysiologic mechanisms for the development of acute kidney injury due to contrast administration [13]. Additionaly, previous studies have shown that endocan is a potential immunoinflammatory marker that may be linked to CIN and is highly expressed in glomeruli, and especially increases by glomerular damage and by the deterioration of glomerular filtration rate, its clearance decreases and its levels raise to higher extents [12,14].

According to these pathological mechanisms, testing novel biomarkers in the patients undergoing CAG may help determination of potential risks for acute kidney injury and may reduce the development of CIN. Therefore, we aimed to evaluate the relationship between serum endocan levels and the risk of CIN in the patients undergoing CAG.

Methods

We prospectively observed 92 consecutive patients undergoing CAG at the Cardiology Department. CAD was defined according to the current guidelines [15]. According to power analysis based on these data (alpha 0.05, power 95%), minumum a total of 87 patients were planned to be included in the study. We excluded the patients with a severe valvular heart disease, severe or decompensated heart failure, acute coronary syndromes, end stage kidney disease, severe liver disease, connective tissue disease and patients undergoing urgent cardiac surgery for revascularization. We

included the patients with angina pectoris who had positive stress test (exercise ECG, myocardial perfusion imaging or stress echocardiography). Serum creatinine concentration levels were observed at hospital admission, every following day and at hospital discharge. Glomerular filtration rate (eGFR) was calculated using the modified formula of Levey et al [16]. Contrast-induced nephropathy was defined as an increase in creatinine 25% or 0.5 mg/dl from the baseline value within the 48- 72 hour period following CAG [17]. In all patients, serum endocan levels were assessed at hospital admission. Endocan (Cloud-Clone Corp., Houston, USA), concentrations in patients' sera were analyzed using sandwich enzyme-linked immunosorbent assays (ELISA) according to the manufacturer's instructions. Values were normalized to standard curve. The intra-assay and interassay variances for serum endocan was <10% and <12%, respectively. A nonionic, low-osmolality contrast agent (iopromide) was used for performing CAG. In the cases who had heart failure and chronic kidney disease, for preventing the development of CIN, saline infusion (intravenously at a rate of 1 mL/(kg h) (0.5 mL/[kg h]) was applied during the periprocedural period. Also, in these cases, for preventing the development of CIN, the use of the nephrotoxic drugs such as non-steroid anti-inflammatory drugs, metformin, angiotensin converting enzyme inhibitors, angiotensin receptor blockers and diuretics were stopped at least 48 hours prior to the procedure. Transthoracic echocardiography was performed for all patients (Epiq 7; Philips Ultrason System, Amsterdam, Netherlands) and left ventricle ejection fraction (LVEF) was measured using the Simpson method.

Hypertension [16] was defined as blood pressure> 140/90 mm Hg or being on treatment with antihypertensive medications. Also, diabetes mellitus (DM) was defined as fasting glucose levels >126 mg/dL or being on treatment with oral antidiabetic drugs or insulin. Finally, hyperlipidemia (HL) was defined by the references of the current guidelines [18]. The study was approved by the Local Ethics Committee (2015.096.IRB.036) and informed consent was taken from all participants. This article does not contain any studies with human participants or animals performed by any of the authors.

Statistical analysis

The statistical analysis was performed by using SPSS version 22 for Windows (SPSS Inc, Chicago, Illinois). Numerical variables were expressed as mean (standard deviation) (SD) and nominals as percentages. All variables were evaluated by Kolmogorov Smirnov Test to determine the normality of distribution. Parametric variables were compared using the Student-T test. The Mann Whitney U-test was used for the evaluation of nonparametric variables. The chi-square test was used to compare categorical data. Correlations were studied by the Pearson's correlation test. ROC analysis was performed to determine the sensitivity and specificity values of serum endocan. To evaluate the effects of various factors on CIN development, multivariate regression analyses were performed by using the backward Logistic Regression method. All p values less than 0.05 were accepted as statistically significant.

Results

92 patients were included in this study and 32 (34.8%) of them had CIN. There were no significant differences between the two groups in terms of age and gender. General risk factors, hypertension, diabetes mellitus, previous history of CAD, smoking and family history of CAD were same in both groups. Additionally, previous medications, contrast volume and coronary angiography findings did not differ between two groups. Only, GFR basal and LVEF were significantly lower in patients with CIN. Additionaly, C-reactive protein (CRP) was higher in patients with CIN. The baseline clinical and procedural characteristics of patients were shown in Table 1. Patients with CIN had higher admission serum endocan levels (3.68 ng/dl; IQR, 0.78-17.3 vs 1.81 ng/dl; IQR, 0.19-17.4, p:0,002) than patients without CIN (Figure 1). Additionally, log10 endocan parameters (0.58 ± 0.38 ng/dl vs 0.27 ± 0.44 ng/dl, p:0,001) were found higher in the patients with CIN than patients without CIN.

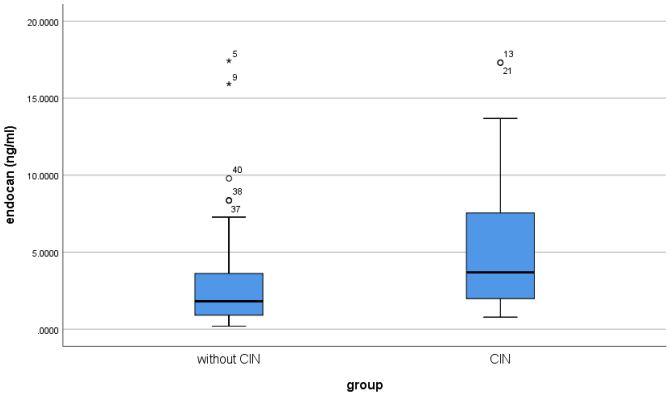

Figure 1. Serum endocan levels with and without CIN patients.

{Values more than three IQR's from the end of the box are labeled as extreme, denoted with an asterisk (*). Values more than 1.5 IQR's but less than 3 IQR's from the end of the box are labeled as outliers (<)}.

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Table 1. Baseline and laboratory characteristics of the study population.			
Clinical characteristics	CIN group (n=32)	Non-CIN group (n=60)	p
Age (years)	69.3 ± 9.4	66.3 ± 6.7	0.074≠
Gender (Male/Female)	75/25	62/38	0.250¶
Hypertension (%)	81	68	0.224¶
Diabetes Mellitus (%)	56	35	0.076¶
Family history of CAD (%)	40	28	0.251¶
Previous history of CAD (%)	34	23	0.257¶
Smoking (%)	50	38	0.376¶
Previous medication			
Angiotensin-converting-enzyme inhibitors (%)	28	21	0.489¶
Angiotensin II receptor blockers (%)	37	20	0.129¶
Calcium canal blockers (%)	40	32	0.390¶
Beta-blockers (%)	53	40	0.228¶
Diuretics (%)	18	10	0.142¶
Alpha-blockers (%)	12	13	0.910¶
Nitrates (%)	10	5	0.418¶
Lipid lowering drugs (%)	50	35	0.162¶
Antiaggregant treatment (%)	50	33	0.119¶
Metformin (%)	25	15	0.239¶
Other oral antidiabetics (%)	34	27	0.439¶
Insulin (%)	18	7	0.076¶
Coronary angiography findings			
Number of patients with obstructed coronary arteries (>%50)	18	28	0.381¶
Number of patients without obstructed coronary arteries (<%50)	9	21	0.409¶
Number of patients with normal coronary arteries (n)	5	11	0.744¶
Obstructed arteries (n)	2 (0-3)	2 (0-3)	0.426*
Left main coronary artery obstruction percentage (%)	0 (0-60)	0 (0-60)	0.458*
Left anterior decending artery obstruction percentage (%)	80 (0-100)	70 (0-100)	0.088*
Circumflex artery obstruction percentage (%)	60 (0-100)	55 (0-100)	0.806*
Right coronary artery obstruction percentage (%)	80 (0-100)	40 (0-100)	0.184*
Coronary stent implantation (%)	47	38	0.507¶
Coronary bypass surgery (n, patient)	3	5	0.344¶
Laboratory and echocardiographic findings			
Left ventricle ejection fraction (%)	51.2 ± 10.7	56.5 ± 8.1	0.011≠
Fasting glucose (mg/dl)	137.6 ± 55.8	123.7 ± 30.3	0.155≠
BUN basal (mg/dl)	29.9 ± 16.7	21.8 ± 10.0	0.005≠
Creatinine basal (mg/dl)	1.21 ± 0.3	1.09 ± 0.3	0.045≠
GFR basal (ml/dk/1.73m2)	57.7 ± 19.3	67.0 ± 16.1	0.016≠
Contrast volume $ (ml)	170 (25-600)	127.5 (40-600)	0.218*
BUN (post contrast) (mg/dl)	39 ± 21.5	21.3 ± 8.7	<0.001≠
Creatinine (post contrast) (mg/dl)	2.01 ± 1.0	1.13 ± 0.3	<0.001≠
GFR (post contrast) (ml/dk/1.73m2)	37.6 ± 16.8	65.4 ± 16.9	<0.001≠
Sodium (mmol/l)	139.9 ± 3.7	140.9 ± 3.3	0.172≠
Potassium (mmol/l)	4.3 ± 0.4	4.4 ± 0.5	0.367≠
Uric acid (mg/dl)	7.06 ± 2.23	7.09 ± 1.92	0.950≠
C-reactive protein (mg/l)	16.1 ± 16.5	8.8 ± 8.2	0.026≠
Hemoglobin (g/dl)	12.2 ± 2.1	13.0 ± 2.1	0.125≠
Leukocytes (K/ul)	7.0 (4.2-10.2)	7.4 (4.2-10.7)	0.448*
Serum endocan (ng/ml)	3.68 (0.78-17.3)	1.81 (0.19-17.4)	0.002*
Log10endocan	0.58 ± 0.38	0.27 ± 0.44	0.001≠

NS indicates non-significant; BUN, blood urea nitrogen; CAD, coronary artery disease; CIN, Contrast induced nephropathy; GFR, glomerular filtration rate; $ iopromid (0.769 g/ml).
The median (interquartile range) or frequency counts (percentages)' as appropriate.
≠ t test; *Mann-Whitney U test; ¶ Chi-square test

In Pearson correlation analysis, CRP levels correlated positively with uric acid (r = 0.44, p < 0.0005). Also, serum endocan concentrations correlated negatively only with serum sodium (r = - 0.30, p = 0.004).

In ROC analysis, the cut-off value of endocan for CIN patients in this study was > 3.04 ng/ml, with 60% sensitivity, 40% specificity (AUC: 0.70, 95% CI: 0.59-0.81, p=0.002) (Figure 2). There were 19 (59%) patients in CIN group and 22 patients (36%) in nonCIN group whose serum endocan levels were exceeding the standard upper value of 3.04 ng/ml.

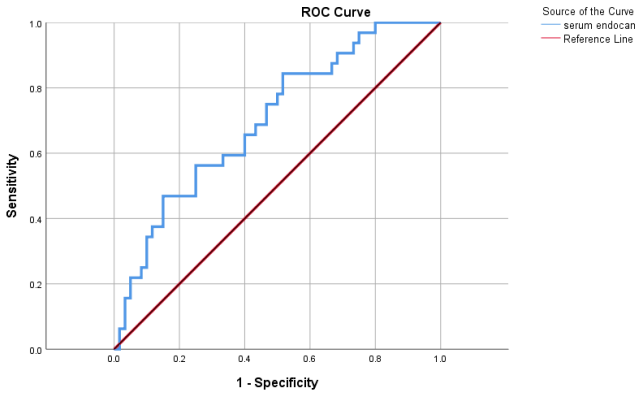
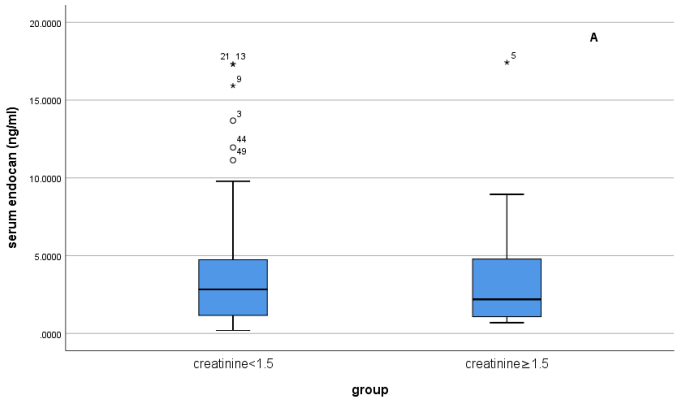


Figure 2. ROC curve analysis for values of serum endocan [3.04 ng/ml, with 60% sensitivity, 40% specificity (AUC: 0.70, 95% CI: 0.59-0.81, p=0.002)].

To analyze the associations of endocan with the potential confounder of creatinine, the study participants were divided into two groups according to creatinine<1.5 mg/dl and creatinine ≥ 1.5 mg/dl. Serum endocan levels did not differ between the creatinine<1.5 mg/dl and creatinine ≥ 1.5 mg/dl groups (2.83 ng/ml; IQR, 0.19-17.31 ng/ml vs 2.19 ng/ml; IQR, 0.68-17.40 ng/ml, p = 0.862) (Figure 3A). Additionally, serum endocan levels were analyzed in the patients with presence or absence of obstructed coronary arteries (>%50). There was not any differences between these groups (2.81 ng/ml; IQR, 0.68-17.40 ng/ml vs 2.84 ng/ml; IQR, 0.19-17.31 ng/ml, p = 0.160) (Figure 3B).



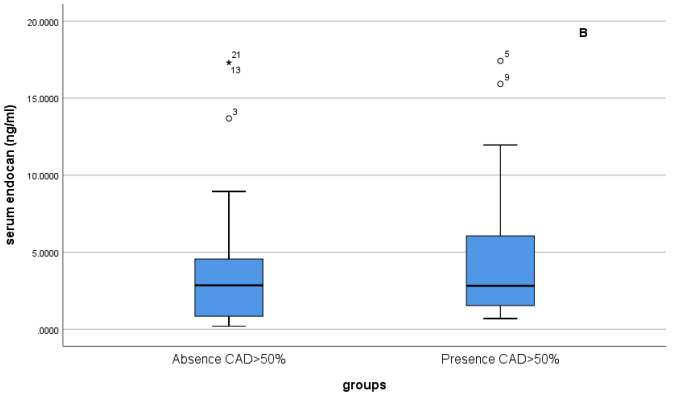


Figure 3. A) Serum endocan levels according to creatinine levels (creatinine <1.5 mg/dl compared to creatinine ≥1.5 mg/dl). **B)** Serum endocan levels according to presence or absence of obstructed coronary arteries (>%50).

{Values more than three IQR's from the end of the box are labeled as extreme, denoted with an asterisk (*). Values more than 1.5 IQR's but less than 3 IQR's from the end of the box are labeled as outliers (<)}.

Additionaly; basal GFR (p= 0.014), contrast volume (p= 0.024), serum endocan level (p= 0.026) and LVEF (p= 0.044) were detected as independent risk factors of CIN in logistic regression analysis (r2= 0.66, p= 0.00, odds ratio= 0.554 for model) (Table 2).

Table 2. The contrast induced nephropathy associated with variables according to binary stepwise logistic regression.

Variables	Logistic regression analysis Method: Backward stepwise (R2: 0.66, p: 0.00)		
	Exp (B)	% 95 CI	p
Hypertension	0.36	0.01-9.91	0.550
Uric acid	0.89	0.55-1.44	0.654
C-reactive protein	0.94	0.86-1.03	0.221
Left ventricle ejection fraction	0.91	0.83-0.99	0.044
Glomerular filtration rate (basal)	0.94	0.89-0.98	0.014
Contrast volume	2.55	1.13-5.77	0.024
Endocan	2.45	1.11-5.42	0.026

CI, confidence intervals.

4 patients from the contrast induced nephropathy group needed HD. Only one time HD was performed for these patients. Hydration therapy was applied to the other patients. All of the patients with CIN healed and their renal function came back to the previous values.

Discussion

CIN is a common cause of hospital acquired acute kidney injury. Because of CIN effects on morbidity and mortality, identifying the risk of CIN is important. Some conditions such as previous history of CAD, diabetes, dehydration, advanged age, use of diuretics, repeated contrast exposure, use of high osmolar contrast agent are related with CIN development [19]. After the contrast exposure, endothelial dysfunction and deterioration in the balance of the vasoconstrictor and vasodilator factors could cause renal hypoxia and injury [20].

In the general population, the incidence of CIN is estimated to be 1% to 6%. However, the risk may be as high as 50% in some patient subgroups (diabetes, chronic kidney disease, other comorbidities) [21]. In this study, 32 patients (34.8%) had CIN. This finding might be related with lower basal GFR and LVEF values than non-CIN group .

In our study, we found that CIN rate was significantly increased in patients with high endocan levels and also demonstrated that the endocan levels were independently associated with CIN. Endocan is also a useful biomarker for evaluation of renal injury. Gunay et al. showed high endocan levels in patients with acute kidney injury [22]. In addition, serum endocan levels were found inversely correlated with estimated GFR [14]. Yılmaz et al. reported that raised endocan levels could predict all-cause mortality and cardiovascular events in patients with chronic kidney disease [12]. Li et al. reported in the renal transplantation patients that serum level of endocan signifies the degree of endothelial cell injury and it has the potential to show glomerular/endothelial cell injury as a highly sensitive and specific biomarker [23]. Therefore, evaluation of serum endocan levels may help the clinicians for the early detection of CIN.

The amount and the type of the contrast volume is important for the patients undergoing coronary angiography because of the CIN risk, especially if these patients had chronic kidney disease [24]. Thus, contrast agent dose optimization and periprocedural hydration are very important. Therefore, we tried to use a relatively small amount of contrast in this study, and the dose of contrast used was not found different between the patients with and without CIN [25]. However, according to logistic regression analysis diabetes mellitus, contrast volume, serum endocan level and LVEF were independent risk factors of CIN in this study. Serum endocan levels may be a possible significant biomarker for development of CIN together with the known risk factors in this study. High serum endocan levels detected in this study could reflect endothelial dysfunction which is associated with inflammation. Serum endocan levels can be measured easily at the preprocedural period and intravenous hydration, sodium bicarbonate, and N-acetylcysteine for prophylactic prevention of CIN may be applied before the procedure. Thus, in comparison to other available CIN risk stratification tools, serum endocan evaluation is a simple test and therefore may be easily applied to the daily practice.

This study had some limitations. First, it was a single-center study. Second, this study's cohort was relatively small. Third, neither serum endocan levels nor urine endocan levels were not evaluated after the procedure.

Conclusion

Serum endocan levels could be associated with a increased risk for CIN in the patients undergoing CAD and it can be used as a new, simple, and reliable test to predict CIN in patients who underwent urgent CAG.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

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Original Article

The evaluation of ventricular arrhythmia risk by using electrocardiographic parameters in patients with dipper and non-dipper hypertension

Dipper ve nondipper hipertansiyonda ventriküler aritmi riskinin elektrokardiyografik parametreler üzerinden değerlendirilmesi

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Abstract

Aim: Non-dipper hypertension (NDHT) is associated with increased cardiovascular mortality. Lots of different electrocardiographic parameters can be used for this purpose. Some electrocardiographic repolarization parameters and some particular parameters obtained from 24 hours holter recordings frequently were used. The aim of this study was to evaluate ventricular arrhythmia risk by using most of this electrocardiographic parameters in patients with dipper hypertension (DHT) and NDHT.

Material and methods: 220 patients with hypertension were included this study. Patients were divided into two groups as DHT and NDHT according to the 24 hours ambulatory blood pressure monitoring. Two groups were compared with electrocardiography and echocardiography parameters and also were compared with heart rate variability (HRV) and heart rate turbulence (HRT) parameters.

Results: There were no significant differences between DHT and NDHT groups with regard to demographic and laboratory datas. Also echocardiography parameters normally distributed and have no significant differences between two groups. There were no significant differences between DHT and NDHT groups with regard to left ventricular mass index (p=0.280). Although QT, QT dispersion, HRV and HRT parameters differences were not statistically significant , results were in favour of DHT in terms of ventricular arrhythmia risk.

Conclusion: When hypertensive patients having no statistically significant differences in terms of left ventricular diamaters and left ventricular mass between them were divided as DHT and NDHT; there were no statistically significant differences between two groups with regard to electrocardiographic ventricular arrhythmia parameters although results were in favour of DHT.

Keywords: hypertension; dipper; non-dipper; ventricular arrythmia parameters

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Öz

Amaç: Non-dipper hipertansiyon (NDHT) artmış kardiyovasküler mortalite ve morbidite ile ilişkilidir. Çeşitli çalışmalar çok sayıda farklı elektrokardiyografik parametrenin bu amaçla kullanılabileceğini göstermektedir. Özellikle bazı elektrokardiyografik repolarizasyon parametreleri ve 24 saatlik holter kayıtlarından elde edilen bazı özel parametreler sıklıkla kullanılmıştır. Bu çalışmada amaç dipper hipertansiyonlu (DHT) ve NDHT hastalarda ventriküler aritmi riskinin bu elektrokadiyografik parametrelerin çoğunun birlikte kullanılarak değerlendirilmesidir.

Gereç ve Yöntemler: Çalışmaya esansiyel hipertansiyon tanısıyla izlenen 220 hasta alındı. Hastalar 24 saatlik ambulatuvar kan basıncı izlemesi sonuçlarına göre iki grupta değerlendirildi. Sistolik ve/veya diyastolik kan basıncı gece değerleri ortalaması gündüz değerleri ortalamasından %10 veya daha fazla düşük olanlar DHT grubuna, %10'dan az düşük olanlar NDHT grubuna alındı. İki grubun kan basıncı, ekokardiyografi, laboratuar verileri, EKG ve 24 saatlik ritim holter kaydından elde edilen kalp hızı değişkenliği (KHD) ve kalp hızı türbülansı (KHT) verileri karşılaştırıldı.

Bulgular: Demografik bulgular, laboratuar verileri ve ekokardiyografik veriler normal dağılıma uymakta idi ve gruplar arasında anlamlı fark yoktu. Her iki grup arasında sol ventrikül kitle indeksi açısından fark saptanmadı (p=0,280). QT, QT dispersiyonu, KHD, KHT parametrelerinde de istatistiksel anlamlı fark tespit edilememesine rağmen ventriküler aritmi riski açısından verilerin DHT lehine olduğu görüldü. Ayrıca NDHT' da otonom fonksiyonlarda sempatik sistem lehine baskınlığı teyit edecek şekilde ortalama kalp hızı istatistiksel olarak anlamlı olacak şekilde daha yüksek bulundu.

Sonuç: Sol ventrikül çapları ve kitleleri bakımından aralarında anlamlı fark olmayan hipertansif hastalar, dipper ve non-dipper olarak ayrıldığında elektrokardiyografik ventriküler aritmi öngördürücüleri bakımından veriler iki grup arasında dipper lehine olmasına karşın bu fark istatistiksel olarak anlamlı düzeye ulaşmamıştır.

Anahtar kelimeler: hipertansiyon; dipper; non-dipper; ventriküler aritmi parametreleri

Introduction

Cardiovascular diseases (CVD) are seen as the primary cause of death in the world. Hypertension (HT) is one of the main causes of CVDs and an important risk factor for sudden cardiac death. The incidence of sudden cardiac death increases with elevated blood pressure (BP) in parallel with BP values [1]. There is a strong relationship between the systolic BP and diastolic BP and the cardiovascular (CV) risk. HT is responsible for 45% of heart disease-related deaths and 51% of stroke-related deaths [2]. There are studies showing that the frequency of ventricular arrhythmia and consequently the risk of sudden death increases in patients with HT. However, there are limited data on which HT patients have a higher tendency to ventricular arrhythmia.

It has been shown that BP levels obtained by ambulatory measurement are more valuable in predicting HT complications and CV morbidity when compared with BP levels measured in the office [3]. BP changes with circadian rhythm during the day. Studies have shown that BP shows a nocturnal decline in healthy individuals. The rate of this decline varies from person to person. According to ambulatory blood pressure monitoring (ABPM) data obtained from healthy individuals, BP is highest in the morning, shows a slow decrease during the day, and remains at its lowest levels during the night [4]. The circadian rhythm of BP has led to the development of a new classification which is made by ABPM. A decrease in BP of ≥ 10% when compared to daytime was defined as dipper hypertension (DHT) and a < 10% decrease as non-dipper hypertension (NDHT).

In our study, we separated HT patients as DHT and NDHT. Our aim was to determine which group had a higher risk of ventricular arrhythmia and sudden cardiac death and whether this classification is associated with the risk of arrhythmia by using ventricular arrhythmia parameters.

Material and Methods

Our study included 220 HT patients. They rested for at least five minutes before measuring tension. They were seated with their feet on the ground. Their arm was supported by bringing it to the heart level. The cuff of the sphygmomanometer was placed 2.5-3 cm above the bend of their elbows wrapping at least 80% of their arms and the measurement was performed. It was repeated at least ten minutes later. A blood pressure of ≥ 140/90 mmHg at each measurement was diagnosed as HT. Cases with and suspected to have secondary HT were excluded from the study. The exclusion criteria for all groups were non-reliable T-waves on the electrocardiograhpy (ECG), atrial fibrillation, bundle branch block, moderate or severe valvular heart diseases, thyroid disorders, cardiomyopathies,

congenital heart diseases, malignancy, pulmonary HT, electrolyte disturbances, acute coronary syndromes, heart failure, history of myocardial infarction, history of coronary artery bypass grafting, implanted permanent pacemaker, and left ventricular segmental wall-motion defects in the echocardiographic exam. The local ethics committee approval and informed consent from all patients were obtained (Tokat Gaziosmanpasa University ethics committee with project number 14-KAEK-208). All people included in the study signed the informed consent form.

Electrocardiographic examination

A 12-lead superficial ECG was recorded from all patients. 12-lead electrocardiography was performed in a supine position at a rate of 25 mm/sec and an amplitude of 10 mm/mV after 20 minutes of rest (Cardiofax V; Nihon Kohden Corp., Tokyo, Japan). The ECG images of the patients were scanned and examined at a magnification of 400% using the Adobe Photoshop software. The RR distance from the DII lead was calculated.

QT times for each derivation were measured separately. QTcs were calculated by using the Bazet formula. QTc dispersion was calculated. Tp-e times were also calculated from leads V2 and V5. QTc/Tp-e times were calculated. Each measurement was repeated at least twice by two separate researchers and the means of the data were used.

Ambulatory blood pressure monitoring

ABPM was performed using a noninvasive recording system. The device (SunTechAccuwin ProV3) was programmed to perform the measurement for 24 hours, every 30 minutes during the day (07.00-22.00) and every 60 minutes at night (22.00-07.00). The mean levels of ≥ 10% of the daytime levels were in the DHT group and those of <10% were in the NDHT group.

24-hour ECG Holter recording

24-hour holter, a non-invasive recording of the electrocardiogram, was performed using a device with a three-channel analog recording system. The device's software was used to calculate the parameters. Ambulatory ECG values were measured by digital recording on a flashcard using a DL 700 Digital Holter recorder (Ela medical SyneScope V3.10). The minimum and maximum distances between the heart rate variability (HRV), heart rate turbulence (HRT), lowest and highest heart rate values, and the consecutive R waves were calculated by the 24-hour ECG Holter recording.

The same recording device (Ela medical SyneScope V3.10) was used to calculate the HRV. We made the time-domain analysis of the HRV as follows: We obtained the average heart rate for 24 hours and for the day- and night-time separately. We used the ratio of the number of intervals to the total number of R-Rs (pNN50) where the difference between the consecutive R-R intervals was over 50 milliseconds. We used the ratio of the number of intervals to the total number of R-Rs (pNN30) where the difference between the consecutive R-R intervals was over 30 milliseconds. We used the arithmetic mean (RMSSD) of the square root of the difference between consecutive R-R intervals. We obtained the standard deviation (SDNN) of the time (R-R interval) between consecutive normal QRS complexes. For 24 hours, we used the standard deviation (SDANN) and the variability index (VarIndex) of the average R-R intervals of five-minute recordings.

The total power (TP) (<0.4 Hz) obtained from the 24-hour recordings by frequency-domain method, the lowest frequency (VLF) (0.003-0.04 Hz), the low frequency (LF) (0.04-0.15 Hz), high frequency (HF) (0.15-0.40 Hz) and, normalized (nu) equivalents of these values were evaluated. These variables were digitized using power spectral curves and expressed as Ln (ms2/Hz). LF/HF ratio was determined. All measurements were made according to the recommendations of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [5].

Using ventricular premature beats that met the eligibility criteria for HRT measurement, turbulence onset (TO) and turbulence slope (TS) values were automatically calculated from the Holter recording by the software program (HRT View Version 0.60-0.1). TO indicating an early acceleration phase was measured as follows: the two sinus rhythm lengths measured immediately prior to the ventricular premature beats were subtracted from the sum of the two sinus rhythm lengths measured after the ventricular premature beats. The result was divided into two sinus rhythms measured before the ventricular premature beat and expressed as a percentage (%). TS showing late deceleration was calculated by determining the length of the five most sloping sinus cycles in 20 sinus cycles measured after ventricular premature beat and expressed in milliseconds. Levels <0% were considered normal for TO, and > 2.5 ms/RR for TS. Turbulence loss was accepted as an increase in TO and a decrease in TS.

Echocardiographic examination

All echocardiography examinations (General Electric Vivid S5, Milwaukee, WI, USA) were performed by an experienced cardiologist in all subjects using a 2.5–3.5 MHz transducer in the left decubitus position. Two-dimensional and pulsed Doppler measurements were obtained using the criteria of

the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Twelve left ventricular ejection fraction (LVEF) was assessed using Simpson's method [6]. Left ventricular mass was calculated using the Devereux formula. The body surface area of the patients was calculated by the Dubois formula and left ventricular mass index (LVMI) was calculated by dividing the left ventricular mass into the body surface area. LVMI values above 125 g/m2 in men and 110 g/m2 in women were accepted as left ventricular hypertrophy (LVH) findings [7].

Statistical analysis

SPSS 18.0 software package (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. All values are given as mean ± standard deviation. Mean values of continuous variables were compared between the groups using the Student's t-test or the Mann-Whitney U test, according to whether normally distributed or not, as tested by the Kolmogorov-Smirnov test.

We used Pearson's correlation test to evaluate the relationship between normally distributed parameters, and Spearman's Rho correlation test to examine the relationship between non-normally distributed parameters.

Results

Evaluation of basic clinical and demographic characteristics revealed no statistically significant difference between the two groups in terms of age, gender distribution, body mass index, and smoking status (Table 1).

Table 1: Basic clinical, demographic and laboratory data of patients

	DHT	NDHT	P value
Age	55 ± 8.367	52.94 ± 8.247	0.243
Sex (male %)	34 (%37.7)	30 (%27.7)	0.902
BMI (kg/m^2)	26.76 [26-30.4]	27.58 [26,6-30,4]	0.282
Smoking	5 (%15.2)	8(%17)	0.823
Glucose (mg/dL)	97.85 [93.7-104]	97 [89.8-113.7]	0.494
Sodium (mmol/L)	141 [139-142]	140 [139-142]	0.319
Potassium (mmol/L)	4.4 ± 0.28	4.5 ± 0.4	0.125
Calcium (mg/dL)	9.6 ± 0.4	9.4 ± 0.3	0.079
Magnesium (mg/dL)	2.205 [2.11-2.315]	2.25 [2.06-2.345]	0.965
TSH (µIU/mL)	1.41 [1.12-1.86]	1.39 [1.0-2.26]	0.953
Kreatinin (mg/dL)	0.8 [0.7-0.965]	0,76 [0,62-9]	0.049

TSH: Thyroid Stimulating Hormone, BMI:Body mass index

DHT was detected in 90 patients (40.9%) and NDHT in 130 patients (59.1%) according to their ABPM results. There was no statistically significant difference between patients with DHT and NDHT in terms of echocardiographic left ventricular parameters (Table 2).

Table 2: Echocardiographic data of patient groups

	DHT	NDHT	P value
LVDd (mm)	45 [43.5-48]	46 [44-48.5]	0.659
LVSd (mm)	30 [26-53.3]	30 [28-32]	0.616
IVS(mm)	11 [10-12]	10 [9-11]	0.176
Posterior wall (mm)	10 [9-11]	10 [8-10]	0.280
Left atrium (mm)	36.88 ± 3.7	35.77 ± 4.4	0.243
LV EF (%)	60 [60-65]	65 [60-65]	0.219
LV Mass Index	86.4 ± 99.19	80.15 ± 91.18	0.280

EF: Ejection Fraction, IVS: Interventricular septum, LVH: Left Ventricle, LVDd: Left Ventricular End Diastolic Diameter, LVSd: Left Ventricular End Systolic Diameter

When the DHT group and the NDHT group were compared, we observed that almost all of the electrocardiographic data showed elongation in milliseconds in the NDHT group. However, this difference did not reach statistical significance.

QTc dispersion was also higher in NDHT group, however, there was no statistically significant difference (Table 3).

Table 3: Comparison of ECG data between the patient groups

	DHT	NDHT	P value
QTV2 (millisecond)	372 [352-383]	376 [347-386]	0.528
QT V5	377 ± 25	367 ± 31	0.153
QTc V2	414 ± 28	414 ± 25	0.952
QTc V5	423 ± 28	411 ± 26	0.060
QTc dispersion	35 [29-58]	44 [27.5-59.5]	0.494
TPe V2	103.44 ± 17.16	105.66 ± 16.01	0.555
TPe V5	91.52 [81.36-96.61]	91.52 [86.44-101.69]	0.654
TPe /QT V2	0.280 ± 0.04	0.285 ± 0.04	0.623
TPe/QT V5	0.244 ± 0.04	0.248 ± 0.03	0.653
TPe/QTc V2	0.250 ± 0.04	0.255 ± 0.03	0.564
TPE /QTc V5	0.217 [0.196-0.228]	0.222 [0.199-0.239]	0.356

The average heart rate was significantly higher in the NDHT group with 78 ± 8.1 and in the DHT group it was 73 ± 8.3 group (p = 0.032). Furthermore, the minimum heart rate values were found to be 61 ± 7.2 in NDHT and 58 ± 7.8 in DHT, and these values were found to be statistically significant (Table 4).

Table 4: Comparison of General ECG Holter Data Between the Patient Groups

	DHT	NDHT	P value
Minimum Heart Rate	58 ± 7.8	61 ± 7.2	0.036
Maximum Heart Rate	101 ± 11.8	97 ± 13.6	0.223
Average Daytime Heart Rate	71 ± 11.4	75 ± 8.5	0.052
Average Night-time Heart Rate	77 ± 10.7	81 ± 9.8	0.079
Average Heart Rate	73 ± 8.3	78 ± 8.1	0.032

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There was no statistically significant difference between the patient groups in parameters related to HRV and HRT data (Table 5) and both were obtained by time-domain and frequency-domain methods (Table 5).

Table 5: Comparison of Time-Domain and Frequency-Domain Method and HRV Data, Comparison of HRT data

	DHT	NDHT	P value
PNN50 (%)	4.61 [1.67-11.34]	2.22 [1.14-6.19]	0.141
PNN30 (%)	16.27 [7.41-24.89]	12.43 [5.17-20.52]	0.206
RMSSD (ms)	28.57 [19.54-35.68]	23.43 [18.09-30.49]	0.324
Variable Index	2.07 [1.64-2.69]	1.96 [1.6-2.4]	0.594
SDNN (ms)	48.14 ± 15.25	46.29 ± 11.7	0.544
SDANN (ms)	105.9[89.46-139.84]	97.85 [86.76-108.37]	0.052
Total Power	2465 [1234-3379]	1947 [1463-2621]	0.629
VLF Power (ms^2)	1726 [825-2251]	1342 [1021-1799]	0.625
LF Power (ms^2)	248 [246-691]	341 [238-474]	0.261
HF Power (ms^2)	151 [65-270]	106 [59-168]	0.123
LF nu	61 [51-66]	63 [54-68]	0.356
HF nu	23 ± 9	20 ± 10	0.124
Turbulence Onset	-0.002 [-0.03-0.006]	-0.053 [-0.01-0.001]	0.968
Turbulence Slope	5.8 [3.8-12.3]	5 [2.4-7.8]	0.111

PNN50: the ratio of the number of intervals where the difference between consecutive R-R intervals is greater than 50 milliseconds to the total number of R-Rs, PNN30: the ratio of the number of intervals where the difference between consecutive R-R intervals is over 30 milliseconds to the total number of R-Rs, RMSSD: the arithmetic mean of square root of the difference between consecutive R-R intervals, SDNN: the standard deviation of time (R-R interval) between consecutive normal QRS complexes, SDANN: the standard deviation of average R-R intervals of five minute recordings over 24 hours, HF:High Frequency, LF:Low Frequency, VLF:Very Low Frequency

The correlation analysis between the LVMI and QTc data measured separately from each lead in the ECG data were examined. There was a statistically significant difference in the results regarding QTc V3 ($p = 0.04$), QTc V2 ($p = 0.01$), QTc V1 ($p = 0.04$), and QTc D1 ($p = 0.04$).

Discussion

To the best of our knowledge, if there is no cardiac end-organ damage, the separation between DHT and NDHT has no effect on the risk of arrhythmia. HT is one of the important risk factors of CVDs. The prevalence of HT in society is increasing, both in relation to the ease of access to diagnosis and healthcare centers and to the increase in other CVD risk factors. HT-related research answers questions about etiology, classification, and treatment. However, regardless of other factors, it has not yet been elucidated what role personal differences play in the risk levels of different people with close BP values [8].

There are many studies showing that ABPM predicts CV mortality and morbidity better and that they are higher in NDHT [9]. There is a physiological decline in BP at night. This reflex reduces with age. The reasons for this condition are thought to be as follows: Vascular elasticity decreases due to aging and atherosclerosis. The regulation of the autonomic nervous system is impaired and the vasoconstriction associated with the sympathetic nervous system dominates the vasodilatation relevant to the parasympathetic nervous system [10]. There are several causes of night-time BP decline in the normal circadian rhythm, such as decreased blood levels of cortisol, adrenaline, and noradrenaline. Patients with NDHT have lower levels of decline than those with DHT. In addition, an increased α1 adrenergic receptor response and a decreased parasympathetic activity were found in NDHT patients [11]. It is known that lack of expected decrease in night-time BP is associated with increased CV morbidity. CV risk factors such as a decrease in HRV, an increase in plasma creatinine level, and a decrease in high-density lipoprotein level are more common in patients with low BP at night [12]. It has been shown that target organ damage is higher in NDHT due to greater deterioration in endothelial functions than in DHT [13].

The risk of ventricular arrhythmia and sudden death is increased in hypertensive patients. Data on the incidence of arrhythmia in HT and the prognostic value of these indicators are limited. Some data even contain contradictions. There are limited studies on the relationship between ambulatory measured BP data and non-invasive ventricular arrhythmia parameters.

HT is a pathologic condition known as hypertensive heart disease, which develops as a result of structural and functional adaptation with hemodynamic effects. It manifests itself as blood flow disorders due to increased LV mass, diastolic dysfunction, congestive heart failure, arrhythmia, and microvascular diseases [14]. One of the most common cardiac complications is LVH. In our study, no significant difference was found between the two groups in terms of LVH.

Studies investigating the relationship between the diurnal course of BP and the LVH found that night-time BP values were more correlated with LVH [15,16]. However, in the study performed by Grandi et al., no correlation was found between LV morphology and night-time BP elevation [17]. In LVH, the coronary reserve is reduced resulting in ischemia and fibrosis which may impair homogeneity in myocardial repolarization. Therefore, the variability in QT interval is an indicator of arrhythmogenicity. It was reported that there was a linear relationship between the

LVMI and QTd in HT [18]. QTd was increased in non-proportional LVH, such as HT, while it was found normal in proportional LVH, such as an athlete's heart [19].

Cavallini showed that QTd increased in HT and LVH patients, but this increase was not associated with complex ventricular arrhythmias [20]. Galinier followed up 214 hypertensive patients (33.7% of whom were hypertrophic) after an average of 42 months. He found an increased QTd (>80 ms) associated with cardiac mortality in univariate analyses. He reported that this relationship was absent in multivariate analyses. In our study, we found that there was an increase in QTd duration in the NDHT group compared to the DHT group, but this increase was not statistically significant.

Recently, new electrocardiographic parameters Tpe, Tpe/QT, and Tpe/QTc parameters have emerged in relation to increased repolarization dispersion [21]. These markers can be used as an electrocardiographic predictor for ventricular arrhythmogenicity and sudden cardiac death [22]. Demir et al showed that Tpe and Tpe/QT ratio increased in patients with NDHT [23]. In our study, there were differences in Tpe interval, Tpe/QT and Tpe/QTc ratios between the

groups. The NDHT group had higher results than the DHT group. However, these differences were not statistically significant. It is clear that more studies are needed to demonstrate the relationship between the patients with NDHT and ventricular arrhythmias and the Tpe interval and Tpe/QT ratio.

Our study showed that HRV parameters were generally smaller in the NDHT group than in the DHT group, but this difference was not statistically significant. Similarly, Poanta et al. compared normotensive patients with type 2 diabetes and NDHT. In their study, HRV parameters were smaller in the NDHT group. However, very few of these parameters showed a statistically significant change [24]. This result was attributed to the fact that autonomic functions may be impaired in relation to the pathophysiology of diabetes. In our study, the small number of patients may be the reason why the results did not reach statistical significance. Another recent study by Dauphinot et al. examined the relationship between DHT and NDHT risk changes and a decreased autonomic nervous system activity assessed by HRV parameters in the elderly population [25]. In their study, increased risk of the non-dipper pattern was detected in patients with low autonomic nervous system activity. Regardless of HT, a decreased autonomic nervous system activity was associated with non-dipper blood pressure pattern. This study also demonstrated that autonomic dysfunction may be a predictive and etiological factor in non-dipper blood pressure pattern.

In our study, we also evaluated TO and TS, which are HRT parameters. There was no statistically significant difference between the groups. This may be associated with the small size of the selected patient population.

Autonomic nervous system dysfunction is usually associated with non-dipper BP phenomenon [26]. HRV and HRT reflect a reduced cardiac autonomic nervous system activity, a particularly increased sympathetic activity, and a decreased parasympathetic activity [27]. These two methods can evaluate cardiac autonomic dysfunction as noninvasive and have been accepted as new risk parameters for sudden cardiac death [28].

According to the European Society of Cardiology, HRT is an independent predictor of total mortality after myocardial infarction and a marker of vagal activity [29]. In one study, the average heart rate was found to be higher in non-dipper patients than in dipper patients. This may be due to the predominance of sympathetic activity due to cardiac autonomic dysfunction in subjects with nondipper blood pressure pattern [30]. In our study, the average heart rate supporting this data was found to be statistically higher in the NDHT group.

Study limitations

The main limitation of our study was the small number of patients. In addition, only individuals with HT were included in the study and therefore no comparison was made with healthy controls. In addition, since there was no follow-up study, the effects of duration of exposure to DHT and NDHT on the risk of arrhythmias were not taken.

Conclusion

When HT patients were grouped as DHT and NDHT, there was no difference between the two groups in terms of the risk of ventricular arrhythmia, the HRV and HRT parameters evaluated by ECG parameters, and the HRV and HRT parameters evaluated with a 24-hour Holter. As a result, if there is no cardiac end-organ damage, the separation between DHT and NDHT has no effect on the risk of arrhythmia. It was concluded that this may be due to the fact that there was no difference between the groups in terms of left ventricular functions, left ventricular masses, and LVMI between our DHT and NDHT groups.

Declaration of conflict of interest

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Original Article

Enchondromas of the hand: Retrospective evaluation of 33 cases

Elin enkondromları: 33 vakanın retrospektif değerlendirilmesi

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Abstract

Aim: To present the demographic evaluation and distribution of the enchondromas of the hand which were treated by curettage with bone grafting or isolated curettage.

Material and Methods: We retrospectively evaluated the 798 patients who were operated because of hand tumors and pathological diagnosis was made in the same hospital between 2007 and 2019. Age, gender, affected side and location of the tumor of the patients who were diagnosed with enchondroma of the hand and could be follow-up minimum of one year were evaluated accordingly.

Results: A total of 33 patients (mean age 36.4 years; range 6 to 77 years) with 34 enchondromas of the hand were included. Fifteen (45%) out of 33 patients were male and 18 (55%) were female. Twenty (61%) out of 33 had enchondroma on the right hand and 13 (39%) had on the left. One patient (3%) had enchondroma on his two fingers. Seventeen (52%) patients had enchondromas on their proximal phalanges, seven (21%) had on the middle phalanges, seven (21%) had on the distal phalanges (Total eight distal phalanges) and two (6%) had on metacarpals. One patient (3%) had enchondroma on her thumb, six (18.2%) had on the index finger, five (15.1%) had on the third finger, 11 (33.3%) had on the ring finger and nine patients (27.3%) had enchondromas on their little finger.

Conclusion: Enchondromas are usually seen on the ulnar side of the right hand and frequently seen on the proximal phalanges and may cause pathological fractures.

Keywords: enchondroma; enchondroma of the hand; hand; hand tumors; tumor

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Öz

Amaç: İzole küretaj ya da küretaj ve greftleme ile tedavi edilmiş elin enkondromlarının demografik değerlendirmesini ve dağılımlarını sunmak.

Gereç ve Yöntemler: 2007-2019 yılları arasında el tümörü nedeniyle opere edilen ve patolojik tanısı aynı hastanede konulan 798 hasta retrospektif olarak değerlendirildi. Enkondroma tanısı konulan ve bu sebeple opere edilen, en az bir yıl süre ile takip edilen hastaların yaşı, cinsiyeti, etkilenen tarafları ve tümör yerleşimi değerlendirildi.

Bulgular: Toplam 33 hasta ve onların 34 elde yerleşen enkondroması dahil edildi (Ortalama 36,4 yıl; 6-77 aralığında). 33 hastanın 15'i (%45) erkek, 18'i (%55) kadındı. 33 hastanın 20'sinin (%61) enkondroması sağ elde, 13'ününki (%39) sol elde yerleşimliydi. Bir hastanın (%3) iki parmağında enkondroma mevcuttu. 17 hastanın (%52) enkondroması proksimal falanksta, yedi hastanınki (%21) orta falanksta, yedi hastanın (%21) distal falanksta (toplam sekiz distal falanks) ve iki hastanınki (%6) metakarplarındaydı. Bir hastanın enkondroması (%3) başparmakta, altı hastanınki (%18.2) 2.parmakta, beş hastanınki (%15,1) 3.parmakta, 11 hastanınki (%33,3) 4.parmakta ve dokuz hastanınki (%27,3) ise 5.parmakta idi.

Sonuç: Enkondromlar genellikle sağ elin ulnar tarafında, sıklıkla proksimal falankslarda görülür ve patolojik kırıklara sebep olabilir.

Anahtar kelimeler: enkondrom; elin enkondromu; el; el tümörleri; tümör

Introduction

Enchondromas are the most common primary bone tumors of the hand [1]. They frequently consist of hyaline cartilage, calcification, usually located in the hands and settles intramedullary [2,3]. Patients often suffer from pain due to the growth of the tumor or pathological fracture. But it may also be determined incidentally in hand radiography which was taken for any other reasons [3].

Enchondromas are usually inclined to appear on the ulnar side and develop in the third and fourth decades of life [1-3]. Diagnosis can be made on plain radiography and they are frequently determined on the proximal phalanx and on the little fingers [4].

The treatment of enchondromas changes according to the size and the presence of a pathological fracture. In a normal way, the treatment modality varies from a follow-up to surgical excision and curettage with bone grafting. It has to be kept in mind that enchondromas may rarely malignant transform to chondrosarcoma. Pain in rest, concomitant soft tissue mass, and cortical destruction are the suspicious factors for a possible malignant transformation to chondrosarcoma [3,5].

In this retrospective study, we aimed to present the demographic evaluation and distribution of the enchondromas of the hand which were treated by curettage with bone grafting or isolated curettage.

Material and Methods

In this study, we retrospectively evaluated the 798 patients who were operated because of hand tumors and pathological diagnosis was made in the same hospital between 2007 and 2019. Age, gender, affected side and location of the tumor of the patients who were diagnosed with enchondroma of the hand and could be follow-up minimum of one year were evaluated accordingly. The folder archives, pathological records and the computer archiving system of the XXX Akdeniz University hospital (Mia-Med version 1.0.1.2808, Mia Technology A.Ş, Ankara, Turkey) and Picture Archiving and Communication System (PACS) of the same XXX Hospital were used for the retrospective evaluation. A descriptive statistical analysis was performed for the comparison of the distribution of the enchondromas. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Thirty-six patients with 37 tumors were diagnosed as "enchondroma" of the upper extremity. Two out of 36 didn't have a detailed description of the location and one of the enchondromas was on the distal ulna. At last, a total of 33 patients (mean age 36.4 years; range 6 to 77 years) with 34 enchondromas of the hand were included in the study. Mean follow-up period was 22,2 months (range 12 to 48 moths).

Fifteen (45%) out of 33 patients were male and 18 (55%) were female. Twenty (61%) out of 33 had enchondroma on the

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right hand and 13 (39%) had on the left. One patient (3%) had enchondroma on his two fingers. Seventeen (52%) patients had enchondromas on their proximal phalanges, seven (21%) had on the middle phalanges, seven (21%) had on the distal phalanges (Total eight distal phalanges) and two (6%) had on metacarpals. One patient (3%) had enchondroma on her thumb, six (18.2%) had on the index finger (Figure 1), five (15.1%) had on the third finger, 11 (33.3%) had on the ring finger and nine patients (27.3%) had enchondromas on their little finger. One patient (3%) had enchondromas on the distal phalanges of both his index and ring fingers (Table 1).

Table 1: Demographic datas and distribution of the enchondromas

Parameter	Description
Age	Mean age 36.4 years; range 6 to 77 years
Gender	15 Male, 18 female
Side	20 right, 13 left
Location	
1st finger	1 patient
2nd finger	6 patients
3rd finger	5 patients
4th finger	11 patients
5th finger	9 patients
Two fingers	1 patient
Proximal phalanx	17 patients
Middle phalanx	7 patients
Distal phalanx	7 patients
Metacarpals	2 patients

Figure 1: Middle phalanx of the index finger with an enchondroma; a, Preoperative anteroposterior X-Ray view, b, Six months after operation, calcified matrix is visible.

Eleven patients were treated with curettage alone (33.3%) and other 22 were treated by curettage and grafting (66.6%). Autograf was harvested from ipsilateral metaphysis of the radius in three cases, ipsilateral olecranon in three cases and ipsilateral iliac wing in 16 cases.

One of our patients applied to the emergency department after falling from a height and a pathological fracture was diagnosed on his proximal phalanx of the ring finger of the right hand. He was operated for his proximal phalanx fracture and open reduction-internal fixation with screws was performed (Figure 2). We had no malignant transformation in any patient in the postoperative first year. Just two of patients complained from graft donor site pain and both of them healed at the end of first year. The graft donor site was iliac wing in both of the cases. We had no wound complication.

Figure 2: Pathological fracture of the proximal phalanx of the fourth finger; a, Preoperative anteroposterior X-Ray view of the fracture line, b, Three months after operation, callus is visible on fracture lines.

Discussion

Enchondromas of the hand should be evaluated with a wide range of morbidity intervals. They may be asymptomatic, may be a reason for a pathological fracture and also may cause a malignant transformation. It's impossible to report an exact incidence of the enchondromas due to the absence of symptoms [6]. The results of the distribution according to finger and phalanges of the present study supported the literature: they usually occurs on the third and fourth decade of life, they are inclined to present on the ulnar side, and on the proximal phalanges [1,3,4,7].

Tumorous conditions of the hand are frequently treated by both orthopedic surgeons and hand surgeons throughout their working period. Enchondromas comprise a wide area in the daily practice of a hand tumor surgeon due to its frequency [8,9,10]. A patient with an enchondroma even it was detected incidentally should always be followed-up in a period of time. The treatment modality changes according to its' size, cortical destruction. Curettage alone and curettage with bone grafting can also be used for the cases with enchondromas [11,12]. Even if enchondromas are the most common primary bone tumors of the hand, any standard operative treatment algorithm for a symptomatic enchondroma has not been established yet [13]. In our case series, we performed both curettage and curettage with bone grafting. The 0% recurrence rate for the follow-up of the first postoperative year made it not feasible to evaluate the demographic factors and also the distribution of the enchondromas affecting and related to the recurrence rate.

The donor sites were olecranon, distal radius and iliac wing in our study. Even iliac wing was the most used one as a donor site the donor site morbidity rate was also lower than the literature [14].

Our study has some limitations. The one year follow up period would be much more to have an ideal idea about the recurrence rate. Prospective randomized trials with a tumor and patient-specific approach would be more evidence based instead of a retrospective study.

Conclusion

Enchondromas are usually seen on the ulnar side of the right hand and frequently seen on the proximal phalanges and may cause pathological fractures. Both isolated curettage and curettage with bone grafting are used in the treatment.

Declaration of conflict of interest

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There is no conflict of interest.

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Orijinal Makale

Ön çapraz bağ rekonstrüksiyonunda transtibial ve anteromedial portal tekniklerin fonksiyonel olarak karşılaştırılması

Functional comparison of transtibial and anteromedial portal techniques in anterior cruciate ligament reconstruction

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Öz

Amaç: Bu çalışmada, otojen hamstring tendon grefti kullanılarak ön çapraz bağ (ÖÇB) rekonstrüksiyonu yapılan hastalarda, transtibial (TT) ve anteromedial portal (AMP) tekniklerin fonksiyonel sonuçlarının karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler: 2010-2018 yılları arasında, TT ve AMP teknik ile ÖÇB rekonstrüksiyonu yapılan toplam 80 hasta çalışmaya dahil edilmiştir. Hastaların 40 tanesi TT teknik ile 40 tanesi AMP teknik ile ameliyat edildi. Hastaların ameliyat sonrası takiplerinde, diz hareket açıklığı (fleksiyon- ekstansiyon), eklem kararlılık testleri (Lachman, ön çekmece, pivot-shift testleri) ve fonksiyonel skorları (IKDC, Lysholm, Cincinnati and Tegner diz skorları) kaydedildi.

Bulgular: Her iki grup için ameliyat öncesi ve ameliyat sonrası yapılan ölçümler arasında istatistiksel olarak anlamlı fark bulunmuşsa da, TT ve AMP grupların birbirleri ile karşılaştırılmasında, diz hareket açıklığı, kararlılık ve fonksiyonel skorların sonuçları açısından fark bulunmadı.

Sonuç: Her iki grup için, otojen hamstring tendon grefti ile yapılan artroskopik ÖÇB rekonstrüksiyonunun erken fonksiyonel sonuçları tatmin edici ve benzerdir.

Anahtar kelimeler: ön çapraz bağ; transtibial teknik; anteromedial portal teknik.

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Abstract

Aim: This study aimed to compare the functional results of transtibial (TT) and anteromedial portal (AMP) techniques in patients who underwent anterior cruciate ligament (ACL) reconstruction using the autogenous hamstring graft.

Material and Methods: Fourty patients with TT technique and 40 patients with AMP technique who underwent arthroscopic ACL reconstruction between 2010-2018 were included in this study. During follow-up, range of motion (flexion-extension), stability (Lachman, anterior drawer, pivot-shift tests), functional scores (IKDC, Lysholm, Cincinnati and Tegner knee scores) were recorded.

Results: Although there were statistically significant results between preoperative and postoperative values in each group, there was no statistically significant difference between groups for knee range of motion, stability, functional results.

Conclusion: For both groups, early postoperative functional results of arthroscopic ACL reconstruction with autogenous hamstring tendon graft were found to be satisfactory.

Keywords: anterior cruciate ligament; transtibial technique; anteromedial portal technique.

Giriş

Günümüzde sportif faaliyetler günlük hayatın bir parçası haline gelmiş, bunun sonucu olarak da spor yaralanmalarında önemli bir artış olmuştur. Ön çapraz bağ (ÖÇB) yaralanması, spor yaralanmalarının en sık görülenlerinden biridir.[1-4] Yüksekten düşme, trafik kazası gibi yüksek enerjili travmalar da ÖÇB yaralanmasına neden olabilirler.

ÖÇB, dizin ön-arka ve rotasyonel stabilitesinde görev aldığından, ÖÇB yaralanması sonrası dizde instabilite meydana gelmektedir. Kişinin günlük hayatını etkileyen ve diz içerisinde daha ileri hasar meydana gelmesine neden olan ÖÇB yaralanmalarında tedavinin önemi bir kat daha artmaktadır.[5]

ÖÇB yaralanmalarında yapılan cerrahi tedavinin temel amacı normal diz kinematiği ve stabilitesini sağlayıp, ileride dejeneratif değişikliklerin ortaya çıkmasını önlemektir.[6] Literatürde birçok cerrahi teknik tanımlanmış olsa da günümüzde anatomik rekonstrüksiyonlar giderek popüler hale gelirken, en sık artroskopik transtibial (TT) ve anteromedial portal (AMP) teknikleri kullanılmaktadır.[7,8]

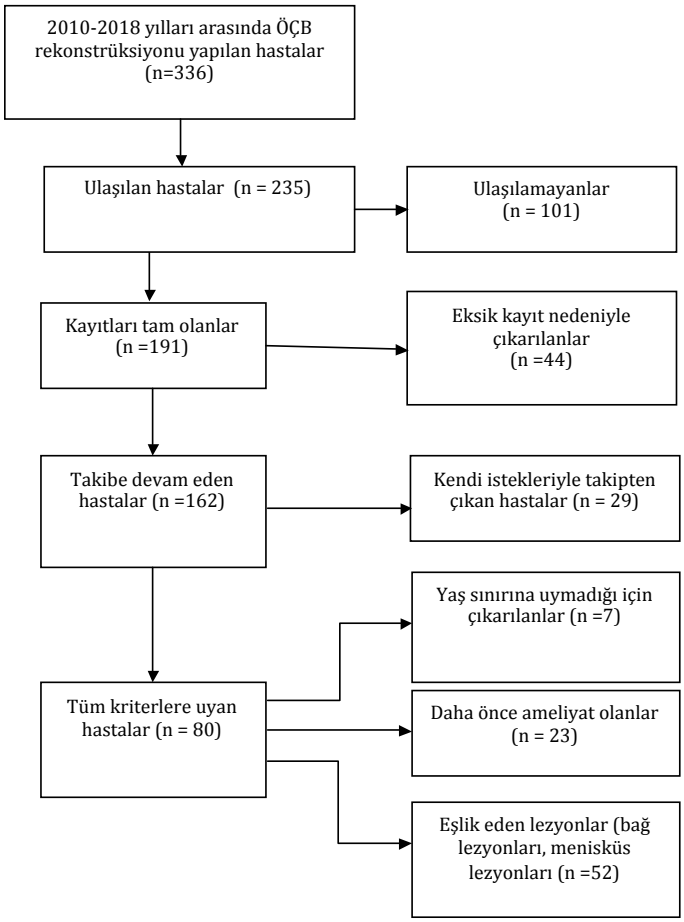
Bu çalışmada TT ve AMP teknikleri fonksiyonel açıdan kıyaslandı. Hastaların operasyondan maksimum fayda görmelerini sağlamak amacıyla, günlük aktivite ve sportif faaliyetlere en hızlı dönüşü sağlayacak yaklaşım tespit etmeye çalışıldı.

Gereç ve Yöntemler

T.C. Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'nun 17/12/2018 tarih ve 57/13 karar numarası ile onaylanmış bu çalışma, Helsinki İlkeler Deklerasyonu'na uyularak yapılmıştır.

Bu çalışmada 2010-2018 yılları arasında, T.C. Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi Ortopedi ve Travmatoloji Kliniği'nde ÖÇB rüptürü nedeniyle otojen hamstring grefti kullanılarak, TT ve AMP tekniği ile artroskopik ÖÇB tamiri yapılan ve takiplerine devam eden, toplam 80 hasta dahil edildi. Toplam 336 hastanın 151 tanesi TT teknik ile geri kalanı AMP tekniği ile ameliyat edilmiştir. Çalışmaya 18-50 yaş arasında, daha önce diz ameliyatı geçirmemiş, her iki dizinde ek patolojisi (arka çapraz bağ (AÇB), iç yan bağ, dış yan bağ lezyonları veya tamir gerektiren kompleks menisküs patolojisi) olmayan hastalar dahil edildi (Tablo 1).

Tablo 1. Hastaların çalışmaya dahil edilme süreci



Retrospektif bu çalışmada, ÖÇB rüptürü tanısı alan hastaların, muayene bulguları ve manyetik rezonans görüntüleme tetkiki sonuçları tekrar değerlendirildi. Kliniğimizde ÖÇB tamiri yapılan hastaların rutin kontrolleri 2. hafta, 6. hafta, 3. ay, 1. yılda yapılmakta, sonrasında yıllık kontrollere çağrılmaktadır. Tüm hastaların sosyodemografik özellikleri (yaş, vücut kitle indeksi, cinsiyet), taraf, yaralanma sebebi ve mekanizması, yaralanma ve ameliyat arasında geçen süre, ameliyat öncesi şikayetleri (ağrı, efüzyon, boşalma hissi, güvensizlik hissi), ameliyat sırasında tespit edilen menisküs ve/veya kıkırdak patolojisi, ameliyat sonrası aktiviteye dönme süreleri kaydedildi. Hastaların ameliyat sonrası minimum 12. ayda maksimum 48. ayda yapılan ölçümlerinden faydalanıldı.

Cerrahi Teknik

Hastalara turnike altında, aynı cerrah tarafından standart artroskopi protokolü uygulandı. Buna göre, usulüne uygun açılan anteromedial ve anterolateral portallerden girilerek suprapatellar boşluk, lateral ve medial gutter, patellofemoral eklem, medial ve lateral kompartmanlar değerlendirildi. Eklem faresi varlığı, osteokondral lezyonlar ve menisküslerin değerlendirilmesi yapıldı. Anteromedial portal tekniğinde, femoral tünel tibial tünelden bağımsız olarak açıldı. Lateral femoral kondilin medial duvarı shaver ile temizlenip, "Resident's Ridge" tam olarak görüldükten sonra kondil posterioru probe ya da spinal iğne ile değerlendirildi. Femoral tünel açıldıktan sonra, ÖÇB'ın tibia anatomik lokalizasyonu shaver yardımıyla temizlendi. ÖÇB'ın tibia anatomik lokalizasyonuna gönderilen kılavuz tel üzerinden daha önce belirlenen greft çapına uygun çaptaki oyucu ile tibial tünel açıldı.

Transtibial teknikte ise ilk olarak tibial tünel açılmakta ve tibial tünel üzerinden femoral tünel açılmaktadır. ÖÇB tibia anatomik lokalizasyonu shaver yardımıyla temizlenerek, kılavuz insizyonun içinde kalacak şekilde diğer ucu anteriordan açılan portalden içeri sokularak, AÇB'ın ortalama 5-7 mm önüne ve medial eminensin lateral kenarına yerleştirildi. Gönderilen kılavuz telin çıkış yeri, femur lateral kondil medial duvarına doğru yönlendiği bölge, açılacak olan femoral tünel için ulaşılabilecek giriş noktası ve buna bağlı sıkışma olup olmayacağı kontrol edildikten sonra, kılavuz tel üzerinden direkt olarak daha önce belirlenen greft çapına uygun çaptaki oyucu ile tibial tünel açıldı. Daha sonra femoral kılavuz, tibial tünel içerisinden geçirildikten sonra çentiği posterior kortekse dayanacak şekilde yerleştirilip, kılavuz tel gönderildi. Ardından daha önce belirlenen greft çapına uygun çaptaki oyucu ile femoral tünel açıldı.

Femoral stabilizasyon için AMP teknikle rekonstrüksiyon yapılan hastaların tamamında Endobutton Cl kullanılırken, TT teknikle rekonstrüksiyon yapılan 37 hastada Endobutton Cl ve 3 hastada Crosspin kullanıldı. Tibial stabilizasyon için her iki grupta da interferans vidası ve staple kullanıldı.

Değerlendirme

Çalışmaya katılmayı kabul eden tüm hastaların ameliyat sonrası diz eklem hareket açıklığı (EHA) muayenesi, Lachman testi, ön çekmece testi ve Pivot Shift testi yapıldı. Lachman testi (-), (+), (++) olarak, ön çekmece testi ve Pivot shift testi (+) ve (-) olarak derecelendirildi. Ameliyat öncesi ve ameliyat sonrası takiplerde tüm hastalara IKDC, Lysholm, Cincinnati ve Tegner skorlama sistemleri kullanılarak anket yapıldı. Gruplar arasında ameliyat öncesi ve sonrası skorlama sonuçları açısından fark olup olmadığı değerlendirildi.

İstatistiksel Analiz

Verilerin istatistiksel değerlendirmesi Statistical Package for the Social Sciences (SPSS) for Windows sürüm 20.0 kullanılarak yapıldı. Kategorik değişkenler için tanımlayıcı istatistikler, sayı ve yüzdeler hesaplandı. Sayısal verilerin analizinde normal dağılıma uygunluk "Kolmogrov Simirnov" ve "Shapiro-Wilk" testleri ile incelenmiş olup, normal dağılıma uygun olan bağımsız değişkenler için iki grup arasındaki ortalama farkı "Student t testi" ile, ikiden fazla grup arasındaki ortalama farkı ise "OneWayAnova" testi ile incelenmiştir. Normal dağılıma uygun olmayan bağımsız değişkenler için iki grup arasındaki medyan farkı "Mann-Whitney U" testi ile, ikiden fazla grup arasındaki medyan farkı ise "Kruskal-Wallis H" testi ile incelenmiştir. Normal dağılım gösteren bağımlı değişkenlerin analizi "Paired Samples T testi", normal dağılım göstermeyen bağımlı değişkenlerin analizi ise "Wilcoxon testi" kullanılarak yapılmıştır. Kategorik değişkenlerin kendi aralarındaki analizleri "Chi-Square" koşulu sağlandığı durumlarda "ChiSquare" test istatistiği, sağlanmadığı durumlarda ise "Fisher's Exact Test" istatistiği kullanılarak gerçekleştirilmiştir. Veriler %95 güven düzeyinde incelenerek p değeri 0,05'ten küçük ise testler anlamlı kabul edildi.

Bulgular

TT grubun yaş ortalaması 33,18 (18-50), AMP grup yaş ortalaması 26,82 (18-50) olarak tespit edildi. TT grup 35 erkek, 5 kadın hastadan, AMP grup 36 erkek, 4 kadın hastadan oluşmaktaydı. Taraf tutulumu incelendiğinde AMP grup 21 sağ, 19 sol taraf, TT grup 25 sağ, 15 sol taraf tutulumu ile benzerdi. Vücut kitle indeksi (VKİ), her iki grupta anlamlı bir farklılık göstermiyordu. (Tablo 2)

Tablo 2. Hastaların demografik bilgileri

		Yaş		Cinsiyet				Taraf		VKİ					
				Kadın		Erkek		Sağ	Sol	Zayıf 18.5'tan az		Normal 18.5-24.9 arası		Fazla Kilolu 25-29.9 arası	
Ameliyat Tekniği	AMP	26,83	44,7%	4	10,0%	36	90,0%	21	19	6	15,0%	27	67,5%	7	17,5%
	TT	33,18	55,3%	5	12,5%	35	87,5%	25	15	3	7,5%	33	82,5%	4	10,0%

Yaralanma mekanizması AMP grubunda %42,5 oranında spor yaralanmaları iken, TT grupta bu oran ancak %20 idi. Aynı zamanda yaralanma sonrası ameliyata kadar geçen süre TT grupta daha kısa iken, aktiviteye dönme zamanları diğer gruba nazaran daha geç olmuştu. Her iki parametre açısından sırasıyla p=0,044 ve p=0,040 değerleri ile istatistiksel olarak anlamlı bir fark olduğu tespit edildi. (Tablo 3)

Ameliyat öncesi şikayetler her iki grupta benzer olmakla birlikte, efüzyon ve intraartiküler hasar varlığı (menisküs lezyonu, kondral hasar) TT grupta anlamlı olarak fazla idi. (p=0,024, p=0,025, p=0,034) Ağrı, güvensizlik ve boşalma hissi her iki grupta benzer orandaydı. (Tablo 4)

Her iki grupta ameliyat sonrası eklem hareket açıklığı ölçümlerinde anlamlı bir fark tespit edilmedi. Stabilite testleri (lachman, ön çekmece ve pivot shift) arasında her iki grup için istatistiksel olarak anlamlı bir fark yoktu. (Tablo 5 ve 6)

Tablo 3. Yaralanma tipi, mekanizma ve ameliyat zamanı

		Yaralanma Sebebi				Oluşum Mekanizması				Ameliyat Zamanı (p=0,044)						Aktiviteye Dönme Zamanı (p=0,040)					
		Spor		Diğer		Direk		İndirek		<6 ay		6 ay-1 yıl		>1 yıl		<6 ay		6 ay-1 yıl		>1 yıl	
Ameliyat Tekniği	AMP	17	42,5%	23	57,5%	22	55,0%	18	45,0%	22	55,0%	9	22,5%	9	22,5%	12	30,0%	18	45,0%	10	25,0%
	TT	8	20,0%	32	80,0%	31	77,5%	9	22,5%	31	77,5%	7	17,5%	2	5,0%	7	17,5%	12	30,0%	21	52,5%

Tablo 4. Ameliyat öncesi bulgular

		Ağrı (ameliyat öncesi)				Efüzyon (ameliyat öncesi)				Güvensizlik (ameliyat öncesi)				Boşalma Hissi (ameliyat öncesi)			
		Yok		Var		Yok		Var		Yok		Var		Yok		Var	
Ameliyat Tekniği	AMP	15	37,5%	25	62,5%	22	55,0%	18	45,0%	15	37,5%	25	62,5%	12	30,0%	28	70,0%
	TT	7	17,5%	33	82,5%	12	30,0%	28	70,0%	22	55,0%	18	45,0%	19	47,5%	21	52,5%

Tablo 5. Ameliyat sonrası EHA muayenesi

		Fleksiyon (ameliyat sonrası)				Ekstansiyon (ameliyat sonrası)					
		>120°		100°-120° arası		Fleksiyon Kontraktürü (>0°)		Tam (0°)		Recurvatum (<0°)	
Ameliyat Tekniği	AMP	26	65,0%	14	35,0%	9	22,5%	31	77,5%	0	0,0%
	TT	33	82,5%	7	17,5%	7	17,5%	32	80,0%	1	2,5%

Tablo 6. Ameliyat sonrası muayene bulguları

		Pivot Shift (ameliyat sonrası)				Ön Çekmece (ameliyat sonrası)				Lachman (ameliyat sonrası)					
		Negatif		Pozitif		Negatif		Pozitif		Negatif		+		++	
Ameliyat Tekniği	AMP	39	97,5%	1	2,5%	36	90,0%	4	10,0%	31	77,5%	8	20,0%	1	2,5%
	TT	36	90,0%	4	10,0%	35	87,5%	5	12,5%	28	70,0%	10	25,0%	2	5,0%

Fonksiyonel sonuçlar (IKDC, Lysholm, Cincinnati ve Tegner skorları) açısından, hastaların ameliyat öncesi ve ameliyat sonrası değerlendirmeleri hem grup içinde hem de gruplar arasında karşılaştırıldı. Buna göre gerek TT gerekse AMP grupta hastaların ameliyat öncesi ve sonrası fonksiyonel skorlarında anlamlı bir iyileşme görülürken, gruplar arasında bir fark ortaya konulamadı. (Grafik 1,2,3,4)

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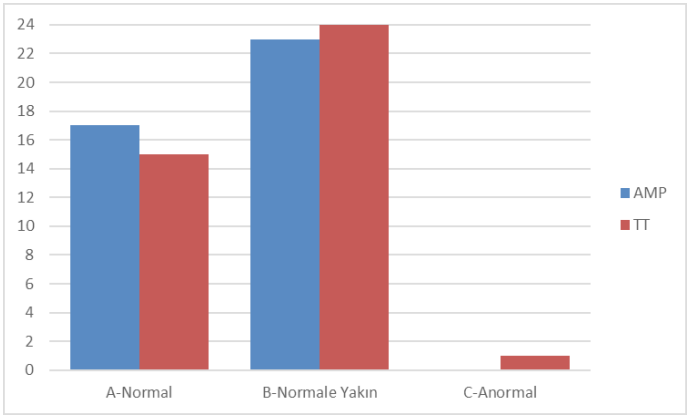
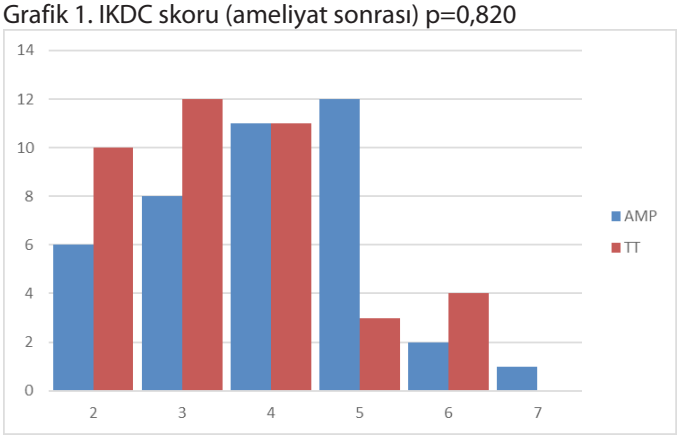
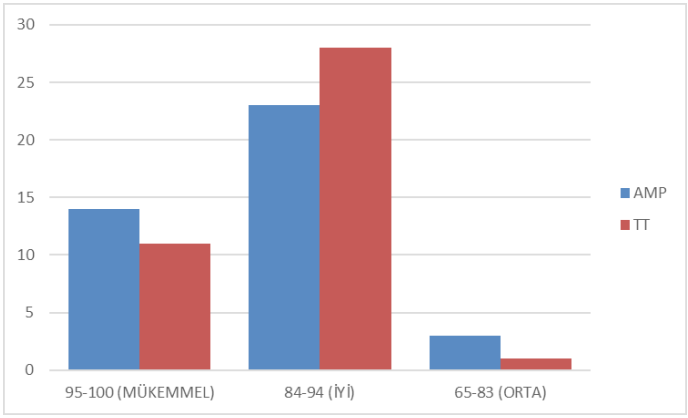


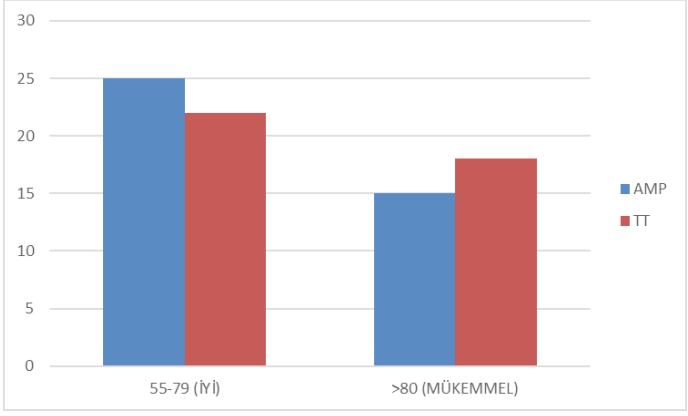
Grafik 1. IKDC skoru (ameliyat sonrası) p=0,820



Grafik 2. TEGNER skoru (ameliyat sonrası) p=0,098



Grafik 3. LYSHOLM skoru (ameliyat sonrası) p=0,403



Grafik 4. CINCINATI skoru (ameliyat sonrası) p=0,496

Hastaların ikisi rerüptür/laksite (TT grup), bir tanesi menisküs yırtığı (AMP grup) ve bir tanesi eklem içi enfeksiyon (AMP) sebebiyle tekrar ameliyat edilmiştir.

Tartışma

Ortopedi ve travmatoloji, günlük pratiği teknolojik ilerleme ve yeniliklerden en çok etkilenen branşlardan biridir. 2014 senesi sonlarından günümüze kadar, kliniğimizde AMP tekniği ile ÖÇB tamiri uygulanmakta ise de bu tekniğin tercih edilme sebebi diğer tekniğin eksikliklerinden ziyade, günün gelişmelerine ayak uydurma, daha iyi, daha farklı tedavi seçeneklerine ulaşma ihtiyacıdır.

Her ne kadar son dönemde, özellikle son 15 yılda anatomik rekonstrüksiyonların popülaritesi artmış ve pek çok taraftar kazanmış olsa da literatürde iki tekniği karşılaştıran çalışmalarda, AMP tekniğin daha başarılı olduğu yönünde bir fikir birliği yoktur.[9]

Bu çalışmada, AMP ve TT hasta gruplarının karşılaştırılması neticesinde, ameliyat sonrası erken dönem fonksiyonel sonuçlar açısından istatistiksel olarak anlamlı bir fark tespit edilmedi. (IKDC p= 0,820, Tegner p=0,098, Lysholm p=0,403, Cincinnati p=0,496) Bu durum literatürle uyumlu olup, yapılan çalışmalarda ya fark olmadığı ya da küçük farklarla AMP tekniğinin daha iyi olduğu ancak istatistiksel anlam ifade etmediği yönünde pek çok sonuç bildirilmiştir. [15-22]

Çalışmamızda, TT grubunun daha erken ameliyat olmasına rağmen AMP grubunun daha kısa sürede normal aktiviteye döndüğünü bulduk. Bu bulgular istatistiksel olarak da anlamlı idi. Literatürde AMP teknikte normal aktiviteye dönüş için çalışmamızla benzer sonuçlar bildirilmiştir.[9,17] Normal aktiviteye dönüşün TT grupta daha erken ameliyat olmalarına rağmen gecikmesini, gruplar arası yaş ve yaralanma mekanizması vb. faktörlerin farklı olmasına da bağlayabiliriz. TT grup nispeten daha yaşlı, daha sedanter ve ameliyat öncesi daha belirgin şikayetleri olan hastalardan, AMP grup daha genç, daha aktif ve daha az şikayeti olan hastalardan oluşmuş görülmektedir. Ameliyat öncesi şikayetlerin fazlalığı TT grubu daha önce ameliyat olmaya yöneltmiş olabilir. Aktivitesi daha yüksek ve genç olan AMP grubunda ise ameliyat sonrası normale dönüşün pozitif yönde etkilendiğini düşünüyoruz.

Son olarak, yaptığımız bu çalışma retrospektif bir çalışma olup, kısa dönem sonuçlar bildirilmiştir. Daha önce bahsedildiği ve son zamanlardaki yayınların çoğunda olduğu gibi, biz de

prospektif karşılaştırmalı ve uzun dönem sonuçların konu edildiği çalışmaların gerekliliğini vurgulamak isteriz. Diğer bir husus ise tüm gayretimize rağmen hasta sayımızın istenilen düzeyde olmamasıdır. Özellikle ulaşılamayan ve çalışmaya katılmak istemeyen hastaların çokluğu dikkat çekicidir. Sık sık değişen ve her seferinde arşivimizden bir şeyler götüren takip programlarının katkısı kadar, hastalardaki çalışmalara karşı duyulan kaygının yenilememiş olmasının da payı büyüktür. Daha çok sayıda hastanın katılımı ile yapılacak bir çalışma daha anlamlı sonuçlar verecektir.

Sonuç

Otojen hamstring tendon grefti ile yapılan artroskopik ÖÇB rekonstrüksiyonunun gerek TT gerekse AMP teknikle yapılsın, erken dönem fonksiyonel sonuçları tatmin edici ve benzerdir.

Maddi Destek ve Çıkar İlişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur.

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Orijinal Makale

Ekstrahepatik yerleşimli primer intraabdominal kist hidatiklere cerrahi yaklaşım

Surgical approach to primary intraabdominal hydatid cysts with extrahepatic location

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Öz

Amaç: Kist hidatik ülkemiz için yaygın bir sağlık sorunu olarak önemini korumaktadır. En sık karaciğer ve akciğer yerleşimli olup karın içi diğer organların primer tutulumu oldukça nadirdir. Ekstrahepatik primer intraabdominal hidatik kist nedeniyle cerrahi tedavi ettiğimiz olguları literatür eşliğinde incelendik.

Gereç ve Yöntemler: Ekstrahepatik primer intraabdominal hidatik kist tanısıyla opere edilen toplam 9 hastanın tıbbi kayıtları geriye dönük olarak incelendi.

Bulgular: Hastaların 6'sı kadın, 3'ü erkek olup yaş ortalamaları 49,6 (22-74) olarak saptandı. Polikliniğe basvurma şikayetleri; 3'ünde mide ağrısı, 5'inde şişkinlik, 1'inde ise sarılık idi. Kist yerleşimi 5 olguda dalak, 3 olguda retroperitoneal, 1 olguda gastrokolik ligament olarak saptandı.Kist boyutu ortalama 9,5 (5-13) cm olarak hesaplandı. Hastaların 4'üne splenektomi,1'ine laparoskopik splenektomi, 2'sine total perikistektomi ve 2'sine total perikistektomi+kolesistektomi yapıldı.Mortalite olmadı .Hastaların 2'sinde yara yerinde Hematom 1 'inde yara yeri enfeksiyonu gelişti.Ortalama hastanede yatıs 5,2 gün(4-8) idi. Taburculuk sonrası hastalara 6 ay andazol baslandı.Hastaların hepsi 6 ay sonra kontrole cagrıldı ve Usg ile kontrol edildi.Ortalama takip süresi 18,1 (6-43) ay idi. Takip sürelerinde herhangi nükse rastlanılmadı.

Sonuç: Echinococcus granulosus'un her organı tutabileceği unutulmamalıdır. Bu yüzden KC ve AC tutulumu olmasa bile tüm sistem tetkik edilmelidir. Batın içi kitlelerde özellikle endemik bölgelerde Ekstrahepatik primer intraabdominal hidatik kist akla getirilmelidir ve tedavide nüksü tamamen ortadan kaldıran total perikistektomi veya organ rezeksiyonu seçilecek tedavi yöntemdir.

Anahtar kelimeler: ekstrahepatik kist hidatik; total perikistektomi; nüks

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Abstract

Aim: Hydatid cyst maintains its importance as a common health problem for our country. It is the most common liver, lung and primary involvement of other intra-abdominal organs is extremely rare. We reviewed the cases that we treated surgically for extrahepatic primary intraabdominal hydatid cyst in the light of the literature.

Methods: Medical records of 9 patients who were operated with extrahepatic primary intraabdominal hydatid cyst diagnosis were analyzed retrospectively.

Results: Six of the patients were female and 3 were male and their mean age was 49.6 (22-74). Complaints about applying to the outpatient clinic; There were stomach pain in 3, bloating in 5 and jaundice in 1. Cyst placement was determined as spleen in 5 cases, retroperitoneal in 3 cases and gastrocolic ligament in 1 case. The cyst size was calculated as an average of 9.5 (5-13) cm. Splenectomy was performed in 4 patients, laparoscopic splenectomy in 1 patients, total pericystectomy in 2 patients, and total pericystectomy + cholecystectomy in 2 patients. No mortality occurred. Two of the patients developed hematoma at the wound site and 1 of them developed wound infection. The average hospital stay was 5.2 days (4-8).After discharge, the patients were started on 6 months of andazole. All of the patients were called for control after 6 months and checked with USG. The mean follow-up time was 18,1 (6-43) months. No recurrence was observed during follow-up.

Conclusion: It should be remembered that Echinococcus granulosus can hold every organ. Therefore, the entire system should be examined even if there is no involvement of liver and lung. Extrahepatic primary intraabdominal hydatid cyst should be considered in intra-abdominal masses, especially in endemic regions, and total pericystectomy or organ resection is the treatment method to be selected in the treatment that completely eliminates recurrence.

Keywords: extrahepatic cyst hydatid; total pericystectomy; recurrence

Giriş

Kist Hidatik tarım ve hayvancılıkla uğraşan insanlarda görülen, hayvanlardan insanlara geçen endemik paraziter bir hastalıktır. Birçok ülkede, insanların, sahip olduğu koyun, köpek gibi hayvanlarla yakın temasları parazitin hayat zincirinin kalıcı olmasını sağlar.[1] Bu helmintik hastalık dünya çapında izlenmekte olup Akdeniz havzası, Kuzey ve Doğu Afrika, Asya, Güney Amerika ve Avustralya ülkeleri gibi pek çok bölgede endemik olarak izlenmektedir.[2]

Kist Hidatik etkeni Sestod gurubunda yer alan bir parazit olup 4 alt grubu vardır ve en sık görülenleri Echinococcus granulosus ve Echinococcus multilocularis(alveolaris) dir.

Kist Hidatik tüm organları tutabilmekle birlikte en sık karaciğer (%70) ve akciğeri (% 15-20) tutar. Dalak tutulumu % 0,9-% 8 sıklıkla bildirilirken, izole dalak tutulumu çok nadirdir. Nadiren yumuşak dokular, kas-iskelet sistemi, kalp ve mesane gibi bölgelerde de görülebilir.[3] Parazit genellikle hematojen veya ince barsak lenfatikleri yoluyla yayılır; ancak batın içi yayılımı primer kistin spontan rüptürü ve parazitin intraperitoneal sıvı ile dolaşarak diğer organlara ekilmesi yoluyla da gerçekleşebilir.[4]

Genellikle asemptomatik olup, klinik ya bası bulgularına ya da kistin komplikasyonlarına baglı olarak ortaya çıkmaktadır.

Tanı için ultrasonografi (USG), bilgisayarlı tomografi (BT) ve manyetik rezonans inceleme (MRI) kullanılmaktadır.[5]

Kist hidatik (KH) tedavisinde temel prensipler; hastalığa sebep olan parazitin, ara konak formunun öldürülmesi ve/veya vücuttan uzaklaştırılması; kistin yol açabileceği komplikasyonların önlenmesi boşaltılması ve sorunsuz kapanmasının sağlanmasıdır. İdeal tedavi, hem hastalığın iyileştirilmesini tam olarak sağlamalı; hem de morbidite mortalitesi minimal olmalıdır.[6]

Ekstrahepatik primer intraabdominal hidatik kist nedeniyle cerrahi tedavi ettiğimiz olgular literatür eşliğinde incelendi ve yapılan cerrahinin nüks üzerine etkisine bakıldı.

Gereç ve Yöntemler

Mart 2017- Nisan 2020 yıllarına ait arşiv kayıtları esas alınarak, vakalar patoloji sonucu KH tanısı almış olgular olup toplam 56 hasta retrospektif olarak incelendi. Bunlardan extrahepatik primer KH 9 hasta çalışmaya dahil edildi. Olgular, yaş, cinsiyet ve lokalizasyonlarına göre sınıflandırıldı. Tüm hastalarda tanı aşamasında klinik öykü, fizik muayene, laboratuvar testleri ve radyolojik yöntemlerden yararlanıldı. Ameliyat öncesinde hastalara akciğer grafisi, US ve BT yapıldı. İndirekt hemaglütinasyon (IHA) testinde ≥1/160 serum titreleri pozitif olarak kabul edildi. Klinik öykülerinde daha önce hidatik kist nedeniyle te-

davi görmedikleri ve ilk tanı olduğu öğrenildi. Hastaların tamamı elektif şartlarda opere edildi.Ameliyat sonrası hastalar 6 ay andozal kullandı ve kontrol USG ile takipleri yapıldı.

Tanı amacı ile laboratuvar testleri, immünolojik yöntemler ve radyolojik görüntüleme yöntemleri kullanıldı. Extrahepatik yerlesimli primer kist hidatik saptanan hastalara sistemik tarama yapıldı. Operasyon öncesi tüm hastalar hem USG hem de batın BT istendi ve tanıları konuldu.

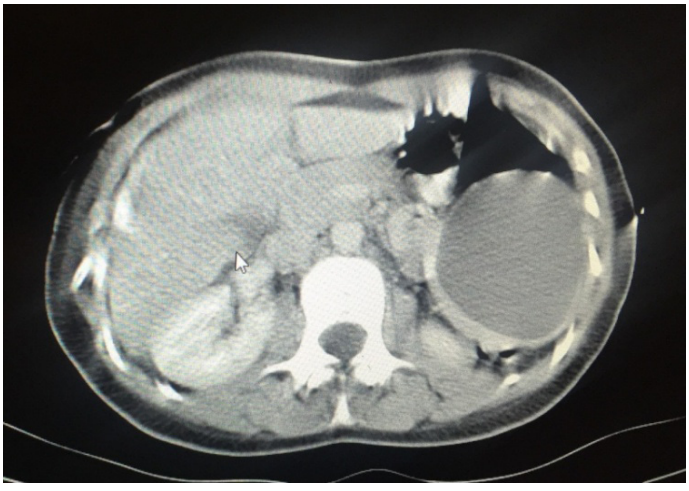
Çalışma Helsinki Deklerasyonu kararlarına, hasta hakları yönetmeliğine ve etik kurallara uygun olarak planlandı. Çalışma öncesinde Ankara Numune Eğitim ve Araştırma Hastanesi etik kurulundan onay alındı.(Tarih:21.05,2020 ve Karar no:2020-247) Hastalara aydınlatılmış onam belgesi imzalatıldı.

İstatistiksel Analiz

Verilerin analizi SPSS for Windows 11,5 paket programında yapıldı. Sürekli değişkenlerin dağılımının normale yakın olup olmadığı Shapiro Wilk testiyle araştırıldı. Tanımlayıcı istatistikler sürekli değişkenler için ortalama ± standart sapma veya ortanca (minimum-maksimum) olarak kategorik değişkenler ise olgu sayısı ve (%) şeklinde gösterildi.

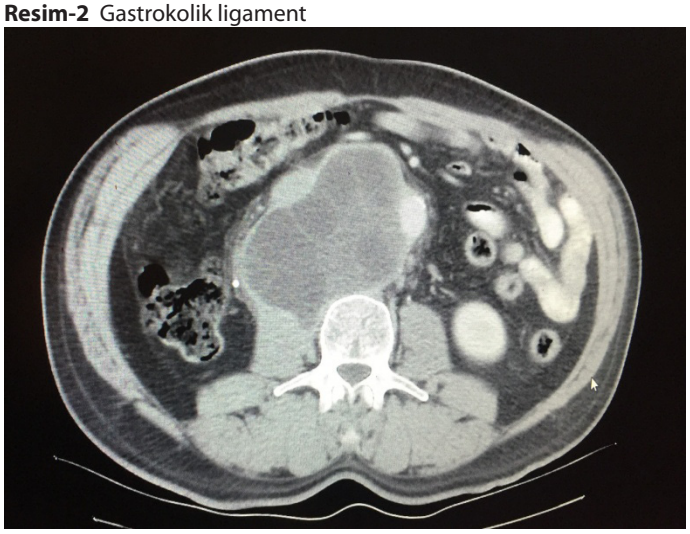
Bulgular

Çalışmaya dahil edilen 9 hastanın 6'sı kadın, 3 'ü erkek olup yaş ortalamaları 49,6 (22-74) olarak bulundu. Polikliniğe başvurma şikayetleri; 3'ünde mide ağrısı, 5'inde şişkinlik, 1'inde ise sarılık idi. Kist yerleşimi BT'ye göre 5 olguda dalak (resim 1), 3 olguda retroperitoneal (resim 2), 1 olguda gastrokolik ligament (resim 3) yerleşimli olarak saptandı. Kist boyutu ortalama 9,5 (5-13) cm olarak hesaplandı.(şekil 1)

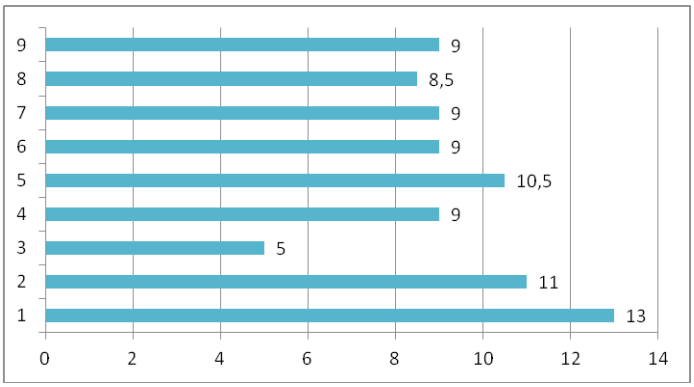


Resim -1 Dalak Kist Hidatik

Resim-2 Gastrokolik ligament



Resim -3 Retroduedonal



Sekil 1: Kist çapı (cm)

Tanı amacı ile laboratuvar testleri, immünolojik yöntemler ve radyolojik görüntüleme yöntemleri kullanıldı. Extrahepatik yerlesimli primer kist hidatik saptanan hastalara sistemik tarama yapıldı. Hastalar da İmmünolojik test olarak kullanılan İHA testinin 2 (%22,2) hastada pozitif olduğu görüldü. Operasyon öncesi tüm hastalar hem USG hem de BT istendi ve tanıları konuldu.

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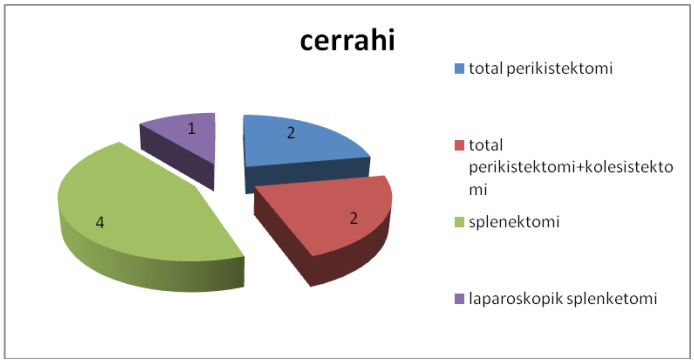
Hastalar genel anestezi altında, skolosidal ajan olarak % 3 hipertonik solusyon kullanıldı.Hastaların 4'üne splenektomi ,1 'ine laparoskopik splenektomi, 2' sine total perikistektomi ve 2'sine total perikistektomi+kolesistektomi yapıldı (şekil-2). Mortalite olmadı. Hastaların 2'sinde yara yerinde Hematom 1 'inde yara yeri enfeksiyonu gelişti.Ortalama hastanede yatış 5,2 gün (4-8) idi.



Sekil 2: cerrahi operasyon

Taburculuk sonrası hastalara 10 mg/kg dozunda 6 ay andazol başlandı. Hastaların hepsi 6 ay sonra kontrole çağrıldı ve USG ile kontrol edildi. Ortalama takip süresi 18,1 (6-43) ay idi.Takip sürelerinde herhangi nükse rastlanılmadı.

Tartışma

Ekinokokkus özellikle Avrupa, Asya, Akdeniz, Güney Amerika ve Afrika ülkelerinde endemik olarak görülmektedir.[7] Ülkemiz de KH açısından endemik bir bölge olarak değerlendirilmektedir.Türk toplumunda KH görülme sıklığı 1/2000 olarak bildirilmiştir.[8] Hidatik kist halen endemik bölgelerde yaygın olarak görülmektedir. Çoğunlukla karaciğer (%70) ve akciğerde (%20) yer almaktadır.[9,10] Ancak diğer organları da tutabilir. Ekstrahepatik intrabdominal hidatik kist tutulumu primer ya da sekonder olabilir. Primer ekstrahepatik intraabdominal hidatik kist oldukça nadirdir. Literatürde dalakta %2,2, pankreasta %1,1, periton, pelvis ve mezokolonda %2,2, safra kesesinde %0,6 ve sürrenal bezde %0,6 olarak bildirilmiştir.[11] Bu çalışmada tüm hastaların 9'unun (%6,1) primer ekstrahepatik intraabdominal hidatik kist olduğu saptandı. Bu hastaların da 5'inde dalak, 3'ünde retroperiton, bir olguyla da gastrokolik ligament içinde saptandı.

Dalak, üçüncü sıklıkta tutulan organ olmasına rağmen, endemik bölgelerde bile az görülen (%2,5–5,8) bir durumdur. Dalak yerleşimli KH'lerde, sistemik inceleme yapılmalı ve diğer organlarda bir tutulum olup olmadığı araştırılmalıdır.[12] Hastalık tablosu çoğunlukla sessiz olmasına rağmen, kistin enfekte olması, karın boşluğuna rüptür, gastrointestinal sisteme fistülizasyon ya da perforasyon gibi komplikasyonlar gelişebilmektedir .Bu çalışmada, izole dalak tutulumu; 5 vaka da saptandı ve tüm hastalara batın BT ve USG yapıldı.

Gastrokolik ligamentteki KH, oldukça nadir görüldüğü bölgelerdendir ve genellikle diğer organ tutulumuna ikincil olarak veya cerrahi sonrası görülür.[13] Kulaçoğlu ve ark. tarafından yapılan çalışma 3 vakada gastrokolik ligamentte KH saptanmıstır.[14] Bu çalışmada mide ağrısı ile gelen hastada yapılan BT de kist hidatik olduğu saptandı ve total perikistektomi uygulandı. Tüm tetkiklerde başka sistemlerde de kist hidatik olmadığı görüldü. Çok nadir görülen gastrokolik kist hidatik olarak tanımlandı.

Litaratürde retroperitoneal paraduedonal kist hidatikler hakkında çok az bilgi mevcut olup az görülmesine rağmen literatürde bildirilen toplam 4 vaka olup bu çalışmada 3 vakada olup 2 tanesine kolesistektomi+total perikistektomi birine de total perikistektomi yapıldı.

Klinik bulgular genelde asemptomatik olup semptomlar tutulan organlara, kistin büyüklüğüne ve organdaki yerleşimine, genişleyen kist ile kiste komşu organ yapıları arasındaki ilişkiye, kistin rüptürü sonucunda gelişen komplikasyonlara bağlıdır. [15,16] Bu çalısmada; karında şiskinlik hissi olan 5 olgu, 3 hastada mide ağrısı ve 1 hastada basıya bağlı sarılık yakınması vardı.

IHA testi sıklıkla tercih edilmekte olup, duyarlılığı %65-96.8 ve özgüllüğü %90-100 dür.[17] USG ve BT tanıda oldukça yardımcı modalitelerdendir. US'nin tanısal duyarlılığı %93-98, BT'nin ise %97'dir.[18] Ekstrahepatik intraabdominal yerleşimli hidatik kist olgularında da genellikle USG ve batın BT yapılmaktadır.[19] Tanıda ilk önce, ucuz ve kolay uygulanabilir bir yöntem olan US tercih edilmelidir. Ancak ekstrahepatik karın içi hidatik kist olguları nadir görüldüğünden genelde tanıları BT ile konulmaktadır. Çalısmada preoperetif tüm hastalara hem USG hem de batın BT yapıldı.

Tedavi yöntemleri cerrahi, medikal ve perkütan aspirasyon injeksiyon reaspirasyon (PAIR) olmak üzere üç başlık altında incelenebilir. Semptomatik ve büyük intraabdominal kistler komplikasyon gelişmeden önce ameliyat edilmelidir.[20] Genellikle organ rezeksiyonu yapılmadan kistin tamamının çıkarılması uygundur.[21] Bu çalısmada sarılık ve mide agrıs şikayetiyle gelen 2 hasta koledok basısı ve kolelithiazis olması nedeniyle kolesistektomi+total perikistektomi yapıldı. Diğer 5

vakada dalak hilus ile ilişkili olduğundan organ rezeksiyonuyla yapıldı. Çalısmada tüm hastalarda total perikistektomi yapıldığından takiplerinde nüks olmadığı saptandı.

Sonuç

Batın içi kitlelerde özellikle endemik bölgelerde Ekstrahepatik primer intraabdominal hidatik kist akla getirilmelidir. Hastalık tablosu çoğunlukla sessiz olmasına rağmen, kistin enfekte olması, karın boşluğuna rüptür, gastrointestinal sisteme fistülizasyon ya da perforasyon gibi komplikasyonlar gelişebilmektedir.Bu yüzden tedavide nüksü tamamen ortadan kaldıran total perikistektomi veya organ rezeksiyonuyla beraber total perikistektomi yapılmasını önermekteyiz.

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Orijinal Makale

Kronik spontan ürtikerde omalizumab tedavisinin etkinliği: Retrospektif bir çalışma

The efficacy of omalizumab therapy in chronic spontaneous urticaria: A retrospective analysis

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Öz

Amaç: Bu çalışmada tedaviye dirençli kronik spontan ürtiker (KSÜ) nedeni ile omalizumab tedavisi kullanan hastaların klinik ve demografik özelliklerinin yanısıra omalizumab etkinliği ile yan etkilerinin geriye dönük olarak değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Kliniğimizde 2014-2017 yılları arasında H1-antihistaminiklere direnç nedeni ile 300 mg/ay subkutan omalizumab başlanan KSÜ hastalarının kayıtlı bilgisayar verileri taranarak retrospektif olarak incelendi. Hiç ürtikeryal plağı ve kaşıntısı olmayanlar tam yanıtlı, tedavi başlangıcına göre hayat kalitesi artan ve semptomlarında belirgin iyileşme olanlar kısmi yanıtlı, semptomlarında hiç iyileşme olmayanlar yanıtsız olarak kabul edildi.

Bulgular: Tedaviye dirençli KSÜ nedeniyle omalizumab verilen 71 (41 K, 30 E) hasta çalışmaya dahil edildi. Bu hastaların ortalama hastalık süresi 54.6±52.9 (min-maks:8-360) ay olup, yaş ortalaması 43.6±16.4 (min-maks: 14-83) yıl idi. Omalizumab tedavisi 3. ayı sonunda hastaların yapılan değerlendirilmesinde, 14 (19.7%) hastada tam yanıt, 36 (50.7%) hastada kısmı yanıt görülürken, 21 (%29,6) hastada yanıt alınamadı. Başlangıç total IgE ve CRP düzeyleri, hastalık süresi, hasta yaşı, cinsiyeti, astım öyküsü ve immünsupresif kullanım öyküsü açısından 3. ay sonu omalizumab tedavisi yanıt grupları arasında herhangi bir istatistiksel farklılık tespit edilmedi (p>0.05). Hastalarda ciddi bir yan etki saptanmadı.

Sonuç: Bu çalışmada, KSÜ nedeniyle takip edilip omalizumab kullanılan hastalarda, omalizumab tedavisinin etkin ve güvenilir olduğunu tespit ettik.

Anahtar kelimeler: ürtiker; omalizumab; immunoglobulin e

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Abstract

Aim: In this study, it was aimed to evaluate the clinical and demographic features of patients using omalizumab therapy for treatment-resistant CSU, as well as the efficacy and side effects of omalizumab retrospectively.

Material and Methods: In our clinic, we retrospectively checked the computer data of CSU patients who began subcutaneous omalizumab 300 mg / month due to H1-antihistamin resistance between 2014 and 2017. Those without urticaria plaque and itching were considered to be a complete response; those with improved quality of life relative to the onset of treatment and significant improvement in their symptoms were considered to be a partial response; and those with no improvement in symptoms were considered to be unresponsive.

Results: Seventy-one (41 F, 30 M) patients who received omalizumab for treatment-resistant CSU were included in the study. The mean disease duration of these patients was 54.6 ± 52.9 (min-max: 8-360) months and the mean age was 43.6 ± 16.4 (min-max: 14-83) years. In patient evaluation at the end of the third month of treatment with omalizumab, 14 (19.7%) patients had complete response, 36 (50.7%) patients had partial response, whereas 21 (29.6 %) patients had no response. At the end of the 3rd month there was no statistical difference between the omalizumab treatment response groups in terms of baseline total IgE and CRP levels, disease duration, patient age, sex, history of asthma, and history of immunosuppressive use. There were no significant side effects in the patients.

Conclusion: In this study, we found that treatment with omalizumab was effective and safe in patients who were being followed up due to CSU and used omalizumab.

Keywords: omalizumab, urticaria, immunglobulin e

Giriş

Heterojen bir hastalık olan ürtikerin klinik görünümüne göre değişik alt tipleri olsa da, gözlenen ortak deri reaksiyonu kaşıntılı eritemli ödemli ürtikeryal deri lezyonları ve/veya anjiyoödemdir.[1,2] Yaklaşık olarak insanların %9'unun tüm hayatı boyunca en az bir kez ürtiker atağı geçirdiği ve bu olguların da %0,1-1'inde 6 haftadan daha uzun süreli ürtikeryal lezyonlar ile karakterize kronik ürtiker (KÜ) geliştiği düşünülmektedir. En sık görülen ürtiker tipi olan ve herhangi bir dış uyaran olmaksızın meydana gelen spontan ürtiker tablosuna kronik spontan ürtiker (KSÜ) adı verilmektedir.[2] KSÜ tablosunun oluşumunda gıda ve ilaçlara karşı intolerans reaksiyonları, enfeksiyonlar ve otoreaktif mekanizmalar gibi altta yatan çeşitli faktörlerin rol oynadığı düşünülmektedir.[1,2]

Kronik ürtiker klavuzu, KSÜ tedavisinde üç basamaklı bir yaklaşım önermektedir. Birinci basamakta, ikinci kuşak antihistaminik ilaçlar kullanımını, bu tedaviye yanıt vermeyen hastalarda ikinci basamakta dört katına kadar doz artırımını önermektedir. Semptomların devam etmesi halinde ise üçüncü basamak tedavide omalizumab veya siklosporin A veya lökotrien reseptör antagonisti (LTRA) kullanımı önermektedir.[3] Omalizumab, serum immunglobulin E (IgE)'lerine bağlanarak, IgE'nin mast hücre ve dolaşan bazofiller üzerindeki yüksek afiniteli IgE reseptörüne bağlanmasına engel olmaktadır. Böylelikle IgE'nin efektör fonksiyonlarını inhibe ederek selüler medyatörlerin salınımını inhibe etmektedir.[4] Sonuçta omalizumab duyarlı allerjenle tetiklenen efektör hücre aktivasyonunu önlemekte ve allerjenlere karşı gelişen hem erken hem de geç faz yanıtlarını azaltmaktadır.[5] Güvenilirlik açısından bakıldığında ise bir çok derleme ve meta-analizde omalizumab tedavisinin genel yan etki insidansını arttırmadığı gösterilmiştir.[6,7]

Literatür incelendiğinde bu konuda gerçek yaşam deneyimini sunan, Güneydoğu Anadolu Bölgesinde yapılmış az sayıda çalışma olduğu saptanmıştır.[8,9] Çalışmamızda, 3. basamak bir sağlık kurumu olan hastanemizde tedaviye dirençli KSÜ nedeni ile omalizumab tedavisi kullanan hastaların klinik ve demografik özelliklerinin yanısıra omalizumab etkinliği ile yan etkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler

Kliniğimizde 2014-2017 yılları arasında tedaviye direnç nedeni ile omalizumab başlanan KSÜ hastaların kayıtlı bilgisayar verileri taranarak omalizumab etkinliğinin ve yan etkilerinin retrospektif olarak incelenmesi planlandı. Hastaların dosyalarından yaş, cinsiyet, hastalık süresi, daha önce kullanılan tedaviler ve labarotuvar testlerinden tam kan sayımı ve total IgE düzeylerinin kaydedilmesi planlandı.

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Omalizumab tedavisi başlanmadan önce tüm hastaların en az altı ay süre ile ikinci kuşak antihistaminik tedavisi kullanmış olması gerekmektedir. İkinci kuşak antihistaminik olarak desloratadin, loratadin, setirizin, levosetirizin, feksofenadin veya rupatadinden en az biri standart dozda kullanılmaktadır. Bu tedavilere rağmen ürtiker semptomları kontrol altına alınamayan KSÜ'li hastalar antihistaminik tedavisine dirençli kabul edilmektedir ve omalizumab tedavisi, subkutan enjeksiyon olacak şekilde başlanmaktadır.

Hastalar aylık kontrollerinde omalizumab sonrası enjeksiyon yerinde ağrı, morarma, şişme, kızarıklık ve kaşıntı gibi geçici enjeksiyon bölgesi reaksiyonları açısından ve nazofarenjit, üst solunum yolu infeksiyonu, baş ağrısı ile sinüzit gibi yan etkiler açısından değerlendirilmektedir.

Kliniğimizde Omalizumab dozu şu an için Sağlık Bakanlığı tarafından KSÜ için geri ödeme kapsamında olan 300 mg/ay olarak verilmektedir. Tedaviye yanıtsız hastalar için sağlık bakanlığına doz artırımı için başvuruda bulunulmaktadır.

Hastalar tedavi yan etkisi ve etkinlik açısından aylık olarak dermatoloji uzman hekimi tarafından değerlendirilmektedir. 3 aylık tedavi sonrasında hiç ürtikeryal plağı ve kaşıntısı olmayanlar tam yanıtlı, tedavi başlangıcına göre hayat kalitesi artan, ürtikeryal plağı ve kaşıntısı azalan ancak hala tam geçmeyen hastalar kısmi yanıtlı, semptomlarında hiç iyileşme olmayanlar yanıtsız olarak kabul edilmiştir. Bu çalışma için etik kurul izni Sanko Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu'ndan alınmıştır. Hastalara aydınlatılmış onam belgesi imzalatılmıştır.

İstatistiksel Analiz

Tanımlayıcı istatistik olarak; ölçümle belirtilen sürekli değişkenler için ortalama ve standart sapma veya medyan ve minimum-maksimum değerleri, nitel değişkenler için frekans ve yüzde değerleri verilmiştir. Grup karşılaştırmalarında; ölçümle belirtilen sürekli değişkenler için parametrik test koşullarının sağlanması durumunda iki ortalama arasındaki farkın önemlilik testi, parametrik test koşullarının sağlanmadığı durumlarda Mann-Whitney U testi kullanılmıştır. Nitel değişkenlerin grup karşılaştırmaları için ki-kare testi kullanılmıştır.

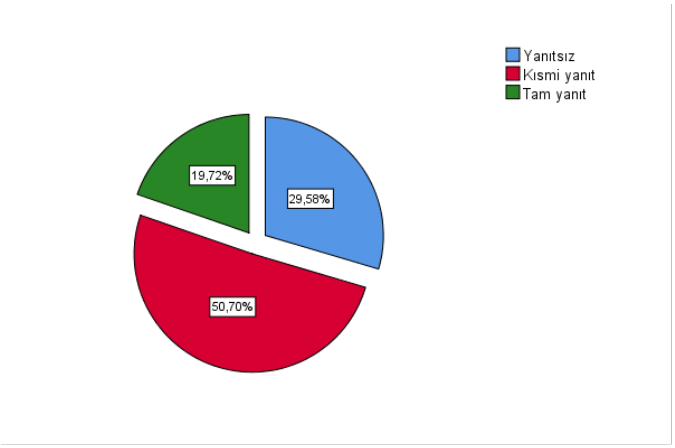
Bulgular

Çalışmaya alınan hastaların demografik ve klinik özellikleri Tablo 1'de belirtildi. Tedaviye dirençli KSÜ nedeniyle omalizumab verilen 71 (41 K, 30 E) hasta çalışmaya dahil edildi. Bu hastaların ortalama hastalık süresi 54.6±52.9 (min-maks:8-360) ay olup, yaş ortalaması 43.6±16.4 (min-maks: 14-83) yıl idi. Ortalama omalizumab kullanma süresi 6.2±4.1 (min-maks:2-19) ay idi. Hastaların başlangıç total IgE düzeyleri ortalaması 6.2±4.1(min-maks:18-5660) IU/ml idi. 27 (34,2) hastanın başlangıç CRP düzeyleri normalden yüksek idi. 39 (%49,4) hasta omalizumab tedavi öncesinde sistemik steroid kullanmış iken, 10 (%12,7) hasta da immünsupresif (siklosporin) kullanma öyküsü mevcuttu. 9 (%11,4) hastanın astım öyküsü mevcuttu.

Tablo 1: Hastaların klinik ve demografik özellikleri

Parametreler	**Bulgular**
Yaş (ort ± SD) (yıl)	43.6±16.4
Kadın (n) (%)	41 (%51,9)
Hastalık süresi (ort ± SD) (ay)	54.6±52.9
Omalizumab tedavi süresi (ort ± SD) (ay)	6.2±4.1
IgE [IU/ml]	625,2±946,3
Eozinofil %	2,2±3,5
CRP pozitiflik (n) %	27(%34,2)
Sistemik steroid kullanım öyküsü n(%)	39(%49,4)
Sistemik immünsupresif kullanım öyküsü n(%)	10(%12,7)
Astım öyküsü n(%)	9(%11,4)

Omalizumab tedavisi 3. ayı sonunda hastaların yapılan değerlendirilmesinde, 14 (19.7%) hastada tam yanıt, 36 (50.7%) hastada kısmı yanıt görülürken, 21 (%29,6) hastada yanıt alınamadı (Şekil 1). Tedavi esnasında kaydedilen yan etkiler incelendiğinde sadece iki (2,8%) hastada uygulama bölgesinde lokal eritem tespit edildi. İlaç ile ilişkili olduğu düşünülen sistemik bir yan etki görülmedi. Hastaların takiplerinde klinik değerlendirilmesinde ve fizik muayenesinde herhangi bir sorun saptanmadı. Omalizumab tedavisinin iyi tolere edildiği tespit edildi.



Şekil 1. Omalizumab tedavisinin 3. ay sonunda hastaların değerlendirilmesine göre elde edilen sonuçlar

Başlangıç total IgE, eozinofil, bazofil ve CRP düzeyleri, hastalık süresi, hasta yaşı, cinsiyeti, astım öyküsü ve immünsupresif kullanım öyküsü açısından 3. ay sonu omalizumab tedavisi yanıt grupları

arasında herhangi bir istatistiksel farklılık tespit edilmedi (p>0.05).

Hasta dosyaları incelendiğinde 22 (%30,9) hastanın halen ilaç kullanımına devam etmekte olduğu tespit edildi. Tedaviye devam etmekte olan iki hastada yetersiz yanıt nedeni ile omalizumab dozunun iki katına çıkarıldığı tespit edildi. Yine tedaviye devam etmekte olan üç hastanın ise omalizumab tedavisine ek olarak siklosporin kullandığı tespit edildi. Tedaviyi bırakan 25 (%35,2) hastada tam remisyon gözlendiği için tedavinin kesildiği saptandı. 15 (%21,1) hastanın ise tedavi yanıtsızlığı nedeni ile tedaviyi bıraktığı tespit edildi. 8 (%11,3) hastanın ise tedaviyi bırakma sonrasında antihistaminik kullanmaya devam eden kısmi yanıtlı olan hastalar olduğu tespit edildi.

Tartışma

Kronik spontan ürtiker; kronik ve nükseden seyri, nükslerin öngörülemezliği ve şiddetli kaşıntılı lezyonlar nedeni ile genellikle hastalar üzerinde ağır bir psikososyal yük oluşturur.[10] Tedavinin amacı hastalığa bağlı semptomları yan etkileri olmayan tedavilerle kontrol etmektir. Tedavide ilk seçenek olarak ikinci nesil ve sedatizasyon özelliği olmayan H1 bloke edici antihistaminikler tercih edilmektedir. Bununla birlikte, hastaların önemli bir oranı yüksek dozlarda antihistaminiklere yanıtsız seyretmektedir. Son yıllarda ise antihistaminiklere yanıtsız KSÜ hastalarında bir anti-IgE monoklonal antikoru olan omalizumab, tedavi kılavuzları tarafından etkili ve güvenli bir ajan olarak önerilmektedir.[11]

Erken faz 2 ve faz 3 randomize plasebo kontrollü, çok merkezli çalışmalarda H1 antihistaminikleri lisanslı dozlarda daha önce kullanılmasına rağmen halen semptomatik olan KSÜ hastalarında omalizumabın semptomları kontrol etmede yararlı etkinlik gösterdiği saptanmıştır.[12,13] Maurer ve ark.'nın [13] 2013 yılında yaptıkları faz 3 çok merkezli randomize çift kör çalışma ile Metz ve ark.'nın [14] 4 yıllık retrospektif analizinde hem KSÜ hem de kronik indüklenebilir ürtiker hastalarında omalizumab tedavisinin hızlı, yüksek oranda etkili ve güvenilir bir tedavi seçeneği olduğu sonucuna varılmıştır. Yapılan pek çok gerçek yaşam çalışmasına rağmen günümüzde omalizumab tedavisinin ne kadar sürmesi ve nasıl kesilmesi gerektiği ve uzun dönem yan etkileri gibi bir takım soru işaretleri halen mevcuttur. Bu nedenle daha fazla sayıda gerçek yaşam verisi içeren çalışmaya ihtiyaç halen devam etmektedir. Bu çalışmada omalizumab kullanan KSÜ hastalarının gerçek yaşam verilerinin belirlenmesi amaçlanmıştır ve dirençli KSÜ'de omalizumabın güvenli ve etkili bir tedavi seçeneği olduğu gözlenmiş olup bu sonuçlar bugüne kadarki literatür verilerini destekler niteliktedir.

Bu çalışmada 3 ay sonunda 14 (19.7%) hastada tam yanıt, 36 (50.7%) hastada kısmi yanıt görülürken, 21 (%29,6) hastada yanıt alınamadığı tespit edilmiştir. Omalizumab kullanan hastalarda gerçek yaşam verilerinin değerlendirildiği ve 45 çalışmanın dâhil edildiği ve 1158 hastanın sonuçlarının değerlendirildiği son bir metaanalizde %30 ile 100 arasında değişen ve ortalaması %76 olarak tespit edilen tam yanıt oranları bildirilmiştir.[15]. Ülkemizde yapılan gerçek yaşam verilerinin değerlendirildiği çalışmalarda ise elde edilen tam yanıt oranları %13,3 ile %76,9 arasında değişmektedir.[8,9, 16-19] Literatürde elde edilen farklı sonuçların çalışmalarda hastalara uygulanan omalizumab dozlarının farklı olmasına, klinik yanıtın değerlendirilme farklılıklarına ve etnik farklılıklara bağlı olabileceğini düşünmekteyiz. Bazı çalışmalarda klinik cevap yanıt var veya yok şeklinde sınıflandırılırken, bazı çalışmalarda ise klinik yanıt çalışmamızda olduğu gibi tam yanıt, kısmi yanıt ve yanıtsız şeklinde sınıflandırma yapılmıştır.[15] Ayrıca yapılan çalışmaların çoğunda kullanılan ek tedavilerle ilgili bilgilendirme eksikliği tespit edilmiştir.[20] Çalışma sonuçlarında ki farklılığın bir nedenide ülkelerin sağlık bakanlıklarının farklı geri ödeme politikaları olabileceğini düşünmekteyiz. Ülkemizde omalizumab daha önce en az 6 ay süreyle antihistaminik tedavisi almış ancak yanıt alınamamış olan hastalarda geri ödeme kapsamındadır.

Bu çalışmada yan etki olarak sadece iki hastada ilacın uygulandığı bölgede lokal eritem görüldü, bu hastaların fiziksel incelemesinde ve takiplerinde herhangi bir sorun tespit edilmedi. Bunun dışında omalizumab ile ilişkili yan etki görülmedi. Tedavi iyi tolere edildi. Literatürde astım ve KSÜ de omalizumab tedavisinin güvenilir olduğu birçok derleme, metanaliz ve çalışmada gösterilmiştir.[3-9]

Astımın aksine, KSÜ'de omalizumab dozu IgE seviyelerinden bağımsız olarak ayarlanmaktadır. Omalizumab'a tam yanıt verenlerde, semptomları bastırmak için gerekli doz ile toplam serum IgE seviyeleri arasında herhangi bir korelasyon saptanmamıştır ve omalizumab tedavisinin etkinliğinin başlangıç total IgE değerlerinden bağımsız olduğu düşünülmektedir.[14] Bu çalışmada yine literatürle uyumlu olarak klinik iyileşmenin başlangıç total IgE düzeylerinden bağımsız olduğu gözlendi.[17,19] Hastalarda tedavi etkinliğinin, hastaların başlangıç IgE değerlerinden çok zaman içerisinde gözlenen IgE artışı ile korelere olduğu yine son zamanlarda yapılan bir çalışmada saptanmıştır.[21]

Bu çalışmanın üstünlükleri, geriye dönük olarak gerçek yaşam deneyimlerini aktarması ve hasta popülasyonunun heterojen olmasıdır. Ek olarak omalizumab kullanım süresinin 6.2±4.1 ay ile yeterli bir süre olduğunu görmekteyiz. Çalışmanın kısıtlılıkları ise tek merkezli bir çalışma olması ve geriye dönük bir çalışma olması nedeni ile hastaların ürtiker aktivite skorlarının değerlendirilmemiş olmasıdır.

Sonuç

Bu çalışmada, kendi hastanemizde KSÜ nedeniyle takip edip omalizumab verdiğimiz hastalarda, omalizumab tedavisinin oldukça etkin ve yan etki açısından da güvenilir olduğunu tespit ettik.

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Orijinal Makale

Üniversite öğrencilerinin yeme davranışlarının Hollanda Yeme Davranışı Anketi (DEBQ) ile değerlendirilmesi: Osmaniye Korkut Ata Üniversitesi Örneği

Evaluation of the eating behavior of university students with the Dutch Eating Behavior Questionnaire (DEBQ): The case of Osmaniye Korkut Ata University

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Öz

Amaç: Üniversite döneminde gençlerin ciddi beslenme sorunları yaşadığı bilinmektedir. Bu çalışmada, üniversite öğrencilerinin cinsiyetlerine, yaşadıkları yerlere, vücut kütle indekslerine ve eğitim alanlarına göre yeme davranışlarının incelenmesi hedeflenmiştir.

Gereç ve Yöntemler: Çalışma, Aralık 2019 – Şubat 2020 tarihleri arasında, Osmaniye Korkut Ata Üniversitesi'nde öğrenim gören 726 öğrenci ile yapılmıştır. Yeme davranışları, Türkiye'de yaşayan insanlar üzerinde geçerliliği ve güvenilirliği 2009 yılında Bozan tarafından uyarlanan ve 33 maddeden oluşan Hollanda yeme davranış anketiyle (DEBQ) değerlendirilmiştir. Bu anket duygusal yeme davranışlarını, dışsal yeme davranışlarını ve kısıtlı yeme davranışlarını değerlendiren 3 alt ölçekten oluşmaktadır. Anketteki her bir madde 5'li Likert skalası (1:hiçbir zaman, 2:nadiren, 3:bazen, 4:sık, 5:çok sık) ile değerlendirilmektedir.

Bulgular: Katılımcıların 387 (%53,3)'si kadın, 339 (%46,7)'ü erkek olup; yaş ortalaması 22±2 (18-30)'dir. Vücut kitle indeksine (VKİ) göre katılımcıların dağılımı incelendiğinde; 66 (%9) zayıf, 371 (%51) normal, 241(%33) fazla kilolu, 51 (%7) ise obezdir. Cinsiyete göre değerlendirildiğinde, duyusal yemenin kadınlarda fazla olduğu bulundu ($p<0,01$). Kısıtlayıcı ve dışlayıcı yemede gruplar arasında anlamlı fark gözlenmedi ($p>0,05$). Eğitim alanlarına göre; kısıtlayıcı yeme açısından gruplar arasında anlamlı fark saptanmazken ($p=0,18$); duyusal ve dışlayıcı yeme açısından anlamlı farklılık saptandı ($p<0,05$, $p=0,02$). Yaşadıkları yere göre; duyusal, kısıtlayıcı ve dışsal yeme açısından anlamlı farklılık saptandı ($p<0,001$, $p=0,03$, $p=0,04$). VKİ' ye göre; gruplar arasında duyusal yeme açısından anlamlı fark saptanmazken ($p=0,74$); dışsal ve kısıtlayıcı yeme davranışı açısından anlamlı farklılık saptandı ($p<0,001$, $p<0,001$).

Sonuç: Çalışmamızda, DEBQ'nun alt ölçeklerini kullanarak, öğrencilerin okudukları alanlara, yaşadıkları yere, VKİ'lerine, cinsiyetlerine göre oluşan verileri analiz ettik, yeme bozukluğu riski yüksek olan popülasyonun VKİ, cinsiyet, okudukları alan ve yaşadıkları çevrenin ilişkili olduğunu gösterdik.

Anahtar kelimeler: yeme bozuklukları; DEBQ; genç; beslenme

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Abstract

Aim: t is known that young people experience serious nutritional problems during university period. In this study, it was aimed to examine the eating behaviors of university students according to their gender, their place of residence, body mass index and education area.

Material and Methods: The study was carried out with 726 students studying at Osmaniye Korkut Ata University between December 2019 - February 2020. Eating behavior, validity and reliability of the people living in Turkey and the Netherlands in 2009. Impairments adopted by the eating behavior questionnaire consisting of 33 items (DEBQ) were evaluated. This questionnaire consists of 3 subscales that evaluate emotional eating behaviors, external eating behaviors and limited eating behaviors. Each item in the questionnaire is evaluated with a 5-point Likert scale (1: never, 2: rarely, 3: sometimes, 4: frequent, 5: very often).

Results: 387 (53.3%) of the participants were women and 339 (46.7%) were men; average age is 22 ± 2 (18-30). When the distribution of participants according to body mass index (BMI) is examined; 66 (9%) are weak, 371 (51%) are normal, 241 (33%) are overweight and 51 (7%) are obese. When evaluated by gender, sensory eating was found to be more in women ($p < 0.01$). No significant difference was observed between the groups in restrictive and exclusive food ($p > 0.05$). According to the fields of education; no significant difference was found between the groups in terms of restrictive eating ($p = 0.18$); There was a significant difference in sensory and exclusive eating ($p < 0.05$, $p = 0.02$). According to where they live; There was a significant difference in sensory, restrictive and exogenous eating ($p < 0.001$, $p = 0.03$, $p = 0.04$). According to the BMI; There was no significant difference in sensory eating between groups ($p = 0.74$); There was a significant difference in terms of external and restrictive eating behavior ($p < 0.001$, $p < 0.001$).

Conclusion: In our study, using the sub-scales of DEBQ, we analyzed the data formed according to the areas where students read, where they live, their BMI, gender, and we showed that the population with a high risk of eating disorder is related to the BMI, gender, the area they study and the environment they live in.

Keywords: eating disorders; DEBQ; young; nutrition

Giriş

Dünya Sağlık Örgütü (DSÖ) sağlığı; sadece hastalık ve sakatlığın olmayışı değil, insanın fiziksel, zihinsel ve sosyal yönden tam bir iyilik halinde olması şeklinde tanımlamıştır [1]. Fetüsün oluşması ile başlayan beslenme; büyüme ve gelişmenin sağlanması, sağlığın korunması, sürdürülmesi, geliştirilmesi ve yaşam kalitesinin yükseltilmesi için vücudun ihtiyacı olan besin öğelerini yeterli miktarlarda ve uygun zamanlarda almak amacıyla, bilinçli yapılması gereken bir eylemdir [2].

Üniversite öğrencilerinin çoğunluğu aile ortamından uzaklaştıkları için üniversite ortamında hiç tecrübe etmediği yeni alışkanlıklar kazanabilirler. Yaşadıkları coğrafyanın değişmesi, ailelerinden ayrı bir evde - yurtta veya apartta yaşamaya başlamaları, yemek hazırlama alışkanlığı edinememeleri, ev yemeği tüketimini azaltmaları, dışarıda yemek yemelerinin daha cazip ve kolay gelmesi gibi dış etkiler ve özgürce karar verebilmeleri sayesinde beslenme alışkanlıkları değişebilmektedir [3]. Bu nedenle üniversite öğrencilerinin çoğunluğu mevcut alışkanlıklarından uzaklaşmakta ve bu yeni ortamda hiç tecrübe etmedikleri beslenme alışkanlıkları ile yetersiz ve dengesiz beslenmeye başlayabilmektedirler [4].

Gençlik dönemi, özellikle 18-24 yaş arası dönem, mevcut sağlığın korunması, geliştirilmesi ve hastalıkların önlenmesi açısından önemli bir yaş dönemi olarak bilinmektedir. Bu nedenle bu yaş döneminde yer alan üniversite öğrencileri, son yıllarda pek çok çalışmanın hedef grubunu oluşturmaktadır [5].

Üniversiteyi yeni kazanmış gençler yaş dönemi olarak incelendiğinde, bu gençlerin ergenliğin son safhalarında oldukları bilinmektedir. Ergenlerde kontrolsüz aşırı yemenin giderek yayıldığı görülmektedir. Obez ergenlerde anksiyete ve depresyon ile kontrol kaybı arasında anlamlı ilişki bulunmuştur. Duygusal yemenin erken tespiti, kilo kontrolünün sağlanması, çarpık yeme bozukluklarının önlenmesi ve tedavisi için önemlidir [6]. Yapılan bir çalışmada genel ebeveynlik ile duygusal yeme arasındaki ilişki incelenmiş, ebeveynlik ve aile etkileşiminin duygusal yeme üzerinde önemli etkiye sahip olabileceği bildirilmiştir. Ailelerinden ayrı yaşamaya başlayan üniversite öğrencilerinde bu durumun görülebileceği unutulmamalıdır [7].

Topham ve arkadaşları Hollandalı ergenlerin eğitiminde, düşük anne desteğinin, yüksek psikolojik kontrolün ve yüksek davranışsal kontrolün artan duygusal yeme ile ilişkili olduğunu belirtmiştir [8].

Ülkemizde gençlerin beslenme alışkanlıkları ile ilgili yapılan araştırmalarda üniversite dönemindeki beslenmede çok ciddi sorunların yaşandığı bildirilmektedir. Öğrencilerin bu dönemde genellikle öğünlerine dikkat etmedikleri, tek öğün yemek yedikleri, sandviç ve simit gibi yiyecekleri daha çok tükettikleri, ekonomik zorlukların yetersiz ve dengesiz beslenme probleminde etkili olduğu, yurtta kalan öğrencilerin yurt şartlarının kötü olmasından dolayı beslenmelerinin iyi olmadığı, sadece karınlarını doyurdukları farklı zamanlarda yapılan araştırmalarda ortaya konulmuştur [9]. Yapılan bir başka çalışmada ise yetersiz ve dengesiz beslenmenin mental gelişme üzerinde de olumsuz etkiler yaptığı, kişilerin zekâ düzeylerinde düşüşe, öğrenmede güçlüğe, davranış bozukluklarına ve neden olduğu belirtilmektedir [10].

Ayrıca duygusal yeme, bulimia ner¬vozada yeme ataklarını tetikleyen muhtemel bir faktör olarak tanımlanmıştır. Buna göre Bulimia nervozada tıkınırcasına yeme atakları¬la var olan stres ve negatif duygu durumunun azaltılacağı görüşü mevcuttur. Aneroksiya nervozadaki duygu durumu ise daha çok kişinin yeme davra¬nışı üzerindeki kontrol mekanizmasını kaybetme korkusu ta¬şıması ile ilişkilendirilmektedir. Her iki durumda da bireyler, içinde bulundukları duygu durumunu tanım¬layamadıkları için duygularla baş edebilmenin bir yolu olarak aşırı yeme ya da yememe davranışı sergilemektedirler [11].

Yemek yeme özellikle genç insanlar için otomatik bir süreç değildir. Her birimizin hissettiği kültürel, sosyal ve psikolojik baskılardan büyük oranda etkilenmektedir. Son 30 yılda, yemek yeme motivasyonunu, yeterli besin alımını ve vücut ağırlığı kontrolünü bozabilecek davranışları değerlendirmek için teoriler geliştirilmiştir. Psikolojik teorilere dayanarak, Van Strien ve ark. üç farklı yeme davranışı tanımladı. "Duygusal yeme", içsel fizyolojik açlık sinyalleri olmadan, tokluk sinyalini göz ardı ederek stresi hafifletmek için olumsuz duygularla baş edebilmek için yemeyi ifade eder. "Dışsal yeme", açlık ve tokluk sinyallerine bakılmaksızın besin tüketimi ile ilgili uyaranlara (besinle karşılaşma veya kokusu) yanıt olarak yeme anlamına gelir. "Kısıtlayıcı yeme" teorisi bilinçli olarak besin alımını kısıtlama derecesini (belirli bir kilo vermek veya korumak için yemekten kaçınma girişimleri) yansıtır [12].

Çoğu çalışma bu üç yeme davranışının beden kitle indeksi (BMI) ile bağlantılı olduğunu göstermiştir [13,14]. Bu üç tür yeme davranışı, Hollanda Yeme Yeme Davranışı Anketi (DEBQ) kullanılarak güvenilir ve geçerli bir şekilde ölçülebilir. DEBQ her birinde 5'li Likert ölçeği ("asla" ile "çok sık" arasında değişen) bulunan 33 maddeden oluşmaktadır . Orijinal DEBQ'nun İngilizce versiyonu birçok dile çevrilmiştir: Tüm sürümler iyi faktöriyel geçerlilik göstermiştir. DEBQ, cinsiyetler, ağırlık kategorileri ve rastgele numuneler arasında stabil bir faktör yapısına sahiptir [15].

Bu çalışmada, üniversite öğrencilerinin cinsiyet, yaşadıkları yer, beden kütle indeksi ve eğitim gördükleri bölümlere göre yeme davranışlarının incelenmesi hedeflenmiştir.

Materytal ve Metod

Çalışmamız; Aralık 2019 – Şubat 2020 tarihleri arasında, Osmaniye Korkut Ata Üniversitesi'nde eğitim ve öğrenim görmekte olan 726 öğrencinin katılımı ile yapılmıştır. Katılımcılar çalışmaya gönüllü olarak katılmışlardır.

Çalışmaya üniversitemiz öğrencisi olan ve herhangi bir kronik hastalık öyküsü olmayan öğrenciler gönüllülük esasına göre dahil edilmiştir. Kronik hastalığı olmak ve üniversitemiz öğrencisi olmamak dışında çalışma harici tutulma kriteri bulunmamaktadır.

Katılımcıların demografik verileri (yaş, cinsiyet), vücut ağırlıkları, boy uzunluğu, eğitim gördükleri fakülte, eğitim süresince konaklama bilgisi sordu ve ardından yeme davranışlarını değerlendirmek amacıyla anket uygulandı.

Araştırmaya katılan bireylerin yeme davranışlarının değerlendirilmesinde Türkçe geçerlilik ve güvenilirliği 2009 yılında Bozan tarafından yapılan [13], 33 maddeden oluşan Hollanda yeme davranış anketi (DEBQ) kullanılmıştır. Bu anket duygusal yeme davranışlarını, dışsal yeme davranışlarını ve kısıtlı yeme davranışlarını değerlendiren 3 alt ölçekten oluşmaktadır. Ankette yer alan maddeler 5'li Likert skalası ile değerlendirilmektedir (1: hiçbir zaman, 2: nadiren, 3: bazen, 4: sık, 5: çok sık). Testin toplam skoru değerlendirilmemekte 3 alt ölçek kendi içinde değerlendirilmektedir. Testin skorlamasında her hangi bir kesim noktası olmazken 3 alt ölçeğin kendi içinde değerlendirilen toplam puanının yüksek olması yeme davranışı ile ilgili olumsuzluğu göstermektedir. Hollanda Yeme Davranışı anketinin Türkçe versiyonunda ilk 10 soru kısıtlı yeme, 11-23 arası duygusal yeme, 24-33 arası ise dışsal yeme tutumunu değerlendiren sorulardır. Dışsal yeme skalasında bulunan 31. soru ise ters sorudur. Verilerin istatistiksel analizinde SPSS (IBM SPSS Statistics 21) paket programı kullanılmıştır. Bulguların yorumlanmasında tanımlayıcı istatistikler kullanılmıştır. Tanımlayıcı değerler sayı (n), yüzde (%), aritmetik ortalama (<<), standart sapma (SS), medyan (M) ve çeyrekler arası (IQR) olarak belirtilmiştir. Parametrik yöntemlere uygun şekilde, iki bağımsız değişkenin karşılaştırılmasında "Indepedent Sample-t" test (t-tablo değeri), ikiden fazla bağımsız değişkenin karşılaştırılmasında One-way ANOVA testi kullanılmıştır. İki nitel değişkenin

birbiriyle olan ilişkilerinin incelenmesinde beklenen değer düzeylerine göre χ2-çapraz tabloları kullanılmıştır.

Bulgular

Çalışmamıza katılan öğrencilerin 387 (%53,3)'si kadın, 339 (%46,7)'ü erkek olup; yaş ortalaması 22±2 (min:18,max:30) idi. Vücut kitle indeksi (VKİ) ortanca değeri 23,9 (IQR: 20,9-26,6). Katılımcıların VKİ'ne göre dağılımı incelendiğinde; 66 (%9) zayıf, 371 (%51) normal, 241(%33) fazla kilolu, 51 (%7) ise obez idi (Tablo 1).

Katılımcıların eğitim gördükleri bölümlere göre dağılımı incelendiğinde; 118'i (%16,3) sağlık bilimleri, 169'u (%23,3) mühendislik, 98'i (%13,5) fen-edebiyat, 68'i (%9,4) ilahiyat, 167'si (%23) iktisadi ve idari bilimler fakültesi (İİBF) ve 106'sı (%14,6) meslek yüksek okulu (MYO) idi (Tablo 1).

Katılımcıların konaklama yeri incelendiğinde; 80 (%11)'ı ailesiyle evde, 143'ü (%19,7) arkadaşlarıyla evde, 56 (%7,7)'sı ailesi ve ev arkadaşı olmadan evde, 368 (%55)'i devlet yurdunda ve 84'ü (%12) ise özel yurtta kalıyordu. Katılımcıların büyük çoğunluğu (%89) Osmaniye dışından gelmişti (Tablo 1).

Tablo 1. Bireylerin demografik özellikleri

N		%
Cinsiyet		
Kadın	387	53,3
Erkek	339	46,7
VKİ		
Zayıf	63	8,7
Normal	371	51,1
Fazla kilolu	241	33,2
Obez	51	7,0
Eğitim alınan alan		
Sağlık	118	16,3
Mühendislik	169	23,3
Fen-edebiyat	98	13,5
İlahiyat	68	9,4
İİBF	167	23
MYO	54	15,8
Yaşadığı yere göre		
Ailesi ile	75	10,3
Arkadaşları ile	143	19,7
KYK	368	50,7
Özel yurt	84	11,6
Evde tek	56	7,7

Cinsiyete göre değerlendirildiğinde, duygusal yeme davranışının kadınlarda erkeklere göre istatistiksel olarak anlamlı farklılık yaratacak düzeyde fazla olduğu tespit edilmişken; kısıtlayıcı ve dışlayıcı yeme davranışında gruplar arasında anlamlı fark gözlenmedi (Tablo 2).

Tablo 2. Cinsiyete göre alt grup farklılıklar.

	Kısıtlayıcı Yeme	Duygusal Yeme	Dışlayıcı Yeme
Kadın	2,26±0,75	2,49±0,99	3,14±0,66
Erkek	2,29±0,78	2,06±0,99	3,10±0,74
p	0,52	0,001	0,51

Katılımcılar eğitim gördükleri bölümlere göre yeme davranışları değerlendirildiğinde; kısıtlayıcı yeme davranışı açısından anlamlı fark saptanmazken (ANOVA, p=0,18); duygusal ve dışlayıcı yeme davranışı açısından anlamlı farklılık saptandı (ANOVA, p<0,05, p=0,02) (Tablo 3).

Mühendislik fakültesi öğrencilerinde, fen-edebiyat (p<0,05) ve İİBF öğrencilerine (p=0,03) göre daha az duygusal yeme davranışı tespit edildi [ANOVA-Tukey (Post-Hoc)] (Tablo 3).

Mühendislik fakültesi öğrencilerinde fen edebiyat fakültesi öğrencilerine göre daha fazla dışlayıcı yeme davranışı tespit edildi [ANOVA-Games Howel (Post-Hoc)] (Tablo 3).

Tablo 3. Eğitim gördükleri bölümlere göre alt gruplar

		DEBQ Skoru		
		Kısıtlayıcı Yeme	Dışsal Yeme	Duygusal Yeme
Eğitim Gördüğü Bölüm	n	X	X	X
Fen Edebiyat Fakültesi	98	2,2327	3,0194a	2,4937c
İkdisadi ve İdari bilimler fakültesi	167	2,2689	3,0802	2,3759
İlahiyat	68	2,3956	3,1912	2,4355
Sağlık Bilimleri Fakültesi	118	2,1280	3,0754	2,3755
MYO	106	2,3000	3,0500	2,2025
Mühendislik Fak.	169	2,3385	3,2751b	2,0442d
p		0,18	0,003	0,02
Za-b: -,25576, Zc-d:,44957				

Katılımcıların beden kitle indekslerine göre yeme davranışları değerlendirildiğinde; duygusal yeme davranışı açısından anlamlı fark saptanmazken (ANOVA, p=0,74); dışsal ve kısıtlayıcı yeme davranışı açısından anlamlı farklılık saptandı (ANOVA, p<0,001, p<0,001) (Tablo 4).

Obez grupta dışsal yeme skoru, zayıf, normal ve fazla kilolu gruplarından daha düşük bulunmuştur. Diğer gruplar arasında farklılıklar anlamlı değildir (Tablo 4).

Kısıtlayıcı yeme skoru, zayıf grupta diğer üç gruba göre daha düşük bulunurken, fazla kilolu grupta normal ve obez gruba göre yeme bozukluğu daha yüksek bulunmuştur. Diğer gruplar arasında anlamlı farklılık yoktur [ANOVA-Games Howel (Post-Hoc)] (Tablo 4).

Tablo 4. Beden kitle indekslerine göre alt gruplar

DEBQ Skoru				
		Dışsal Yeme	Kısıtlayıcı Yeme	Duygusal Yeme
VKİ	n	X	X	X
Zayıf	63	3,3143a	1,5667e	2,1941
Normal	371	3,1671b	2,2615f	2,3212
Fazla kilolu	241	3,0722c	2,4979g	2,2672
Obez	51	2,8000d	2,1765h	2,3575
p		0,001	0,001	0,74

Za-d: ,51429, Zb-d: ,36712, Zc-d:,27220
Z:e-f:-,69479, Ze-g:-,93126, Ze-h:-,60980, Zf-g: -,23647, Zg-h:,32145

Katılımcılar kadın ve erkek grubu olarak beden kitle indekslerine göre yeme davranışları açısından değerlendirildiğinde; her iki grupta da alt grupların yeme skorları (kısıtlayıcı, dışsal ve duygusal yeme davranışları) açısından anlamlı fark vardır (ANOVA, p<0,05) (Tablo 5).

Fazla kilolu grubunda kadınların duygusal yeme skoru, zayıf, normal ve obez gruplarından daha yüksek bulunmuştur. Zayıf grupta Dışsal yeme skoru, normal, fazla kilolu ve obez gruplarından daha yüksek bulunurken, normal grupta obez grubuna göre daha yüksek bulunmuştur. Diğer gruplar arasındaki farklılıklar anlamlı değildir (Tablo 5).

Kısıtlayıcı yeme skoru, zayıf grupta diğer üç gruba göre daha düşük bulunurken, fazla kilolu grupta normal ve obez gruba göre daha yüksek bulunmuştur. Diğer gruplar arasında anlamlı farklılık yoktur [ANOVA-Games Howel (Post-Hoc), p>0,05] (Tablo 5).

Tablo 5: Kadınlarda beden kitle indekslerine göre alt gruplar

DEBQ Skoru				
Kadın		Dışsal Yeme	Kısıtlayıcı Yeme	Duygusal Yeme
VKİ	n	X	X	X
Zayıf	53	3,4132a	1,5434e	2,2337ı
Normal	251	3,1546b	2,3163f	2,4214j
Fazla Kilolu	60	2,9550c	2,6900g	3,1654k
Obez	21	2,8000d	2,1286h	2,1099m
p		0,001	0,001	0,001

Z a-b:,25869 , Z a-c: ,45821, Za-d:,61321, Zb-d:,35458
Z:e-f:-,77294, Ze-g:-1,114660, Ze-h:-,58518, Z f-g: -,37367, Zg-h:,56143
Z:k-ı:,93171, Zk-j:,74399, Zk-m:,1,05549

Erkeklerde duygusal yeme skoru, obez grubunda fazla kilolu grubuna göre daha yüksek bulunmuştur. [ANOVA-Tukey (Post-Hoc)] (Tablo 6).

Obez grupta dışsal yeme skoru, normal ve fazla kilolu gruplarından daha düşük bulunmuştur. Diğer gruplar arasındaki farklılıklar anlamlı değildir (Tablo 6).

Kısıtlayıcı yeme skoru, zayıf grupta diğer üç gruba göre daha düşük bulunmuştur. Diğer gruplar arasında anlamlı farklılık yoktur [ANOVA-Games Howel (Post-Hoc)] (Tablo 6).

Tablo 6. Erkeklerde beden kitle indekslerine göre alt gruplar

DEBQ Skoru				
Erkek		Dışsal Yeme	Kısıtlayıcı Yeme	Duygusal Yeme
VKİ	n	X	X	X
Zayıf	10	2,7900	1,6900d	1,9846
Normal	120	3,1933a	2,1467e	2,1115
Fazla Kilolu	181	3,1110b	2,4343f	1,9694h
Obez	30	2,8000c	2,2100g	2,5308ı
p		0,01	0,032	0,034

Z a-c: ,39333, Za-c:,31105
Z:d-e:-,45667, Zd-f:-,74425, Zd-g:-,52000
Z:k-ı:,93171, Zk-j:,74399, Zk-m:,1,05549

Katılımcılar yaşadıkları yere göre yeme davranışları açısından değerlendirildiğinde; duygusal, kısıtlayıcı ve dışsal yeme davranışları açısından anlamlı farklılıklar saptandı (ANOVA, p<0,001, p=0,03, p=0,04) (Tablo 7).

Aileden ayrı evde tek yaşayanlarda kısıtlayıcı yeme skoru, devlet yurdunda, özel yurtta ve arkadaşları ile yaşayanlara göre daha düşük bulundu (p=0,03, p<0,001, p=0,27).Diğer gruplar arasında anlamlı farklılık yoktur [ANOVA-Games Howel (Post-Hoc)] (Tablo 7).

Dışsal yeme skoru, aile ile yaşayanlarda arkadaşlar ile yaşayanlara göre daha düşük bulundu (p=0,03). Diğer gruplar arasında anlamlı farklılık yoktur [ANOVA-Tukey (Post-Hoc)] (Tablo 7).

Duygusal yeme skoru, özel yurtta yaşayanlarda, arkadaşlarıyla yaşayanlardan ve devlet yurdunda yaşayanlardan daha yüksek bulundu (p<0,001, p=0,02). Diğer gruplar arasında anlamlı farklılık yoktur [ANOVA-Games Howel (Post-Hoc)] (Tablo 7).

Tablo 7. Yaşadıkları yere göre alt gruplar

DEBQ Skoru				
		Kısıtlayıcı Yeme	Dışsal Yeme	Duygusal Yeme
Yaşadığı yere göre	n	X	X	X
Aile	75	2,1573	2,9187e	2,3600
Arkadaş ile	143	2,2671a	3,2790f	2,1065g
KYK (Devlet Yurdu)	368	2,3038b	3,1054	2,2333h
Özel Yurt	84	2,4607c	3,0679	2,7143j
Aileden ayrı evde tek	56	1,9679d	3,1911	2,4629
p		0,04	0,03	0,001

Za-b: ,29928, Zb-d: ,33595, Zc-d:,49286
Z:e-f:-,36035
Zg-j:-,60778, Zh-j:-,48101

Tartışma

Yeme bozuklukları, sağlıkla ilişkili yaşam kalitesinde belirgin

düşüşe neden olan ciddi hastalıklardır [16]. Duygusal yeme, kısıtlayıcı yeme ve dışsal yeme gibi yeme davranışlarının obezite ve yeme bozukları için risk faktörü olduğu daha önce yapılan çalışmalarda bildirilmiştir [17,18]. Duygusal yeme, stres, anksiyete, depresyon ve öfke gibi olumsuz duygularla baş edebilmek için gelişen fazla yeme davranışıdır. Özellikle stresin daha fazla yaşandığı gençlik döneminde duygusal yemenin daha fazla olduğu bildirilmiştir [19]. Dışsal yeme, özellikle besinin görünümü, kokusu gibi dışsal faktörlerin etkisine, açlık hissi gibi içsel faktörlerin etkisine göre daha hassas olan insanlarda görülmektedir. Özellikle obezojenik çevrenin dışsal yemeyi uyardığı bilinmektedir. Kısıtlayıcı yeme, paradoksal olarak, besin alımının azaltılması ile birlikte açlık sırasında aşırı besin tüketimi şeklinde ağırlık artışına neden olur [20].

Bu araştırma, yeme bozukluklarına yakalanma riski yüksek popülasyon olan üniversite öğrencilerinin yeme davranışlarını incelemek amacıyla 387 (%53,3)'si kadın, 339 (%46,7)'ü erkek 726 öğrenci ile yapılmıştır. Öğrencilerin bu yeme davranışları ile cinsiyet, VKİ, yaşadıkları ortam, eğitim aldıkları bölüm arasındaki ilişkiler analiz edilmiştir.

Rusya'da yapılan bir çalışma kadınların her durumda erkeklerden daha yüksek puanlara sahip olduğunu göstermektedir. Rus örneğinde, erkeklerin sadece Kısıtlayıcı yeme skoru ile VKİ ilişkili bulunmuştur. Böylece, Kısıtlayıcı ve Duygusal yeme erkek olmakla daha güçlü ilişkilendirilirken, Dışsal yeme erkekler ve kadınlar arasında eşit ilişkili olarak bulunmuştur. Bu nedenle, bu sonuçları hesaba katarak, öncelikle, genç kadınların kısıtlayıcı yeme ölçeklerinde daha yüksek puanlar aldıkları, kilo ile ilgili problemlerinin olmadığı ve yeme stratejilerinin gıda alımını kontrol etmek için dengeli bir yaklaşım içinde olmadığı, bazen dürtüsüz bir şekilde davranışlarını kısıtladıklarının varsayılabileceği belirtilmiştir. Bu etkinin yaşla birlikte azaldığı, buna göre bu gruptaki beslenme ve beden yaklaşımının yaşla birlikte değiştiği bildirilmiştir [21].

Bizim çalışmamız cinsiyete göre değerlendirildiğinde, duygusal yeme davranışının kadınlarda erkeklere göre istatistiksel olarak anlamlı farklılık yaratacak düzeyde fazla olduğu tespit edilmişken; kısıtlayıcı ve dışlayıcı yeme davranışında gruplar arasında anlamlı fark gözlenmedi. Üniversite popülasyonu zaten yaş dağılımı genç bir grup olduğu için yaşa için farka bakılmamıştır.

Yapılan bir çalışma duygusal yeme, kısıtlayıcı yeme alt boyutları ile antropometrik ölçümler arasında pozitif ilişki olduğunu gösterirken, dışsal yemenin antropometrik ölçümler üzerinde etkisinin anlamlı olmadığını belirtmektedir [22]. Türkiye'de yapılan başka bir çalışmada, üniversite öğrencilerinde kısıtlayıcı yeme ile VKİ arasında pozitif korelasyon bulunurken, dışsal yeme ve duygusal yeme ile VKİ arasında herhangi bir ilişki bulunamamıştır [23]. Yapılan prospektif bir çalışmada ise kısıtlayıcı yemenin VKİ'yi artırdığı gösterilmiştir [24]. İtalya'da yapılan bir çalışmada ise obez bireylerde dışsal yeme ve duygusal yeme puanları normal bireylerden daha yüksek bulunmuştur [15]. Yapılan çalışmalarda elde edilen sonuçların tutarlı olmaması, çalışma popülasyonun ırklarının, yaşadıkları çevrelerinin, beslenme alışkanlıklarının, yeme kültürlerinin, sosyodemografik ve ekonomik özelliklerinin farklı olmasından kaynaklanabilir.

Bizim çalışmamızda da VKİ'ye göre yeme davranışları değerlendirildiğinde; duygusal yeme davranışı açısından anlamlı bir fark saptanmazken; dışsal ve kısıtlayıcı yeme davranışı açısından anlamlı farklılık saptandı.

Dışsal yeme skorunun, VKİ arttıkça azaldığı ve Kısıtlayıcı yeme skorunun, VKİ arttıkça artış gösterdiği bulunmuştur.

Literatürde katılımcıların eğitim gördükleri bölümlere ve yaşadıkları yere göre değerlendirilmelerine rastlanılmamıştır. Eğitim gördükleri bölümlere göre yeme davranışları değerlendirildiğinde; kısıtlayıcı yeme davranışı açısından anlamlı bir fark saptanmazken; duygusal ve dışlayıcı yeme davranışı açısından anlamlı farklılık saptandı.

Mühendislik fakültesi öğrencilerinde, fen-edebiyat fakültesi öğrencilerine göre daha az duygusal yeme gözlenirken, dışsal yeme skorunun daha fazla olduğu gözlenmiştir.

Katılımcıların yaşadıkları yere göre yeme davranışları değerlendirildiğinde; duygusal, kısıtlayıcı ve dışşal yeme davranışları açısından anlamlı farklılıklar saptandı.

Kısıtlayıcı yeme skoru, aileden ayrı evde tek yaşayanlarda daha düşük bulunurken, Dışsal yeme skoru, aile ile yaşayanlarda, arkadaşlarla ile evde yaşayanlara göre daha düşük bulunmuştur. Duygusal yeme skoru, özel yurtta yaşayanlarda daha yüksek bulunmuştur.

Sonuç

Bu çalışmada, genç popülasyonda, DEBQ'nun alt ölçeklerini uyguladığımız katılımcıların yeme davranış skorlarını, alanlarına, yaşadıkları yerlere, VKİ'lerine ve cinsiyetlerine göre değerlendirdik ve yeme bozukluğu riski yüksek olan bu popülasyonda yapılan analiz sonucunda, , cinsiyet ve VKİ'lerinin yeme davranışına etkisi olmasının yanında okudukları alanın ve yaşadıkları sosyal çevrenin de buna etkisinin olduğunu gösterdik.

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Original Article

A technique of hemodialysis in patients with extracorporeal membrane oxygenation

Ekstrakorporeal membran oksijenatörü olan hastalarda bir hemodiyaliz tekniği

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Abstract

Aim: We aimed to evaluate the safety and feasibility of hemodialysis (HD) by using a screw compressor clamp on extracorporeal membrane oxygenation (ECMO) lines without placing a central venous catheter.

Material and Methods: From May 2013 to September 2017, 43 adult patients with ECMO that required renal replacement treatment with HD were included.The inflow of the dialysis machine was connected to the outlet of the oxygenator, and the outflow was connected to the venous line using two 3-way taps. The tool that was used on the outflow circuit to perform HD is a clamp on a screw, allowing us to squeeze and de-squeeze to set the optimal line pressure. Creatinine, blood urea nitrogen, pH, base deficit, lactate dehydrogenase (LDH) values were evaluated, and compared pre/post-HD. Rate and duration of dialysis were also analyzed.

Results: HD was successfully performed in all patients with this technique without additional morbidity and mortality. No related complications due to HD were observed. Blood urea nitrogen, creatinine, pH, base deficit values were decreased to the desired levels after dialysis ($p<0.05$). There was a slight insignificant increase in LDH values after HD ($p=0.446$).

Conclusion: This screw compressor clamp increased the pressure on returning line of HD to the venous ECMO line; and made dialysis and ultrafiltration possible even in low blood pressure. This technique is very simple and allows to perform successful filtration and dialysis using ECMO lines without placing venous catheter.

Keywords: extracorporeal life support; kidney injury; hemodialysis; renal replacement therapy.

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Öz

Amaç: Bu çalışmada santral venöz kateteri yerleştirmeden, ekstrakorporeal membran oksijenasyonu (ECMO) hatlarında farklı bir enstrüman kullanılarak hemodiyalizin (HD) uygulanabilirliliğini ve güvenliliğini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Mayıs 2013 - Eylül 2017 tarihleri arasında kliniğimizde ECMO takılmış, HD ile renal replasman tedavisi gerektiren 43 yetişkin hasta çalışmaya dahil edildi. Diyaliz makinesinin çıkışı, oksijenatörün venöz hattına, diyaliz makinasının girişi ise ECMO'nun arter hattının çıkışına iki 3-yollu musluklar kullanılarak bağlandı. HD gerçekleştirmek için çıkış devresinde basıncı ayarlamak için kullanılan enstrüman, en uygun hat basıncını ayarlamak için sıkıştırmamıza izin veren bir vida üzerinde bir kelepçe olarak tasarlanmıştı. Kan kreatinin, kan-üre nitrojeni, pH, baz açığı, laktat dehidrojenaz (LDH) değerleri değerlendirilerek HD öncesi ve sonrası karşılaştırıldı. Diyaliz sayısı ve süresi de analiz edildi.

Bulgular: Bu teknikle ek morbidite ve mortalite olmaksızın tüm hastalarda HD başarılı bir şekilde uygulandı. HD'ye bağlı hiçbir komplikasyon görülmedi. Diyaliz sonrası kan üre nitrojen, kreatinin, pH, baz açığı değerleri istenilen seviyeye düştü ($p<0.05$). HD'den sonra LDH değerlerinde istatistiksel olarak hafif derecede anlamlı olmayan bir artış görüldü ($p=0.446$).

Sonuç: Kulandığımız bu enstrüman, venöz ECMO hattından HD hattına olan basıncı arttırdı; düşük tansiyonda bile diyalizi ve ultrafiltrasyonu mümkün kıldı. Basit bir teknik ile çalışan bu alet sayesinde venöz kateter yerleştirmeden ECMO hatları kullanılarak başarılı filtrasyon ve diyaliz yapılması sağlanabilir.

Anahtar kelimeler: ekstrakorporeal yaşam desteği; böbrek hasarı; hemodiyaliz; renal replasman terapisi.

Introduction

Extracorporeal membrane oxygenation (ECMO) is a temporary form of life support providing a prolonged biventricular circulatory and pulmonary support for patients experiencing both pulmonary and cardiac failure unresponsive to conventional therapy [1]. Advances in pump and oxygenator technology, patient selection and cannulation strategies have contributed to expanded utilization of this technology. ECMO is simple to establish and allows rapid recovery of impaired organ functions. Despite the improvement in organ functions, deterioration is usually progressive and sometimes requires renal replacement therapy [2].

Haemodialysis (HD) is the proven method of removing waste products and extra fluid, which build up in the blood when the kidneys are no longer able to function properly. To accomplish HD, it is necessary to have an access to the blood vessels. In patients with ECMO, the classical access can be achieved temporarily by placing a specific double-way venous catheter in one of the large veins in the neck or groin to enable dialysis. Rubin et al had modified the classical HD pathway with connecting a circuit to the ECMO directly and reported that 75% of their patients were conducted a temporary HD or haemofiltration without a delay. Furthermore, they found that the presence of renal impairment was an independent predictor of mortality in patients with heart failure [3].

In this study, we present a technique by using a tool "screw compressor clamp" that provides HD in patients with ECMO. This tool allows performing HD via ECMO lines without a need of access to blood vessels with double-way venous catheter.

Material and Methods

From May 2013 to September 2017, 43 adult patients with ECMO due to end-stage heart failure that required renal replacement treatment with HD were included in this study. Cannulation for ECMO was established through the femoral vessels directly or percutaneously in the right groin. In all patients HD was performed through ECMO circuits and access to blood vessels with specific venous catheter was not necessary. Creatinine, blood urea nitrogen, pH, base deficit, lactate dehydrogenase (LDH) values were evaluated pre and post-HD. Rate of HD, HD duration and ultrafiltration rates were also analyzed (Table 1). Hemofiltration/HD techniques were used to remove fluid and waste products from the blood and to correct electrolyte imbalances, as well as acid-base imbalances. The study was approved by the local research ethics committee.

Technique

The inflow circuit from the dialysis machine (Fresenius Medical Care, Bad Homburg Germany) is connected to the outlet of the oxygenator of ECMO (Circuit ECMO type Reims, DataStream pump, Medos, Xenios AG, Heilbronn, Germany), and the outflow circuit is connected to the venous line of ECMO using two 3-way taps (Figure 1). Therefore, two independent extracorporeal circuits, ECMO and HD, are associated with the use of an external dialysis machine. The pressure in the venous line of ECMO is negative, generating suction with a risk of gas embolism. Between the pump and the oxygenator (arterial line of the ECMO), the pressure is the highest due to the constitutive resistance of the oxygenator. This pressure in the arterial line allows an optimal inflow for HD. Since the pressure

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is low in the venous line, there is no resistance in the outflow of dialysis machine; drop-off pressure alarm would soon stop HD, therefore, we use Screw Compressor Clamp (Swinging Jaw Clamp, Humboldt Mfg. Co., IL, USA) to increase the pressure on returning line of HD to the venous ECMO line without placing venous dialysis catheter. Consequently, this technique prevents the alarm and provides successful dialysis and ultrafiltration.

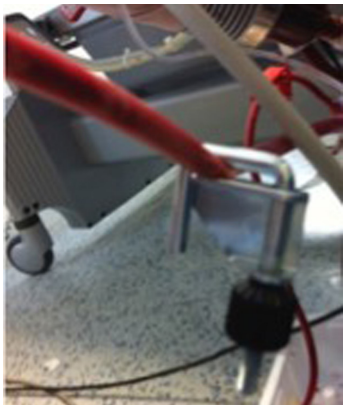

Figure 1: Venous line of extracorporeal membrane oxygenation with Screw Compressor Clamp

This tubing clamp is safe, simple, strong and it can be used on thin or heavy-wall tubing. The clamp is made of plated steel, incorporated a large aluminum and rigid plastic knurled adjusting nut (Figure 2). Substantially, this simple tool is a clamp on a screw, allowing us to squeeze and de-squeeze to set the optimal line pressure.

Figure 2: Screw Compressor Clamp, Swinging Jaw Clamp

Anticoagulation

Anticoagulation was initiated just before the ECMO cannulation procedure with a 50- 100 U/Kg bolus of unfractionated heparin, subsequently continuous unfractionated heparin infusion that targets an activated partial thromboplastin time approximately 1.5 times the normal rate was administered. Therefore, the HD circuit does not require additional anticoagulation.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD), or median values. Categorical variables were expressed as numbers and percentages. Pre/post-operative variables were compared using "chi-square test" for categorical variables. SPSS pocket program, version 14.0 was used for statistical analysis. A p value < 0.05 was accepted as significant.

Results

Mean age was 36.5±11,2(19-56) years. Thirty-one (72%) patients were male. Indications of ECMO support were 60% dilated cardiomyopathy, 9% restrictive cardiomyopathy, 11% ischemic cardiomyopathy, 10% acute rejection after heart transplant, 10% right ventricular failure after left ventricular assist device implantation. Patient characteristics are shown in Table 1.

Table1. Patients' characteristics

	n:43
Gender	
Female	12 (28%)
Male	31 (72%)
Age (year)	36.5 ± 11, 2 (19-56)
Height (cm)	170 ± 8,2 (149-185)
Weight (Kg)	70,1 ± 13 (46-97)
BSA (m2)	1,8 ± 0,1 (1,5-2,2)
BMI (Kg/m2)	24,1 ± 3,9 (17-30)
Indications of ECMO support	
Dilated Cardiomyopathy	26 (60%)
Restrictive Cardiomyopathy	4 (9%)
Ischemic Cardiomyopathy	5 (11%)
Rejection after Heart Transplant	4 (10%)
RVF after LVAD implantation	4 (10%)
PABP (mmHg)	
Systolic Pressure	47,4 ± 13,2 (22-77)
Diastolic Pressure	26,9 ± 10,6 (10-50)
Mean Pressure	25 ± 7,9 (13-45)
PVR (Wood units)	2,8 ± 1,1 (1-5)
TPG (mmHg)	6,6 ± 3,6 (2-15)
CO (L/min)	2,6 ± 0,8 (1,3-4,3)
CI (L/min/m2)	1,5 ± 0,4 (1-2,7)

BSA: Body surface area, BMI: body mass index, ECMO: Extracorporeal membrane oxygenation, RVF: Right ventricular failure, LVAD: left ventricular assist device, PABP: Pulmonary artery blood pressure, PVR: Pulmonary vascular resistance, TPG: transpulmonary pressure gradient, CO: Cardiac output, CI: Cardiac index

HD was successfully performed in all patients, creatinine, blood urea nitrogen, pH, base deficit values were decreased to the desired levels after HD (Mean blood urea nitrogen was 216,8±51,2 (151-294) mg/dl in pre-HD, 128±29,5(83-172)

mg/dl in post-HD). The difference in Pre-HD and post-HD parameters (creatinine, blood urea nitrogen, pH, base deficit) was statistically significant ($p<0.05$). The rate and duration of HD were 8,2±6,9 (2-22) times and 3,4 ± 0,5 (3-4) hours respectively. The amount of ultrafiltration was 2800±447,2 (2000-3000) ml. LDH values were also compared (pre and post-HD values were 483±239.1 (134-840) and 502±245 (221-898) U/L, respectively). There was a slight increase in LDH values after HD, however the difference was not statistically significant (p=0.446). The results are summarized in Table 2. Average systolic arterial pressure was 74±10,5(50-85) mmHg. In ordinary circumstances, it is not possible to perform HD at low mean arterial pressures; however with this technique, HD is not affected by mean arterial pressure and the dialysis machine can operate efficiently (Figure 3). No bleeding or infection due to this technique was found and no other related complications due to hemodialysis were observed.

Table 2: Parameters of Pre-HD and Post –HD

	pre-HD	post-HD	P value
Creatinine (mg/dl)	3,5 ± 1,08 (2,2-4,9)	2,2 ± 0,75 (1,26-3,67)	.001
Blood urea nitrogen (mg/dl)	216,8±51,2 (151-294)	128 ± 29,5 (83-172)	.001
pH	7,36 ± 0,03 (7,3-7,42)	7,42 ± 0,02 (7,38-7,45)	.001
Base deficit	6 ± 2,8 (-6,16-(-8))	2,25 ± 2,2 < (-4) - 3 <	.001
Rate of HD (time)		8,2± 6,9 (2-22)	
HD duration (hour)		3,4 ± 0,5 (3-4)	
Ultrafiltration (UF) (mL)		2800 ± 447,2 (2000-3000)	
Lactate dehydrogenase (LDH) (U/L)	483 ±239.1(134-840)	502±245(221-898)	.446

HD: hemodialysis

Figure 3: Hemodialysis with hypotension

Discussion

Renal dysfunction (RD) and fluid overload are frequent in patients with chronic congestive heart failure [4]. Before the need of ECMO, critically ill patients with heart failure are at high risk of acute RD due to their condition such as sepsis, ischemia, respiratory failure, decompensated cardiac failure, vasopressor requirements and prevalent use of nephrotoxic medication [5]. Unfortunately, in these patients. need for renal replacement therapy (RRT) after ECMO administration and mortality are increased. Lin et al. reported that adults with acute RD had a 78% mortality compared with 20% in non-acute RD patients [6]. Several renal replacement therapy (RRT) techniques such as peritoneal dialysis, intermittent HD, and continuous RRT (CRRT) are available to support ECMO patients with acute RD and/or fluid overload (FO). Each has its own advantages and disadvantages [7, 8, 9]. Patient factors, treatment goals, and center experience play a role in according to the selected RRT. The simplest way to perform HD is through venous access independent from the ECMO circuit. The most frequent venous accesses used are the internal jugular and subclavian veins. The femoral vein is less frequently chosen, due to the infection risk, and the potential risk of thrombosis in the neighborhood of the ECMO cannula. Additionally, if the patient does not undergo previous cannulation with a central venous catheter, new anticoagulation that is required would increase the risk of bleeding, at the same time the catheter drainage would be insufficient and lead to unsuccessful HD [10, 11]. RRT can also be performed by connecting the dialysis circuit to the ECMO circulation. The two most common methods are; the use of an in-line hemofilter or a traditional device connected to the extracorporeal circuit [12]. However, combining two independent extracorporeal circuits may cause several technical problems, most often associated with the dialysis machine's inlet and outlet pressure alarms [11]. It is possible to connect a dialysis machine to the venous line of the ECMO circuit before the pump, which drives the blood from the ECMO circuit into the dialysis machine. After blood purification, the blood is returned to the ECMO circuit before the ECMO pump. Reconnection of the circuit that contains blood returning from the dialysis machine should be prior to the oxygenator in order to trap the air/clots before returning of patient's bloodstream; additionally, venous admixture has also been avoided due to the shunting in the circuit [10]. The pressure in the arterial line of the ECMO is high according to the blood acceleration by the pump and the arterial resistance

of the patient. The inflow catheter of the HD is connected to the venous line and the outflow catheter is connected to the arterial line of ECMO. Although this model is quite easy and "logical", HD is not possible due to permanent high-pressure alarm. Rubin et al [3] reported that the pressure in the venous line was null or negative, generating suction with a risk of gas embolism. Venous pressure was frequently negative during hypovolemia and blood flow rate is the main determinant. In our experience, there was no resistance in the outflow catheter of dialysis machine due to low pressure in the venous line of ECMO; as a result, HD was not possible due to drop-off pressure alarm. We used a Screw Compressor Clamp to increase the pressure on returning line (from HD to the venous ECMO line); consequently, this novel technique provides to stop the alarm and allows to performHD/ultrafiltration possible. In this study, the optimal pressure was achieved by application of this instrument. Maximum care must be taken during the connection of the lines of ECMO and dialysis machine. Simons et al connect the inflow of the dialysis machine to the outlet of the oxygenator, and the outflow circuit that contained returning washed blood was connected to the oxygenator inlet. In their setup, all connections between the ECMO and the dialysis circuits were under positive pressure [13]. They reported that this situation prevented the air from being sucked into the circuit in case of connection failure, therefore, the risk of micro-emboli was reduced. Contrary to Simons' et al. technique in this study, relatively long dialysis lines connected to the cannula as used by Rubin et al was required [3]. Additional attention during patient manipulation to prevent luer connector disconnection or cannula displacement was necessary.

The other disadvantage of combining two independent extracorporeal circuits is hemolysis. Hemolysis could be a specific complication of ECMO, HD or combination of ECMO and HD, with erythrocyte fragmentation caused by the combination of shear stress, positive pressure, wall impact forces and properties of nonendothelialized surfaces [14]. Despite the presence of hemolysis in patients with ECMO that needed HD, the recovery of renal functions seems to be satisfactory. In the absence of primary renal disease, chronic renal failure did not occur in patients with ECMO and these patients weretreated concomitantly with RRT [14, 15, 16]. In our study, there was a slight increase in LDH values after HD however, the difference was not significant.

Study Limitations

The major limitation of this study is its' non-randomized design with a relatively small number of patients. This is also a single center experience; therefore, outcome interpretation is limited by institutional bias.

Conclusion

This technique is a simple, safe and feasible method to perform a successful filtration and dialysis using ECMO lines without placing a specific venous catheter. Screw Compressor Clamp increased the pressure on returning line of HD to the venous extracorporeal membrane oxygenation line; and made dialysis and ultrafiltration possible even in low blood pressure. Further large investigations are needed to demonstrate the validity of this technique.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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Review

Endovascular treatment of native aortic coarctation in adults: Two case reports and detailed review of the literature

Erişkinlerde aort koarktasyonunun endovasküler tedavisi: İki olgu sunumu eşliğinde detaylı literatür derlemesi

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Abstract

Coarctation of the aorta (CoA) forms 6-8% of congenital heart diseases (CHD). This narrowing typically occurs in the proximal descending aorta, close to the insertion of the patent ductus arteriosus and can be found with a number of concomitant diseases. CoA is a common cause of secondary arterial hypertension in young adults. Although CoA can be an isolated CHD, it is also commonly found in other congenital syndromes and cardiovascular anomalies. Herein this review paper we reported a brief history of management of aortic coarctation, and current treatment modalities concentrated on stent placement supported with two novel cases.

Keywords: aortic coarctation; stent placement; endovascular

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Öz

Aort koarktasyonu doğuştan kalp hastalıklarının % 6-8'ini oluşturur. Koarktasyon, tipik olarak proksimal inen aortta, patent duktus arteriyozusun başlangıcına yakın bir yerde meydana gelir ve birkaç eşlik eden hastalıkla birlikte bulunabilir. Aort koarktasyonu, genç yetişkinlerde sekonder arteriyel hipertansiyonun yaygın bir nedenidir, izole bir konjenital kalp hastalığı olmasına rağmen, diğer konjenital sendromlarda ve kardiyovasküler anomalilerde de yaygın olarak bulunur. Bu derleme yazısında, aort koarktasyonunun kısa bir yönetim tarihçesini ve iki yeni vaka ile desteklenen stent yerleştirilmesine yoğunlaşan mevcut tedavi yöntemlerini bildirdik.

Anahtar kelimeler: aort koarktasyonu; stent; endovasküler

Introduction

Coarctation of the aorta (CoA) forms 6-8% of congenital heart diseases (CHD). This narrowing typically occurs in the proximal descending aorta, close to the insertion of the patent ductus arteriosus (PDA) [1], and can be found with a number of concomitant diseases. If left untreated in childhood, CoA has a poor prognosis because of arterial hypertension resulting in various complications such as aneurysms, heart failure, dissection, coronary artery disease, and intracranial hemorrhage.[2-4]

Although first described in the 1700s, the first operations for coarctation were performed in 1944.[5,6] Surgical repair remained the only form of intervention from 1945 until the advent of balloon aortic angioplasty reported in 1982 (7), and the use of balloon-expandable endovascular stents became available in the 1990s firstly introduced by Charles Mullins, a congenital interventional cardiologist.[8,9]

In the current era, the repair of the narrowed section has been performed with surgical treatment in infants, and early childhood. Endovascular treatment (EVT) has generally been the procedure of choice for older school-age, adolescent, and adult patients with native coarctation and those with recurrent coarctation. [10,11] As expected, surgical treatment is more invasive. It may cause complications such as bleeding, wound infection, re-coarctation, systemic hypertension, aortic aneurysm formation, endocarditis, premature coronary atherosclerosis, aorto-bronchial or aorto-esophageal fistulas and pain as well as a faulty cosmetic appearance at the incision site. Besides, open repair of CoA entails the cardiovascular and respiratory risks posed by general anesthesia, in addition to procedural and periprocedural complications. Furthermore, open repair often necessitates a median sternotomy or lateral thoracotomy incision, which can result in significant respiratory morbidity, particularly in a patient who has severe asthma with mild airflow obstruction. Moreover, approximately 10% of patients who undergo initial operative repair of coarctation require a subsequent percutaneous intervention for recurrence of aortic obstruction.[12]

Untreated CoA in adolescents and adults represents a different cohort of patients. These patients may have less severe stenosis of the aorta but present with extensive collateral arterials (Like case 1) as well as more comorbidities such as aortic dilation and heart valve disorders (like Case 2), all of which represent additional difficulties for open surgery.[13] Furthermore, paraplegia is a rare but devastating complication after CoA repair. The protection of the collateral arteries or dedicated monitoring of postoperative coagulation are of great importance. That is another reason why EVT has been preferred in adults.

CoA is a common cause of secondary arterial hypertension in young adults. Although CoA can be an isolated CHD, it is also commonly found in other congenital syndromes and cardiovascular anomalies. The most common cardiovascular malformation associated with CoA is a bicuspid aortic valve (BAV) with up to 45%-62% prevalence of BAV (both cases). [14] As a result, aortic valve replacement and Bentall/David procedure have been two frequently combined procedures.

A stent's radial strength opposes aortic wall recoil, may improve vessel integrity following the trauma inherent to angioplasty, and avoids the need for balloon overdilation of the adjacent normal aorta, thereby decreasing the risk of

aneurysm formation at the dilation site. Covered stents seem to be particularly useful because of their 'sealing' effect on the stenotic area. Because of this, covered stents are effective in preventing aortic dissection or rupture of the vessel wall. [15] Cheatam- Platinum (CP) stent is one of the most widely used stents in the field of cardiology, which is manufactured from 90% platinum and 10% iridium with an expandable polytetrafluoroethylene covering. While it is available at 8 and 10 rows, it is mostly used in 8-zig configuration, which could be dilated up to 28 mm. This stent has an excellent radial coil strength even at larger diameters and also has brilliant visibility on fluoroscopy.[4]

The BIB balloons provide more controlled inflation because serial angiograms can be obtained after inflating the inner balloon to fine-tune the stent position; they are also associated with less stent shortening.

The European Society of Cardiology guidelines for the management of adult CHD recommended intervention in all patients with a non-invasive pressure difference > 20 mm Hg between the upper and lower limbs accompanied by upper limb hypertension (> 140/90 mm Hg) (Class 1C indication). [16] The AHA guidelines recommend stent implantation in all patients with a gradient >20 mmHg, which are of sufficient size for safe stent placement and in which expansion to adult size is possible.[17]

Herein, we reported two cases: a 20-year-old female with hypertension and suffering from severe asthma with mild airflow obstruction who underwent EVT of simple CoA (without any associated lesions) with a covered stent and followed-up for 26-months; and a 34-year old male who had undergone EVT with a bare-stent 3-years ago and suffering from re-CoA and concomitantly severe aortic stenosis with an ascending aortic aneurysm; providing a detailed review of the literature for management of CoA in the adults.

Case 1

A 20-year-old female patient (small body structure- 150 cm / 38 kg) was evaluated by the nephrology clinic due to systemic hypertension. Past medical history was positive for early-onset atopic asthma with mild airflow limitation requiring treatment with high dose inhaled corticosteroids. After a hypertensive episode, she was admitted to the emergency department, and beta-blocker + enalapril treatment was administered. Following further testing, she was referred to the cardiovascular and endovascular surgery outpatient clinic of Numune Research and Training Hospital Ankara, Turkey, in December 2017. Physical examination revealed weak femoral pulses and brachiofemoral pulsation delay. There was a marked difference in blood pressure between the left arm (161/91 mmHg) and ipsilateral leg (87/63 mmHg). A grade 3/6 systolic murmur was auscultated over the precordial and interscapular areas. Laboratory test results and electrocardiogram were normal. Transthoracic echocardiography (TTE) showed normally functioning BAV with mild aortic regurgitation and a 35mmHg gradient in descending aorta. Subsequently, computed tomography angiography (CTA) reported that the descending aorta narrows in a focal area showed critical stenosis of the proximal descending thoracic aorta compatible with CoA (Figure 1).

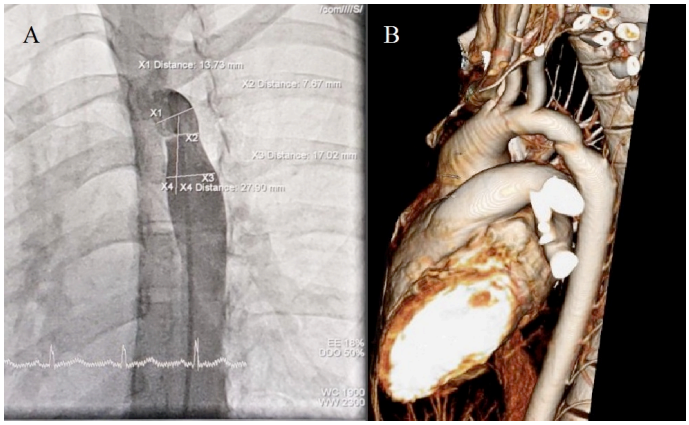

Figure 1. (A)Preoperative angiographic image of case 1. (B) Preoperative 3-D computed-tomography image of case 1

The patient was taken to the angiography suite. Because of severe respiratory status, the procedure was performed under local anesthesia, and mild sedation was provided before and during the deployment of the stent. Under sterile conditions left common femoral artery (CFA) was cannulated following heparin sulfate (100 IU/kg; maximum, 10,000 IU) administration intravenously. The CoA segment was advanced with a 0.035-inch diagnostic guidewire; a marker pigtail catheter was then passed over the wire into the arch of aorta retrogradely. A diagnostic catheterization was performed to determine the exact morphology and the pressure gradient of the stenosis (Figure 1).

We confirmed coarctation in the descending aorta and measured aortic diameter before coarctation (X1=13.73mm), the max-lumen

diameter of the CoA segment (X2=7.67 mm), aortic diameter after the coarctation (X3=17.02 mm) and calculated longitudinal length of the lesion (X4=27.90mm) (Figure 1). The calculated gradient of stenosis was 35 mmHg. Arcus aorta, ascending aorta, and aortic branches were in normal morphology.

The pigtail catheter was changed to a 12F, 75 cm long sheath (Mullins, Cook) over the 0.035-inch exchange guidewire. A manual-mounted eight-zig, with a 22 mm diameter and 3.4 cm long covered CP (NuMED Inc., Hopkinton, NY, USA) stent was loaded on a Balloon-in-Balloon (BIB) delivery catheter with an outer balloon of 14 mm x 3.5 cm (NuMED Inc., Cornwall, Ontario, Canada) was used. All BIBTM catheters have an inner balloon ½ of the balloon diameter of the outer balloon and inner balloon s 1.0 cm shorter than the outer balloon. We delivered the stent using the conventional back-load technique using an Amplatz super-stiff wire that was passed retrograde across the CoA with the help of a JR4 catheter. After ensuring that the stent layout was appropriate, the balloon was manually inflated, according to the manufacturer's recommendations, and the stent was deployed. When the outer balloon was fully expanded (14mm), the stent length shortened to 3.15 cm (a 5.4% shortening), which successfully covered the CoA segment. Angiograms were performed during the stent placement through the sidearm of the sheath to evaluate the results and the presence of any dissection or rupture. Post-treatment angiography showed that the narrowed segment was dilated with no visible gradient (Figure 2)

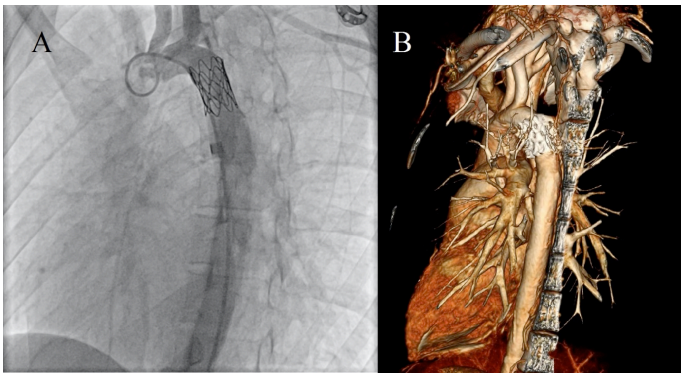

Figure 2. (A)Postoperative angiographic image of case 1. (B) Postoperative 26th month 3-D computed-tomography image of case 1

No complications occurred during and after the procedure. In the immediate postoperative period, strong symmetric pulses were palpable in the lower limbs without pressure gradient between the lower and upper limbs. The postprocedural peak systolic gradient was 0. The diameter of the coarctated segment was increased to 13.67 mm. Postprocedural LMWH and antibiotics were given for 2 days. Aspirin was given 150 mg (5 mg/kg) the night before the procedure and continued for 6 months. Blood pressure was returned to normal limits, as were the discrepancy between upper and lower limbs. The patient was hemodynamically stable and discharged at postoperative 2nd day and has been followed at the outpatient clinic. Follow-up controls were done at 1st, 6th, and 14th and 26th months. CTA was performed at 14th-month control follow-up, which revealed that the stent lumen was open, and there was no re-coarctation re-stenosis or gradient, and no anti-hypertensive treatment was necessary for the follow-up visits. The diameter of the coarctated segment was 13.71 mm.

In 2020, 26th-month CTA control (Figure 2) was revealed no gradient, ascending aorta diameter was 32mm, the coarctated segment was 13.21mm, and aorta and all of the major branches were patent.

Case 2

A 34-year old male was admitted to our clinic because of dyspnea, palpitation, and hypertension. The past medical story included a covered CP stent implantation (12mm x 3.9 cm) to the descending aorta because of CoA 3-years ago in another hospital. He was suffering from intermittent claudication and uncontrolled hypertension despite using three different groups of antihypertensive medications. Physical examination revealed weak femoral pulses and brachio-femoral pulsation delay. There was a marked difference in blood pressure between the left arm (194/112 mmHg) and ipsilateral leg (91/61 mmHg). CTA revealed re-CoA of the previously treated segment and ascending aortic aneurysm with a diameter of 6.8 cm. TTE revealed a BAV with severe stenosis and a gradient of 48mmHg in the coarctated segment. We planned a two-stage procedure. In the first stage, we decided to treat CoA with balloon angioplasty to reduce the afterload. After taking the patient to angio-suite and performing a similar technique with the first case, we measured the length and diameter of stent and aorta, and then we achieved a successful balloon angioplasty for the re-CoA with Z-MED (16x4mm, NuMED Inc., Hopkinton, NY, USA) balloon, which was introduced via 9F catheter and a 0.035-inch guidewire under local anesthesia and sedation. No complications occurred

during and after the procedure. In the immediate postoperative period, strong symmetric pulses were palpable in the lower limbs without pressure gradient between the lower and upper limbs. The postprocedural peak systolic gradient was 3 mmHg. LMWH was administered for 5 days. After ensuring the success of the first stage and the preoperative preparations, a Bentall procedure was performed. The postoperative ICU stay was 2 days, and the hospital stay was 11 days.

Discussion

EVT is now preferred over surgical management in adult patients with discrete coarctation without associated arch hypoplasia.[18] Currently, balloon angioplasty alone is not recommended for the treatment of significant CoA in adults., but it can be preferred for re-CoA.[13] We used balloon angioplasty as a bridge for effective reduction of afterload for a Bentall procedure.

This case also showed that EVT of CoA provides immediate hemodynamic benefit. In both cases, the diameter of the CoA site was increased, and the gradient through the coarctated segment was significantly reduced. Besides, the arm to-leg systolic gradient decreased sufficiently. The results presented in this case confirm the data of other studies that EVT is an effective method of treatment of CoA.[19,20]

Although some operators attempt angioplasty first, balloon-expandable stent implantation is currently regarded as standard-of-care therapy for adolescent and adult patients with primary CoA because stent implantation has proven to reduce the risk of re-CoA as compared with balloon angioplasty by preventing over-dilatation and thereby aortic wall injury and resulting in a lower degree of elastic recoil. [21] The reported risk of aortic aneurysm formation is less than 10% after stent implantation, as compared with 17% in patients after balloon angioplasty alone, and 51% in patients after surgical repair.[22]

A direct comparison between the three main treatment strategies (surgical, balloon, or stent) in CoA is challenging. The initial treatment effect is usually evaluated by the gradient reduction after a repair, but data with regard to residual gradients after surgical repair are lacking. In 2011, Forbes et al. published data of a multicenter, observational, nonrandomized study involving 350 patients from 36 institutions. Compared with surgery, stent placement appeared to produce hemodynamically equivalent results during follow-up observation. Moreover, stenting was associated with significantly fewer complications [2.3% versus 8.1% for surgery and 9.8% for balloon angioplasty ($p < 0.001$)] and shorter hospital stays [2.4 days versus 6.4 days for surgery]. The reintervention rate was higher in the stent group; however, this finding was attributed to staged procedures or patient somatic growth, and all reinterventions carried a similar low risk of morbidity and mortality aortic wall complications of any type occurred significantly more often in the balloon angioplasty group as compared with the surgery or stent repair group.[23] On the other hand, in the Quebec Native Coarctation of the Aorta Study, investigators retrospectively compared surgical repair to angioplasty in 80 patients (mean age, 12 years) treated between 1998 and 2004. Procedure-related complications were far more common in the surgical group (50%) than in the angioplasty group (18%) ($p = 0.005$). The median hospital stay was 7 days for the surgical group and 1 day for the angioplasty group ($p < 0.001$). At 38 ± 21 months, however, the rate of follow-up repeat intervention was higher in the angioplasty group (32%) than in the surgical group (0%) ($p < 0.0001$) (24). The main reason for which surgery favors stent repair is the increased risk for complications after stent repair in children that are not outgrown, which are usually below the age of 8–10 years. The use of bioabsorbable stents may be a promising technique in the setting of coarctation stenting.

The direct end-to-end sutured anastomosis, which had been initially described by Crafoord and Nylin [5] in 1945, has mostly been abandoned due to high rates of re-CoA. Patch aortoplasty, have long been associated with high rates of aneurysmal formation (20–40%) .[25] The addition of polytetrafluoroethylene (PTFE) for aortoplasty lowered rates of aneurysmal disease but, unfortunately, raised the rates of recoarctation to 25%.[26] Surgical repair of CoA can be performed by resection with end-to-end anastomosis, extended end-to-end anastomosis, subclavian flap aortoplasty, graft conduit interposition, bypass graft, or prosthetic patch aortoplasty.[27] Aortic aneurysm formation within the surgical repair group was exclusively found in the subclavian flap and patch angioplasty group.[23] The rate of aneurysm formation has been reported to be between 3% and 20% in long-term

studies of patients who have undergone coarctation repair. Patients repaired with synthetic patch technique are at higher risk of late-term aneurysm development.[14]

Spinal cord ischemia (due to prolonged clamping of the aorta) may cause severe complications, such as paraplegia (0.3% to 2.6%).[22,23] It is especially feared when there is limited collateral flow. In order to avoid spinal cord injury, distal aorta perfusion techniques may be used (i.e., Gott shunt, left heart bypass, femoro-femoral bypass, or cerebrospinal fluid drainage.[13]

The risk of acute complications was lowest after stent repair as compared with after surgery or balloon angioplasty. The overall mortality rates have significantly been more than the stents, such as 30 years after surgery is reported to be 23.7% reintervention 20% as described by Toro-Salazar et al. [28] Longest follow-up balloon angioplasty was performed by Reich et al. with 20 years, and they reported a rate of mortality of 8.1% and reintervention 28.3%.[29] The difference in secondary outcomes partially is attributed to the difference in follow-up durations, as with approximately 10 years after stent repair, 20 years after balloon angioplasty, and up to 50 years after surgery. [30]. However, there are also studies reporting low mortality rates despite extended follow-up as Brown and associates, of the Mayo Clinic, reported an overall 2.4% mortality rate for 819 patients with isolated CoA who underwent primary operative repair between 1946 and 2005 by means of extended end-to-end anastomosis, patch angioplasty, interposition grafting, bypass grafting, or subclavian flap or "other" repair, but they concluded that comparison to age- and sex-matched populations, patients who underwent open repair had reduced long-term survival. Repair at an early age was an independent risk factor for reintervention. At 30 years' follow-up, patients who underwent an initial repair before 1 year of age had an average reintervention rate of 31.1%, and patients who underwent an initial repair before 5 years of age had an average reintervention rate of 73.3% .[31]. A Cochrane review demonstrated that no randomized trials were available to compare surgery and stent repair, which emphasize the need for randomized data to compare different treatment strategies.[32]

Vanagt et al. reported a 9-year experience with CP stents and pointed out

CP as a valuable tool in the management of patients with simple and complex congenital heart disease including CoA, and claimed that the addition of a covering around a stent allows adequate sealing of existing or expected tears, thereby increasing the safety margin with complete dilation of stenotic lesions, with a better expected long-term outcome. [33] Sohrabi et al., evaluated 120 patients with a mean age of 23.60<10.99 years with post-ductal, short-segment, severe native CoA and compared the results of bare CP stent with covered CP stent and concluded that implanting both stents have very high success rates with remarkable hemodynamic effects in severe native CoA patients.[19]

Also, there are several reports in the literature with different uncovered stents such as Kische et al. who treated 52 patients with the Sinus-XL stent concluded that adult coarctation of the aorta treatment utilizing a self-expandable uncovered stent is safe and durable and reported an event-free survival of 82.2±6.3% for 5 years.[34] Tzifa et al. presented the situations where covered stents were chosen: 1) as a rescue treatment in patients with CoA aneurysms or previous stent-relatedd complications 2) in patients at risk of complications because of complex CoA anatomy or advanced age (21) as later confirmed by 2018, AHA/ACC Guideline for the management of adults with congenital heart disease.[35]

Although overall anatomical and hemodynamic results of stent implantation are satisfactory, CoA stenting is not without risk. Frequent complications after stent repair involve difficulties with sheath delivery, vascular complications, restenosis, and aortic aneurysm formation and failure to adapt to the growing child for which dilatation is necessary. One of the most catastrophic complications of CoA stenting is aortic disruption. Stent migration is also one of the most frequently encountered technical complications. The incidence is declared (28/588) 4.8% in multicenter retrospective series. [11] The incidence of peripheral vascular complications after stenting is 2-5% in the literature.[36]

Careful evaluation before the procedure is crucial to prevent vascular complications since covered stent implantation requires an extensive delivery system. After our preoperative evaluation, we decided to cannulate the left CFA instead of the right CFA because of the smaller diameter of the right common iliac artery. BP reduction is a primary goal in the treatment of CoA.[37]

We achieved strict control of blood pressure without medical therapy in approximately 3 years. However, HT may persist after

CoA stenting in adult life, probably due to structural and functional abnormalities of the arterial wall, which can result in diminished arterial wall compliance and increased rigidity.[38] Baykan A et al., after evaluating 20 patients with CP stents because of CoA reported that carotid intima-media thickness, pulse wave velocity (an indirect marker of arterial stiffness), and cardiac output index were found to be significantly higher in CoA patients.[39]

CP stents have also been successfully used for postsurgical recoarctation of the aorta.[40]

In 2018, the AHA/ACC Guideline for the management of adults with congenital heart disease [35] is published. In this guideline, they claimed that multiple factors help to determine whether surgery or stenting is optimal, including anatomic features such as proximity of native coarctation to head and neck vessels or concomitant aneurysm and concluded that, if stenting is the planned strategy for treatment, then a covered stent is needed. Furthermore, they reported that balloon angioplasty alone is associated with a higher rate of intimal tears and aneurysm formation compared with stent placement.

Surgical repair is recommended for most patients with duct-dependent neonatal coarctation, while stent implantation for older children and adults has been shown to have excellent short-term results. Balloon angioplasty for (native) coarctation and re-CoA is effective in leading to an acute gradient reduction [30], as we preferred to perform EVT of CoA with covered stents in Case 1, because of adult age, respiratory problems increase the risk of general anesthesia, extensive collateral development. We preferred to perform balloon angioplasty in Case 2 for re-CoA to provide an immediate hemodynamic reduction of gradient and afterload to be a successful bridge for following the Bentall procedure.

Resection and interposition of a graft conduit is the technique of choice in many centers for adult patients (who have reached their growth potential). It can be surgically tricky due to extensive arterial collaterals -as in our cases- or calcification of the aortic wall (ubiquitous in adult CoA). Furthermore, after EVT, patients often have shorter hospital stays, avoiding many common postsurgical complications such as urinary tract infections, pneumonia- as our patient was vulnerable because of asthma-, and deep venous thrombosis. The role of infections, particularly viral infections, in asthma exacerbations is well-established, and their contribution to asthma development and progression increasingly recognized There is an association between Staphylococcal superantigen-specific IgE antibodies and asthma severity and sinusitis, while fixed airflow limitation has been associated with positive serology for intracellular pathogens, such as Chlamydia pneumonia.[41] Several studies suggest that oxidative and nitrative stress is also increased in severe asthma, deteriorating the postsurgical recovery.

Surgical techniques are mainly reserved for patients with complex aortic arch anatomy such as extended arch hypoplasia or stenosis or para-CoA aneurysm formation. Extended aneurysms can be covered by conformable stents, but stent implantation may require preparative vascular surgery.[42]

Here comes another question. What should we do in the case of post-CoA aneurysmal formation? Theoretically, covered stents have the advantages of reducing the extent of the intimal tear, creating a framework for neointimal growth, and allowing control of the integrity of the aortic wall. For these reasons, they should be the standard of care for managing the coexistent aneurysmal disease.

Here comes another grey-area. The use of a covered stent may be complicated by the occlusion of aortic side branch arteries, and the left subclavian artery is more commonly involved due to the anatomical position. Although it has been suggested that it may be tolerated well, in some cases, it causes claudication of the left arm that requires a carotid to subclavian graft. As a solution, Tufaro et al. dealt with this issue by creating a handmade pinhole in the covered stent before the implantation procedure. By using the stiffer wire in the ascending aorta, they helped the stent to be directed in the standard position. After stent implantation, the pinhole fenestration was adapted to the left subclavian artery size by performing a balloon angioplasty that increased the artery flow. Their technique does not require stent perforation after its deployment, and the most considerable advantage is a significant reduction in the risk of vessel damage.[43]

The ideal patient for stenting has achieved full body growth and has an average transverse aortic arch dimension with a coarctation located at the isthmus, far from the carotid and subclavian arteries. Patients with a gothic geometry of the aortic arch are probably poor candidates for stenting and best treated with an extra-anatomic conduit, which can bypass the aortic arch and the coarctation area. Stenting may be

less successful in patients with suboptimal anatomy, vessel tortuosity, and transverse arch hypoplasia. For these patients, the decision to perform stent placement versus surgical correction must be made case-by-case by the clinical team. [44] A stent provides a more sustainable relief of gradient, with less vascular injury and a more even distribution of forces providing radial support to the vessel wall. Overdistension of the arterial wall, which can cause dissection, is avoided. A stent can seal intimal flaps to the aortic wall, preventing intimal dissection, promoting healing and reinforcing a weakened area [45], but here are also studies in patients with localized native CoA, without isthmic hypoplasia, confirming excellent long-term results with balloon dilatation, as well as a low rate of recurrence and no aneurysm formation.[42]

Conclusion

The endovascular treatment of CoA, as described in this case, is a safe and effective therapeutic option in the selected cases with a low rate of complications and less invasive for adult patients. As an algorithm, native CoA in infants and children should be treated with surgery, Baloon dilatation can be preferred in re-CoA of infants and small children, and as an emergent procedure for bridging the patient to a concomitant procedure. Nevertheless, as a standard, CoA, and reCoA in adults and reCoA in outgrown children should be treated with stents. All patients are prone to aneurysm formation, and recurrent coarctation, so lifelong follow-up is recommended.

Ethical Approval: The study was conducted in compliance with the Declaration of Helsinki with ethics approval provided by our hospital's ethics committees.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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Olgu Sunumu

Nadir görülen bir restriktif kardiyomiyopati olgusu: Hidradenitis suppurativa

Rare reason of restrictive cardiomiyopathy: Hydraadenitis suppuritiva

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Öz

Bu vakada restriktif diyastolik disfonksiyon, nefrotik sendrom ile seyreden bir hidraadenitis suppuritiva (HS) olgusu anlatılacaktır. 46 yaş daha önceden bilinen bir hastalığı olmayan erkek hasta kliniğimize ST elevasyonsuz miyokard infarktüsü, dekompanse kalp yetersizliği, akut böbrek yetersizliği, yeni tanı diyabetes mellitus ön tanılarıyla interne edildi. Hastanın göğüs, gluteal ve aksiller bölgede bir yıldır mevcut HS ile uyumlu nodüler-kistik bir lezyon saptandı. Hastanın ekokardiyografisi grade 3 diyastolik disfonksiyon (restriktif diyastolik disfonksiyon)" ile uyumlu saptandı. Restriktif kardiyomiyopatisi ve nefrotik sendromu olan hastada amiloidoz ön tanısı ile serum amiloid A düzeyi istendi, 120 mg/l (N:0-6.4) bulundu. Restriktif kardiyomiyopatisi ve nefrotik sendromu olan hastada amiloidoz ön tanısı ile serum amiloid A düzeyi istendi, 120 mg/l (N:0-6.4) bulundu. Serum ve idrar proteini elektroforezinde monoklonal gammopati kanıtı bulunamadı. Hidradenitis suppurativaya bağlı sekonder amilodoz ve restriktif kardiyomiyopati tanısı konuldu. Vakamız restriktif kardiyomiyopati olması üzerine araştırılan HS'ye sekonder, sekonder amiloidoz tanısı konulan bir vaka örneği olması nedeniyle özelliklidir. Kronik hastalıklarla birliktelik gösteren sekonder amiloidoz kardiyoloji kliniklerinde diyastolik disfonksiyona eşlik eden kalın duvarlarla birlikte küçük ventrikül hacmi olan hastalarda akla gelmelidir.

Anahtar kelimeler: hidraadenitis suppuritiva; restriktif diyastolik disfonksiyon; nefrotik sendrom

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Abstract

In this case, a case of hydraadenitis suppuritiva (HS) with restrictive diastolic dysfunction and nephrotic syndrome is described. A 46-year-old male patient was hospitalized to cardiology clinic with non-ST elevation myocardial infarction, decompensated heart failure, acute renal failure and new diagnosis of diabetes mellitus. A nodular-cystic lesion in the chest, gluteal and axillary regions of the patient was found to be compatible with HS for one year. Grade 3 diastolic dysfunction (restrictive diastolic dysfunction) was found to echocardiographic examination of patient. The desired serum amyloid A was 120 mg / l (N: 0-6,4) considering systemic amyloidosis in patient with restrictive cardiomyopathy and nephrotic syndrome,. There were no evidence of monoclonal gammopathy in serum and urine protein electrophoresis. Secondary amylodosis and restrictive cardiomyopathy due to hydradenitis suppurativa was diagnosed. Secondary amyloidosis which has been investigated because of restrictive cardiomyopathy and nephrotic syndrome a rare complication of HS. Secondary amyloidosis which are associated with chronic diseases, should be considered in patients with small ventricular volume with thick walls accompanying diastolic dysfunction in cardiology clinics.

Keywords: hydraadenitis suppuritiva; restrictive diastolic dysfunction; nephrotic syndrome

Giriş

Hidradenitis suppurativa (HS), cilt kıvrımlarını etkileyen kronik bir cilt hastalığıdır.

Anemi, proteinüri, lenfödem, nefrotik sendrom, artropati gibi nadir ancak ölümcül komplikasyonları olabilir.[1-3] AA amiloidoz, HS'nin çok nadir bir komplikasyonudur. Bu vakada restriktif diyastolik disfonksiyon, nefrotik sendrom ile seyreden bir HS olgusu sunulacaktır.

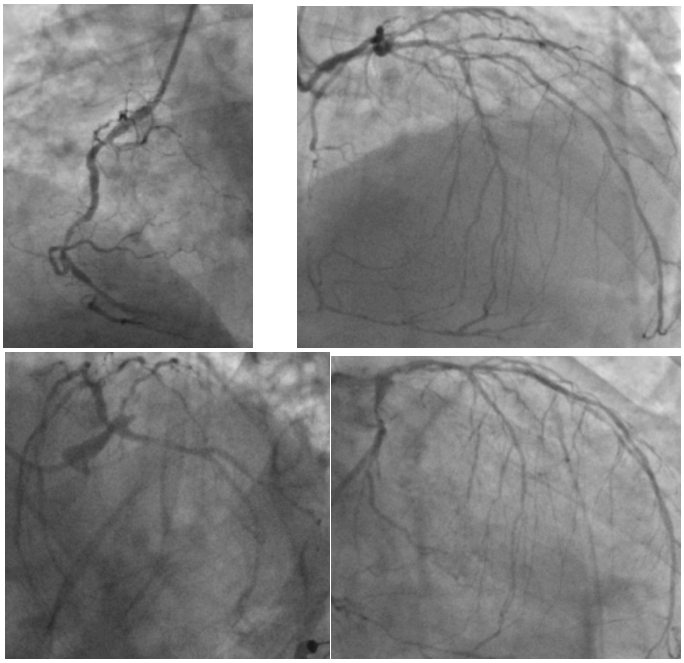
Olgu

46 yaşında, erkek hasta acil servise nefes darlığı, iki gündür ara ara tekrarlayan baskı şeklinde göğüs ağrısı, bacaklarda şişlik şikayeti ile başvurması üzerine istenen kardiyoloji konsültasyonu sonucu değerlendirildi. Daha önceden tedavi aldığı bir hastalığı olmadığı öğrenildi. Yapılan fizik muayenede göğüs bölgesinde bir yıldır kendisinin aralıklı olarak boşalttığını öğrendiğimiz nodüler-kistik bir lezyon vardı ve benzer lezyonlar gluteal ve aksiller bölgede de mevcuttu. Ayrıca bilateral orta-alt zonlarda ral, +++/+++ pretibial ödem, juguler venöz dolgunluk saptandı. Elektrokardiyografisinde sinüs ritmi, anterior derivasyonlarda R progresyon kusuru dışında bir özellik yoktu. Lab değerlerinde kreatin 2,2 mg/dl, glukoz 214 mg/dl, GFR/ckd-epi 35 ml/dk, LDL:187 mg/dl, albümin 30 g/l, HDL 27 mg/dl, troponin 218 ng/l, idrarda +++ protein saptanması üzerine hasta ST elevasyonsuz miyokard infarktüsü, dekompanse kalp yetersizliği, akut böbrek yetersizliği, yeni tanı diyabetes mellitus ön tanılarıyla interne edildi.

Hastanın yapılan ekokardiyografisinde EF %43 (Simpson), septum, apex, anterior ve inferior duvarlar hipokinetik, sağ atriyum 44x44 mm, sol atriyum volüm indeksi (LAVI) 42 ml/m2 (biatriyal dilatasyon), sol ventrikül end diastol çapı 45 mm, interventriküler septum 13 mm, posterior duvar 16 mm, E/A oranı 2, E/e':17, deselerasyon zamanı 99 ms, e' velositiesi 4 mm/sn saptanarak "grade 3 diyastolik disfonksiyon (restriktif diyastolik disfonksiyon)" olarak değerlendirildi. Anlamlı kapak hastalığı mevcut değildi.

Hastaya IV diüretik, antiagregan, antikoagülan, antiglisemik ve statin tedavisi başlandı. Hastanın cilt lezyonları için dermatoloji konsültasyonu istendi. Koltuk altı, göğüs ve gluteal bölgedeki lezyonların HS ile uyumlu olduğu saptandı. 24 saatlik idrarda makroskopik proteinüri mevcuttu. Restriktif kardiyomiyopatisi ve nefrotik sendromu olan hastada amiloidoz ön tanısı ile serum amiloid A düzeyi istendi, 120 mg/l (N:0-6.4) bulundu.

Serum ve idrar proteini elektroforezinde monoklonal gammopati kanıtı bulunamadı. Anti-nükleer antikor, romatoid faktör ve anti-sitrüline peptit antikoru, anti HBV IgG, IgM ve anti-HCV negatif saptandı. Renal ve karaciğer ultrasonunda anormal bulgu yoktu. Sekonder amiloidoz ve buna bağlı restriktif diyastolik disfonksiyon ve nefrotik sendrom tanısı konuldu. Hastaya renal değerleri düzelmesi üzerine koroner anjiyografi planladı. Hastada çoklu koroner arter hastalığı saptanması üzerine koroner arter bypass greftleme önerildi (resim 1). Hidradenitis suppurativaya bağlı sekonder amilodoz saptanan hasta dermatolojiye yönlendirildi.



Resim 1: Hastanın koroner anjiyografi görüntüleri ve çoklu koroner arter hastalığı

Tartışma

HS, ergenlikten sonra, çoğunlukla aksiller, inguinal ve anogenital bölgelerdeki ağrılı, derin yerleşimli lezyonlarla kendini gösterir. Hastalığın kronik seyri sırasında, diğer dokulara fistül veya anemi, sekonder amiloidoz, lenfödem, nefrotik sendrom, artropati gibi birçok lokal ve sistemik komplikasyon ortaya çıkabilir.[4]

İkincil sistemik amiloidoz, dünya çapında en yaygın amiloidoz türüdür.[5] Sistemik AA amiloid, büyük bir akut faz reaktanı olan serum amiloid A proteininin dokuda birikmesinden kaynaklanır.[6] Etkili tedavi olmadan, AA amiloidoz ölümcül olabilir, son dönem böbrek yetmezliği ölümün en önemli nedenidir.[7]

Vakamız restriktif kardiyomiyopati olması üzerine araştırılan HS'ye sekonder, sekonder amiloidoz tanısı konulan bir vaka örneği olması nedeniyle özelliklidir. Hastanın altta yatan koroner arter hastalığına diyabetes mellitusla birlikte nefrotik sendrom ve kronik inflamatuar durum da katkıda bulunmaktadır. Duvarları kalın ve küçük çaplı ventrikül boyutu, azaltılmış stroke hacmi ve sabit kardiyak output kardiak amiloidozun en önemli özellikleridir. Bu hastalarda paradoksik low flow-low gradient aort stenozu da görülebilir.[8]

Sonuç

Atriyal fibrilasyon yaygındır ve sert ventriküller nedeniyle zayıf tolere edilir. Amiloid infiltrasyonuna rağmen, yüksek sol ventrikül dolum basınçları nedeniyle atriyum dilatasyonu mevcuttur. Kronik hastalıklarla birliktelik gösteren sekonder amiloidoz kardiyoloji kliniklerinde diyastolik disfonksiyona eşlik eden kalın duvarlarla birlikte küçük ventrikül hacmi olan hastalarda akla gelmelidir.

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Olgu Sunumu

Toplum kaynaklı metisiline dirençli Staphylococcus aureus'a bağlı boyun bölgesinde karbonkül gelişen olgu

A case with carbuncle in the neck region due community-acquired Methicillin Resistant Staphylococcus aureus

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Öz

Metisiline dirençli Staphylococcus aureus (MRSA)'ya bağlı toplum kaynaklı deri ve yumuşak doku infeksiyonları oldukça nadirdir. Bu yazıda, son 6 ay içinde hastanede yatış öyküsü olmayan 74 yaşında diyabetik bir kadın hastada boyun bölgesinde toplum kaynaklı MRSA bağlı olarak gelişen karbonkül sunuldu. Teikoplanin tedavisi ve aralıklı karbonkül drenajı sonrasında hastanın şikayetleri ve laboratuvar bulguları düzeldi.

Anahtar kelimeler: toplum kaynaklı metisiline dirençli Staphylococcus aureus; deri ve yumuşak doku infeksiyonu; karbonkül

Abstract

Community acquired skin and soft tissue infections due to methicillin-resistant Staphylococcus aureus (MRSA) are extremely rare. In this article, a 74-year-old diabetic woman with no history of hospitalization in the last 6 months presented with a carbuncle in the neck region due to community-acquired MRSA. After teicoplanin treatment and intermittent drainage, the patient's complaints and laboratory findings improved.

Keywords: community acquired methicillin-resistant Staphylococcus aureus; skin and soft tissue infection; carbuncle

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Giriş

Toplum kaynaklı deri ve yumuşak doku infeksiyonları oldukça sık karşılaşılan infeksiyonlardır. Bu infeksiyonlardan başlıcaları; impetigo, erizipel, sellülit, nekrotizan fasittir.[1]

Karbonkül birden fazla fronkülün birbiriyle birleşmesi, apseleşerek yayılması ile oluşan, ayrı ayrı drene olması ile karakterize cilt lezyonudur. Karbonkülde bağ dokusu trabekülaları ile ayrılmış multiple apseler görülebilir. Karbonkül, ense, sırt, uyluk ve gluteal bölgede sık görülür. Karbonkül genellikle yavaş ve skar bırakarak iyileşir. Ateş ve lökositoz eşlik edebilir. Bazen toksemi veya metastatik enfeksiyona bağlı ölüm görülebilir. Altta yatan hastalık olarak sıklıkla diabetes mellitus eşlik edebilir. Karbonküller ve büyük fronküllerde antimikrobiyal tedavi ile birlikte insizyon ve drenaj gereklidir. Tedavide penisilinaza dirençli antibiyotiklerden amoksisilin/klavunat, penisilin alerjisi varsa klindamisin veya makrolidler verilebilir.[2-5] Bu yazıda, diyabeti olan 74 yaşında bir kadın hastada toplum kaynaklı MRSA'ya bağlı olarak karbankül gelişen bir olgu sunularak literatür gözen geçirildi.

Olgu

Yetmiş dört yaşında kadın hasta boyun bölgesinde kızarıklık, kaşıntı ve ağrılı şişlik yakınmaları ile polikliniğe müracaat etti. Anamnezinden diyabet, hipertansiyon ve romatizmal hastalık tanılarının olduğu öğrenildi. Ayrıca, 14 sene önce geçirilmiş serebrovasküler hastalık öyküsü ve buna bağlı sağ bacakta sekel mevcuttu.

Fizik muayenesinde; ateşi 36,4 °C, KB: 110/60 mm/Hg, boyun bölgesinde 2x3 cm boyutlarında etrafı krutlu, karbonkülle uyumlu, pürülan akıntılı lezyon mevcuttu. Diğer sistem muayeneleri normaldi. Laboratuvar testlerinde; lökosit sayısı 22.360 /mm3, sedimantasyon hızı 93 mm/saat, CRP 189 mg/dl idi. Biyokimyasal testleri; AST, ALT, BUN, ve kreatinin değerleri normaldi.

Hastada karbonkül bölgesinden kültür için örnek alındıktan sonra ampisilin/sulbaktam 4x 1.5 gr i.v yolla başlandı.Hastada karbonkül drenaj mayinin kültüründe Staphylococcus aureus (S.aureus) üredi. Disk difüzyon yöntemiyle yapılan antibiyogram sonucunda üreyen etkenin sefoksitin ve benzilpenisilline dirençli, siproflosasin, klindamisin, eritromisin, fusidik asit, gentamisin, tetrasiklin ve vankomisine duyarlı olduğu saptandı.Boyun bilgisayarlı tomografisi '15x60x50 mm boyutlarında apse' şeklinde raporlandı.

İzole edilen suşun VITEK 2 otomatize sistemi (Biomerioux, Fransa) ile de sefoksitine dirençli olduğu belirlendi. Kültürde üreyen etkenin MRSA olması üzerine hastaya ampirik olarak başlanan ampisilin/sulbaktam tedavisi 5. günde kesilerek, teikoplanin tedavisi 12 saat arayla 400 mg intravenöz (I.V.) yükleme, daha sonra 1x400 mg I.V. idame olacak şekilde başlandı.

Hastanın anamnezinden toplum kaynaklı MRSA infeksiyonları için risk faktörü olarak başvurudan birkaç hafta önce lezyon bölgesinde çıkan sivilceyi eliyle patlattığı öğrenildi. Hastada damar içi ilaç kullanımı, saç kesimi, bakım evinde kalma, ailede sağlık çalışanı öyküsü yoktu. Anamnezinden, son 6 ay içinde hastanede yatış ve son 3 ay içinde antibiyotik kullanımı öyküsü olmadığı öğrenildi. Hastadan burunda MRSA taşıyıcılığı açısından burun kültürü alımadı. Tedaviyle hastanın klinik şikayetleri geriledi, laboratuvar bulgularında CRP 1,35 mg/dl, lökosit sayısı ise 9280'e geriledi. Teikoplanin tedavisi 11 gün süreyle uygulanan hasta plastik cerrahi kliniğinde opere edilmek üzere oral fusidik asitle taburcu edildi.

Resim 1. Tedavi öncesi hastanın boyun bölgesinde saptanan 2 x 3 cm boyutlarındaki karbonkül lezyonu

Resim 2. Antibiyotik tedavisi ve aralıklı drenaj sonrasında 6 x6 cm boyutundaki lezyonun görüntüsü

Tartışma

MRSA, hem hastanede yatan hastalarda sağlık bakımıyla ilişkili infeksiyonlara (nozokomiyal, hastane kaynaklı) hem de sağlık bakımı ile ilişkili risk faktörleri olmayan toplum kaynaklı infeksiyonlara neden olabilen önemli bir infeksiyon etkenidir. Toplum kaynaklı metisiline dirençli S. aureus (TK-MRSA), toplumda hızlı bulaş gösterir, agresif seyirli deri ve yumuşak doku enfeksiyonları,toplum kökenli pnömoniye neden olabilir.[6]

Son yıllarda Avrupa ve Amerika başta olmak üzere tüm dünyada bakteriyel deri infeksiyonlarında toplum kökenli MRSA izolasyonunda artış bildirilmiştir .Toplum kaynaklı MRSA infeksiyonlarında bu durumda klindamisin veya kotrimoksazol kullanılabilir. Tedaviye yanıtsız olgularda kültür antibiyogram sonucuna göre tedavi başlamak gerekebilir. Şiddetli MRSA infeksiyonlarında intravenöz vankomisin ilk tercih seçenektir. [7-9] Alternatif olarak tedavide intravenöz linezolid, daptomisin, tigesiklin, telavansin ve seftarolin de tedavide kullanılabilir.[1]

Toplum kökenli (TK) birkaç klonun dünya ölçeğinde yayılmasıyla, özellikle risk faktörü taşımayan genç insanlarda deri ve yumuşak doku infeksiyonlarıyla nekrotizan pnömoni olgularında artış bildrilmiştir. Bu suşların daha virülan olduğu bildirilmektedir. TK-MRSA izolatlarının Panton-Valentin lökosidin (PVL) ve stafilokoksik kaset kromozom mec (SCC mec) tip IV varlığıyla karakterize olduğu, buna karşılık HK-MRSA suşlarında SCCmec tip I-III'in yaygın olduğu bilinmektedir.[5,7]

TK-MRSA infeksiyonları hastane kaynaklı (HK) MRSA'ların aksine büyük çoğunlukla deri ve deriyle ilişkili yapıların infeksiyonları şeklinde görülmektedir.[8] Toplumda sık rastlanan başlıca stafilokokal deri infeksiyonları; impetigo, folikülit, furonkül, apse ve selülit şeklinde sıralanabilir. S.aureus'a bağlı deri infeksiyonlarında hazırlayıcı faktör özellikle S. aureus burun taşıyıcılığıdır.[10]

Dünyanın hemen her bölgesinde TK-MRSA'ya bağlı infeksiyonlar artmaktadır.[6,11,12]

Almanya'da yapılan bir çalışmada TK-MRSA suşlarının Panton-Valentine leukocidin toksini taşıdığı, suşlarda kinolon, klindamisin, ve makrolid direnci yaygın iken, trimetoprim-sulfametoksazol, tetrasiklin, mupirosin, klorheksidin ve fusidikasit direncinin ise düşük olduğu bildirilmiştir.[11]

Ülkemizde poliklinik ve yatan hastalarda yapılmış bir çalışmada infeksiyonlardan 285, kontrol grubu olarak da diğer infeksiyonlardan 161 S. aureus suşu izole edilmiş; deri ve yumuşak doku infeksiyonu olan hastalar arasında %20.3 (n: 58), kontrol grubunda %24.2 (n:39) MRSA saptanmıştır. Her iki grup arasında SCC mec tip paterni açısından istatistiksel fark saptanmazken, hiçbir MRSA suşunda PVL tespit edilmemiştir. SCC mec tip IV taşıyan üç suş deri ve yumuşak doku infeksiyonlarından izole edilmiştir. Bu üç suştan ikisinde SCC mec tip IVa varlığı gösterilmiş olup biri submandibüler apse nedeniyle serviste tedavi alan bir hastadan yatışının ilk günü alınan örnekten izole edildiğinden dolayı TK-MRSA olarak kabul edilmiştir.[12] Sunduğumuz olguda son 6 ay içinde hastanede yatış öyküsü ve son 3 ay içinde antibiyotik kullanımı öyküsü olmaması nedeniyle toplum kaynaklı MRSA infeksiyonu olarak değerlendirildi. Sunduğumuz olguda altta yatan hastalık olarak diabetes mellitus mevcuttu. Olguda izole edilen MRSA suşunda moleküler yöntemlerin çalışılamaması çalışmamızın kısıtlılığı idi.

Sonuç

Sunduğumuz olguda olduğu gibi karbonkül gibi toplum kaynaklı cilt infeksiyonlarında toplum kaynaklı MRSA suşlarının da etken olabileceği akılda tutulmalı, mutlaka lezyondan örnek alınarak kültür ve antibiyotik duyarlılık testleri yapılarak tedaviye karar verilmelidir.

Çıkar çatışması/finansal destek beyanı

Bu yazıdaki hiçbir yazarın herhangi bir çıkar çatışması yoktur. Yazının herhangi bir finansal desteği yoktur.

* Makale için hastadan aydınlatılmış onam belgesi imzalatıldı.

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TURKISH JOURNAL of CLINICS and LABORATORY

Türk Klinik ve Laboratuvar Dergisi

Turkish Journal of Clinics and Laboratory - Türk Klinik ve Laboratuvar Dergisi

Tıp dergilerine gönderilecek makalelerin standart gereksinmeleri ile ilgili tüm bilgileri www.icmje.org internet adresinde bulabilirsiniz

Amaç ve kapsam: "Turkish Journal of Clinics and Laboratory", hakemli, açık erişimli ve periyodik olarak çıkan, DNT Ortadoğu Yayıncılık A.Ş. ye ait bir dergidir. Hedefimiz uluslararası bir tabanda hastalıkların teşhis ve tedavisinde yenilikler içeren yüksek kalitede bilimsel makaleler yayınlamaktır. Yılda dört kez çıkan bir bilimsel bir tıp dergisidir. Hakemli bir dergi olarak gelen yazılar konsültanlar tarafından, öncelikle, biyomedikal makalelere ait Uluslararası Tıp Dergileri Editörleri Komitesi (www.icmje.org adresinden ulaşılabilir) tarafından tanımlanan standart gereksinimler ile ilgili ortak kurallara uygunluğu açısından değerlendirilir. Tıbbın her dalı ile ilgili retrospektif/prospektif klinik ve laboratuar çalışmalar, ilginç olgu sunumları, davet üzerine yazılan derlemeler, editöre mektuplar, orijinal görüntüler, kısa raporlar ve cerrahi teknik yazılarıları yayımlayan bilimsel, uluslar arası hakemli bir dergidir. Başka bir dergide yayımlanmış veya değerlendirilmek üzere gönderilmiş yazılar veya dergi kurallarına göre hazırlanmamış yazılar değerlendirme için kabul edilmez.

On-line makale gönderimi: Tüm yazışmalar ve yazı gönderimleri dergipark üzerinden http://dergipark.gov.tr/tjcl yapılmalıdır. Yazı gönderimi için detaylı bilgi bu internet adresinden edinilebilir. Gönderilen her yazı için özel bir numara verilecek ve yazının alındığı e-posta yolu ile teyid edilecektir. Makalelerin "full-text" pdf formuna http://dergipark.gov.tr/tjcl linkinden ulaşılabilir.

Açık erişim politikası: Turkish Journal of Clinics and Laboratory açık erişimi olan bir dergidir. Kullanıcı lar yazıların tam metnine ulaşabilir, kaynak gösterilerek tüm makaleler bilimsel çalışmalarda kullanılabilir.

Aşağıdaki rehber dergiye gönderilen makalelerde aranan standartları göstermektedir. Bu uluslararası format, makale değerlendirme ve basım aşamalarının hızla yapılmasını sağlayacaktır.

Yazarlara Bilgi: Yazıların tüm bilimsel sorumluluğunu yazar(lar)a aittir. Editör, yardımcı editör ve yayıncı dergide yayınlanan yazılar için herhangi bir sorumluluk kabul etmez.

Dergi adının kısaltması: Turk J Clin Lab

Yazışma adresi: Yazılar e-mail yoluyla sorumlu yazar tarafından, Dergipark ta yer alan Turkish Journal of Clinics and Laboratory linkine girip kayıt olduktan sonra gönderilmelidir.

Makale dili: Makale dili Türkçe ve İngilizcedir. İngilizce makaleler gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Yazıdaki yazım ve gramer hataları içerik değişmeyecek şekilde İngilizce dil danışmanı tarafından düzeltilebilir. Türkçe yazılan yazılarda düzgün bir Türkçe kullanımı önemlidir. Bu amaçla, Türk Dil Kurumu Sözlük ve Yazım Kılavuzu yazım dilinde esas alınmalıdır.

Makalenin başka bir yerde yayımlanmamıştır ibaresi: Her yazar makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, editöre sunum sayfasında belirtmelidirler. 400 kelimeden az özetler kapsam dışıdır. Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal, vb.) yazarlara aittir.

Değerlendirme: Dergiye gönderilen yazılar format ve plagiarism açısından değerlendirilir. Formata uygun olmayan yazılar değerlendirilmeden sorumlu yazara geri gönderilir. Bu tarz bir zaman kaybının olmaması için yazım kuralları gözden geçirilmelidir. Basım için gönderilen tüm yazılar iki veya daha fazla yerli/yabancı hakem tarafından değerlendirilir. Makalelerin değerlendirilmesi, bilimsel önemi, orijinalliği göz önüne alınarak yapılır. Yayıma kabul edilen yazılar editörler kurulu tarafından içerik değiştirilmeden yazarlara haber verilerek yeniden düzenlenebilir. Makalenin dergiye gönderilmesi veya basıma kabul edilmesi sonrası isim sırası değiştirilemez, yazar ismi eklenip çıkartılamaz.

Basıma kabul edilmesi: Editör ve hakemlerin uygunluk vermesi sonrası makalenin gönderim tarihi esas alınarak basım sırasına alınır. Her yazı için bir doi numarası alınır.

Yayın hakları devri: http:/www.dergipark.ulakbim.gov.tr/tjclinlab adresi üzerinden online olarak gönderilmelidir. 1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı yayıncıya aittir.

Makale genel yazım kuralları: Yazılar Microsoft Word programı (7.0 ve üst versiyon) ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçede ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup 500 kelimeyi geçmemelidir. Özet sayfasından sonraki sayfalar numaralandırılmalıdır.

Yazının bölümleri

1. Sunum sayfası: Yazının Turkish Journal of Clinics and Laboratory 'de yayınlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, maddi destek ve çıkar ilişkisi durumu belirtmelidir.

2. Başlık sayfası: Sayfa başında gönderilen makalenin kategorisi belirtilmedir (Klinik analiz, orijinal çalışma, deneysel çalışma, olgu sunumu vs).

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir. Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, unvanları, çalıştıkları kurum, klinik ve şehir yazar isimleri altına eklenmelidir.

Bu sayfada "sorumlu yazar" belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

3. Makale dosyası: (Yazar ve kurum isimleri bulunmamalıdır)

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir.

Özet: Türkçe ve İngilizce yazılmalıdır. Orijinal çalışmalarda özetler, Amaç (Aim), Gereç ve Yöntemler (Material and Methods), Bulgular (Results) ve Sonuçlar (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir. Olgu sunumları ve benzerlerinde özetler, kısa ve tek paragraflık olmalıdır (150 kelime), Derlemelerde 300 kelimeyi geçmemelidir.

Anahtar kelimeler: Türkçe ve İngilizce özetlerin sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir. (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda birebir Türkçe tercümesi verilmelidir.

Metin bölümleri: Orijinal makaleler; Giriş, Gereç ve Yöntemler, Bulgular, Tartışma olarak düzenlenmelidir. Olgu sunumları; Giriş, Olgu sunumu, Tartışma olarak düzenlenmelidir. Şekil, fotoğraf, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli metin içine yerleştirilmemelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Tablolar metin sonuna eklenmelidir. Resimler/fotoğraf kalitesi en az 300dpi olmalıdır.

Etik kurallar: Klinik araştırmaların protokolü etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir. Turkish Journal of Clinics and Laboratory gönderilen yazıların Helsinki Deklarasyonuna uygun olarak yapıldığını, kurumsal etik ve yasal izinlerin alındığını varsayacak ve bu konuda sorumluluk kabul etmeyecektir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Teşekkür yazısı: Varsa kaynaklardan sonra yazılmalıdır.

Maddi destek ve çıkar ilişkisi: Makale sonunda varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve varsa bu kuruluşların yazarlarla olan çıkar ilişkileri belirtilmelidir. (Olmaması durumu da "Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur" şeklinde yazılmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalıdır. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 3 isim yazılıp ve ark. ("et al") eklenmelidir. Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org). Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır. Dergi kısaltmaları "Cumulated Index Medicus" ta kullanılan stile uymalıdır. Kaynak sayısının araştırmalarda 25 ve derlemelerde 60, olgu sunumlarında 10, editöre mektupta 5 ile sınırlandırılmasına özen gösterilmelidir. Kaynaklar metinde cümle sonunda nokta işaretinden hemen önce köşeli parantez kullanılarak belirtilmelidir. Örneğin [4,5]. Kaynakların doğruluğundan yazar(lar) sorumludur. Yerli ve yabancı kaynakların sentezine önem verilmelidir.

Şekil ve tablo başlıkları: Başlıklar kaynaklardan sonra yazılmalıdır.

4. Şekiller: Her biri ayrı bir görüntü dosyası (jpg) olarak gönderilmelidir.

Makalenin basıma kabulünden sonra "Dizginin ilk düzeltme nüshası" sorumlu yazara e-mail yoluyla gönderilecektir. Bu metinde sadece yazım hataları düzeltilecek, ekleme çıkartma yapılmayacaktır. Sorumlu yazar düzeltmeleri 2 gün içinde bir dosya halinde e-mail ile yayın idare merkezine bildirecektir.

Kaynak Yazım Örnekleri

Dergilerden yapılan alıntı;

Özpolat B, Gürpınar ÖA, Ayva EŞ, Gazyağcı S, Niyaz M. The effect of Basic Fibroblast Growth Factor and adipose tissue derived mesenchymal stem cells on wound healing, epithelization and angiogenesis in a tracheal resection and end to end anastomosis rat model. Turk Gogus Kalp Dama 2013; 21: 1010-19.

Kitaptan yapılan alıntı;

Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Tek yazar ve editörü olan kitaptan alıntı;

Neinstein LS. The office visit, interview techniques, and recommendations to parents. In: Neinstein LS (ed). Adolescent Health Care. A practical guide. 3rd ed. Baltimore: Williams&Wilkins; 1996: 46-60.

Çoklu yazar ve editörü olan kitaptan alıntı;

Schulz JE, Parran T Jr: Principles of identification and intervention. In:Principles of Addicton Medicine, Graham AW. Shultz TK (eds). American Society of Addiction Medicine, 3rd ed. Baltimore: Williams&Wilkins; 1998:1-10.

Eğer editör aynı zamanda kitap içinde bölüm yazarı ise;

Diener HC, Wilkinson M (editors). Drug-induced headache. In: Headache. First ed., New York: Springer-Verlag;1988:45-67.

Doktora/Lisans Tezinden alıntı;

Kılıç C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Bir internet sitesinden alıntı;

Sitenin adı, URL adresi, yazar adları, ulaşım tarihi detaylı olarak verilmelidir.

DOI numarası vermek;

Joos S, Musselmann B, Szecsenyi J. Integration of Complementary and Alternative Medicine into Family Practice in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi: 10.1093/ecam/nep019).

Diğer referans stilleri için "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References" sayfasını ziyaret ediniz.

Bilimsel sorumluluk beyanı: Kabul edilen bir makalenin yayınlanmasından önce her yazar, araştırmaya, içeriğinin sorumluluğunu paylaşmaya yetecek boyutta katıldığını beyan etmelidir. Bu katılım şu konularda olabilir:

a. Deneylerin konsept ve dizaynlarının oluşturulması, veya verilerin toplanması, analizi ya da ifade edilmesi;

b. Makalenin taslağının hazırlanması veya bilimsel içeriğinin gözden geçirilmesi

c. Makalenin basılmaya hazır son halinin onaylanması.

Yazının bir başka yere yayın için gönderilmediğinin beyanı: "Bu çalışmanın içindeki materyalin tamamı ya da bir kısmının daha önce herhangi bir yerde yayınlanmadığını, ve halihazırda da yayın için başka bir yerde değerlendirilmede olmadığını beyan ederim. Bu, 400 kelimeye kadar olan özetler hariç, sempozyumlar, bilgi aktarımları, kitaplar, davet üzerine yazılan makaleler, elektronik formatta gönderimler ve her türden ön bildirileri içerir."

Sponsorluk beyanı: Yazarlar aşağıda belirtilen alanlarda, varsa çalışmaya sponsorluk edenlerin rollerini beyan etmelidirler:

1. Çalışmanın dizaynı

2. Veri toplanması, analizi ve sonuçların yorumlanması

3. Raporun yazılması

Kontrol listesi:

1. Editöre sunum sayfası (Sorumlu yazar tarafından yazılmış olmalıdır)

2. Başlık sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Yazarlar, kurumları, sorumlu yazar posta adresi, tüm yazarların e-mail adresleri, sorumlu yazarın telefon numarası)

3. Makalenin metin sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Özet/anahtar kelimeler, Summary/keywords, makale metni, kaynaklar, tablo ve şekil başlıkları, tablolar, şekiller)

4. Tablo ve grafikler metin içinde olmalıdır.

5. Şekiller (En az 300 dpi çözünürlükte) ayrı bir veya daha fazla dosya halinde gönderilmelidir.