International Archives of Medical Research

Cilt/Volume: 14, Sayı/Issue: 1 – 2022
ISSN : 2146-6033

Dergide yayınlanan yazılar izinsiz başka bir yerde yayınlanamaz veya bildiri olarak sunulamaz.

Adress : Dicle Universty,Faculty of Medicine.Department of Microbiology / Diyarbakır
Post Code : 21280
Mail : nakpolat21@gmail.com
web : https://dergipark.org.tr/tr/pub/iamr
Online ISSN : 2146-6033

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ORIGINAL RESEARCH PAPER

Retrospective Analysis of 53 Cases who Developed Colon Fistula

Received Date: 28.12.2021, Accepted Date: 13.06.2022

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Özet:

Özet: *Objektif: Kolon kanseri kadın ve erkeklerde sık görülen kanserler arasındadır. Rezeksiyon sonrası anastomoz ayrılması istenmeyen bir durumdur. Anastomoz kaçağı gelişmesine etkili çeşitli risk faktörleri vardır.*

Metod: *Elliüç kolon anastomoz kaçağı olgusu retrospektif olarak çalışmada yer almıştır. Bu hastalarda demografik özellikler ve yandaş hastalıklar retrospektif olarak değerlendirilmiş ve risk faktörleri literatür ile karşılaştırılmıştır.*

Sonuçlar: *Elliüç olgudan otuz vakada ek hastalık tespit edilmiştir. En çok tespit edilen yandaş hastalık diabetes mellitus(DM) ve hipertansiyon(HT) olup daha az sıklıkta ise kronik obstruktif akciğer hastalığı(KOAH) vb kronik hastalıklar tespit edilmiştir. Fistül gelişen hastalarda mortalite oranı %11 olup mortal olgularda genellikle DM ve HT birliktelik göstermektedir.*

Tartışma: *KOAH'lı hastalarda yetersiz alveoler ventilasyon ve bunun sonucunda hipoksi ve hiperkapni, doku onarım süreçlerinde olumsuz etkiye sahiptir. Mikro sirkülasyondaki değişiklikler ve hastanın diyabetes mellitus (DM) ile ilişkili enfeksiyona daha fazla duyarlılığı postoperatif fistül gelişiminde risk faktörüdür. DM ile birlikte obezite de mevcut ise anastomoz kaçak riski daha da yüksek olabiliyor. Preoperativ diastolik yüksek basınç , anastomoz kaçak riskini arttıran diğer bir faktördür. Sonuç olarak hipertansiyon, obezite, diabet, KOAH , kolorektal cerrahi sonrası anastomoz kaçaklarında etkili risk faktörleridir. Bu risk faktörleri morbidite ve mortalite artışında etkili olmaktadır.*

Anahtar Kelimeler: *Colon, cancer, Anastomosis, Leakage,Fistula*

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Abstract:

Objective: *Colon cancer is among the most common cancers in men and women. Separation of anastomosis after resection is undesirable. There are various risk factors affecting the development of anastomotic leakage.*

Methods: *Fifty-three cases of colon anastomotic leakage were included in the study retrospectively. Demographic characteristics and co-morbidities in these patients were evaluated retrospectively and risk factors were compared with the literature.*

Results: *Additional disease was detected in thirty of fifty-three cases. The most common co-morbidities are diabetes mellitus (DM) and hypertension (HT), while less frequent chronic diseases such as chronic obstructive pulmonary disease (COPD) have been detected. Mortality rate is 11% in patients who develop fistula, and DM and HT usually coexist in mortal cases.*

Conclusion: *Inadequate alveolar ventilation and consequently hypoxia and hypercapnia have negative effects on tissue repair processes in patients with COPD. Changes in the microcirculation and the patient's greater susceptibility to diabetes mellitus (DM)-related infection are risk factors for the development of postoperative fistula. If obesity is present together with DM, the risk of anastomotic leakage may be even higher. Preoperative diastolic pressure is another factor that increases the risk of anastomotic leakage. In conclusion, hypertension, obesity, diabetes, COPD are effective risk factors for anastomotic leakage after colorectal surgery. These risk factors are effective in increasing morbidity and mortality. Key words: colon, cancer, anastomosis, leakage, fistula*

Key words: *Colon, cancer, Anastomosis, Leakage, Fistula*

Introduction

Colon cancer is among the most common cancers in men and women. Colonoscopy is the recommended and frequently used diagnostic method for the prevention and early diagnosis of colon cancer. Thanks to colonoscopy, early diagnosis of colon cancer can be achieved, while polypectomy can prevent cancers that may develop from polyps[1].

Colon cancer surgery is one of the most frequently performed cancer surgeries, as colon cancer is frequently seen. For this reason, the problems related to these surgeries affect more people in the society. In proportion to the frequency of surgeries, the interest of scientists in research on this subject is increasing. Colon fistulas have an important place among the effective factors in morbidity and mortality after surgical treatment of colon cancer. While medical treatment is sufficient in some cases after fistula development, in some cases reoperation may be required for

fistula treatment. Fistulas may heal with medical-surgical treatment or may cause mortality. There are various predisposing risk factors for fistula development. One of these risk factors is comorbidities. Concomitant risk factors were examined in our series [2,3].

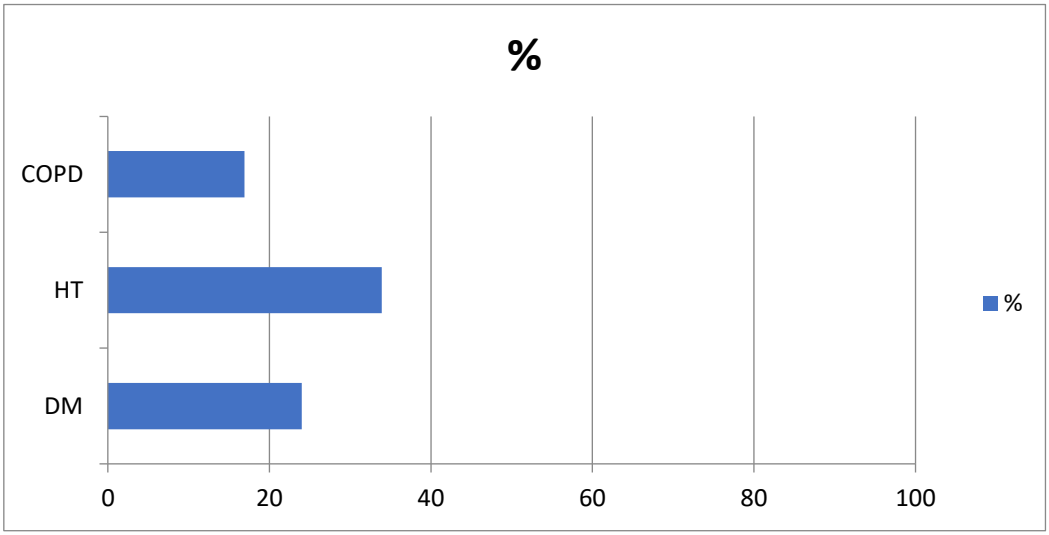
Material and Methods

Fistula cases seen in our colorectal cancer patient who was operated in Tepecik EAH Surgery Clinic between January 1, 2012 and January 1, 2020 were retrospectively analyzed. The demographic characteristics of the patients in our fistula series, co-morbidities were examined and discussed in the light of the literature.Our study was approved by the Tepecik Training and Research Hospital Medical Faculty Ethics Committee.

Result

Between January 1, 2012 and January 1, 2020, 602 colorectal cancer cases were operated in our clinic. Fistula developed in 53 of these patients. The rate of fistula development in our series was 8.8%. The female/male ratio is 25/28. The average age was found to be 61±12 year. Additional disease was detected in 30 of 53 cases. A comorbid condition was detected in some of these 30 cases and more than one comorbid disease in others. Diabetes Mellitus (DM) was detected in 13 (24%) cases, Chronic Obstructive Pulmonary Disease (COPD) was detected in 9(16,9%) cases and Hypertension (HT) was detected in 18(33,9%) cases**(Table 1)**. Chronic diseases such as coronary artery disease, etc. have been detected much less frequently.

Table 1: *Comorbidity ratios in colonic fistula cases*



In our series of 6 patients who died in the first month postoperatively and developed fistula, the mortality rate was 11%. No additional disease was detected in 2 cases in Ex patients. HT and DM were the most common comorbid conditions in the remaining 4 cases. Tumor localizations in our fistula series were determined as follows: 36 rectum, sigmoid 5, left colon 2, right colon 5, cecum 5.

Discussion

Colorectal cancers are among the most frequently performed oncological surgical operations in surgical practice. Compared to the past, more advanced levels have been reached in the diagnosis and treatment of colorectal cancer. Thanks to the diagnostic methods applied today, earlier diagnosis is possible. Colorectal cancers are most common in men (56.8%). The rectum is the most common (55%) site of colorectal carcinoma. The incidence of cancer in other colon segments is less [4,5].

In our fistula series, fistula was most common in males. A positive correlation was observed between the prevalence of colorectal cancers in males and the higher incidence of fistula in males. Fistula was most commonly seen after rectal Ca surgeries. The most common cancer location in the colorectal region is the rectum, and the postoperative fistula location is the rectum [6,7,8,9]. In cases of colorectal cancer, anastomotic leakage after resection may lead to local peritonitis, generalized peritonitis, and sepsis and may lead to a mortal course. In some clinical studies, the mortality rate due to anastomotic leakage was reported as 12.9%. This rate was found to be 11% in our series [10]. Comorbidities have effects on morbidity and mortality. Chronic obstructive pulmonary disease is a common condition in the elderly. Insufficient alveolar ventilation and consequently hypoxia and hypercapnia have negative effects on tissue repair processes in patients with COPD. Experimental studies have shown that hydroxylation of collagen fibrils interacts with hypoxia, resulting in insufficient mechanical resistance. In a clinical study, it was observed that the rate of postoperative colon fistula development was higher in patients with COPD [11,12]. In our fistula series COPD was found of 16,9% Changes in the microcirculation and the patient's greater susceptibility to diabetes mellitus (DM)-related infection are risk factors for the development of postoperative fistula. DM is an effective factor contributing to the development of anastomotic leakage after colon anastomosis. In clinical studies, if obesity is present together with DM, the risk of anastomotic leakage was found to be even higher. In our fistula series DM was found of 24% . In addition, obesity, protein-calorie malnutrition, acute and massive anemia, and blood transfusion can be counted among the effective factors in the development of fistula [11,13,14].

Hypertension is an undesirable condition. It causes many complications in the human body. One of these complications is its effects on colorectal surgery. Preoperative diastolic pressure is a factor that increases the risk of anastomotic leakage. In our fistula series HT was found of 33,9% It has been reported that preoperative diastolic pressure higher than 90mmHg and significant intraoperative hypotension (more than 40% decrease in diastolic pressure) are risk factors for the development of anastomotic leakage [15,16].

Conclusion

In conclusion, in the presence of risk factors, the development of anastomotic leakage can be seen in colorectal surgery. When we examine our series in the light of literature review, hypertension, obesity, diabetes, COPD are effective risk factors in anastomotic leaks after colorectal surgery. These risk factors are effective in increasing morbidity and mortality.

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ORIGINAL RESEARCH PAPER

Why are the First-Line Therapies Used as Injections Discontinued in the Treatment of Multiple Sclerosis?

Received Date: 15.03.2021, Accepted Date: 21.04.2021

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Abstract:

Objective: *Immunomodulatory therapies are used in the treatment of multiple sclerosis considering their efficacy and safety. Although other effective treatments have been used in recent years, the use of immunomodulatory therapies continues. In this study, we aimed to reveal the reasons for the discontinuation of immunomodulatory therapies used as injections.*

Method: *Immunomodulatory therapies data of 1464 patients were collected and analysed from the Imed database, where 20-year data of the patients were entered by us. Groups were divided as; Interferon beta-1a subcutaneous, interferon beta-1a intramuscular, glatiramer acetate and Interferon beta-1b. Age, gender, duration of illness, types of disease onset, time to start the injection, duration of injection therapy, and reason for discontinuation of patients were analysed.*

Results: The most common reason for discontinuation of treatments was found to be disease progression (20.13%, 28.14%, 19.64%, 23.87%). Side effects, increased relapse frequency, patient demand, disease activity detection in imaging methods, and pregnancy planning followed the disease progression respectively.

Conclusion: *Immunomodulatory therapies as an injection form are used in the treatment of multiple sclerosis, considering their effectiveness and reliability. The most common reason for discontinuing treatment is disease progression.*

Keywords: *Multiple sclerosis, immunomodulatory therapy, interferon beta, glatiramer acetate*

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Introduction

Multiple Sclerosis (MS) is a chronic disease of the central nervous system that progresses with loss of myelin and axon damage [1]. Immunomodulatory therapies (IMTs) were currently used to control this disease. Interferon beta-1b (IFN-β1b), approved in 1993, is the first IMT agent for MS treatment. This was followed by intramuscular form of interferon beta-1a intramuscular (IFN-β1a IM) in 1995, glatiramer acetate (GA) in 1996, and interferon beta-1a subcutaneous (IFN-β1a SC) in 1998 [2]. MS disease has been tried to be controlled with the help of these treatments for many years. Although oral, intravenous and monoclonal new treatment options have started to be used in the last 10 years, the molecules used in the form of injection in the traditional MS treatment still maintain their place in the treatment.

IMTs are applied in an algorithm according to their effectiveness and reliability, taking into account the clinical demographics of the patients. In addition to stepwise treatment, the use of high-efficacy treatments is another option at the initial stage [2]. The most decisive limitation for the use of high-efficacy treatments is the side effects. The immunosuppression caused by these treatments may also cause additional problems [3]. For these reasons, injection treatments still maintain their validity and effectiveness, although they do not create high efficacy compared to new treatment options.

For MS patients using injection therapies, it may be necessary to switch to higher-level therapies in cases such as inability to cope with side effects, inadequate relapse control, and disease progression. In the present study, the reasons for discontinuation of IMTs as an injection form during MS treatment are discussed in detail.

Multiple Sclerosis (MS) is a chronic disease of the central nervous system that progresses with loss of myelin and axon damage [1]. Immunomodulatory therapies (IMTs) were currently used to control this disease. Interferon beta-1b (IFN-β1b), approved in 1993, is the first IMT agent for MS treatment. This was followed by intramuscular form of interferon beta-1a intramuscular (IFN-β1a IM) in 1995, glatiramer acetate (GA) in 1996, and interferon beta-1a subcutaneous (IFN-β1a SC) in 1998 [2]. MS disease has been tried to be controlled with the help of these treatments for many years. Although oral, intravenous and monoclonal new treatment options have started to be used in the last 10 years, the molecules used in the form of injection in the traditional MS treatment still maintain their place in the treatment.

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Materials and Methods

After the Ethics Committee of Ondokuz Mayıs University (Samsun, Turkey) approved the protocol of the study (2021/489), previously entered data by expert neurologist to the IMed database were obtained and analysed. The data of 2456 patients followed up in Ondokuz Mayıs University Faculty of Medicine MS Unit of Neurology Department between January 2001 - January 2021 were scanned for the study. Among these patients, 1464 patient-injection therapy matches were identified and included in the study. Age, gender, disease duration, disease onset patterns, injection initiation time, duration of injection therapy, and treatment discontinuation reason of patients were analysed.

Statistical analysis

Data were analysed with IBM SPSS V25 statistical package program. A chi-Square test was used to determine the presence of a significant difference between the treatment groups. One-way analysis of variance (ANOVA) and post-hoc Tukey-Kramer tests were used to compare the duration of discontinuation of treatment among groups. Data are given as mean ± standard deviation or percent (%).

Result

Table 1 reveals demographic profiles on age and disease duration. When this table was analysed, it was determined that there was a similarity among injection groups and there was no significant difference.

Table 1. *Demographic profiles of study participants.*

IMT	Age (years)				Disease duration (years)			
	IMT starting		Current		IMT starting		Current	
	Mean (SD)	Min-Max	Mean (SD)	Min-Max	Mean (SD)	Min-Max	Mean (SD)	Min-Max
IFN-β1a SC	31,95 (9,98)	11,43-61,73	41,01 (11,08)	17,14-72,16	1,98 (3,57)	0-19,84	11,12 (6,35)	0,31-29,44
IFN-β1a IM	31,26 (9,95)	11,01-61,32	42,56 (11,65)	16,37-73,33	1,54 (2,69)	0-13,51	13,47 (5,83)	0,81-30,38
GA	35,54 (10,66)	18,07-60,23	43,93 (11,48)	20,12-73,04	3,05 (4,70)	0-20,64	11,91 (6,62)	0,11-35,78
IFN-β1b	33,44 (10,04)	15,71-63,71	44,54 (11,69)	21,89-74,41	2,15 (3,52)	0-17,77	12,28 (7,25)	0-31,27

IMT: Immunomodulatory therapy, IFN-β1a SC: Interferon beta-1a subcutaneous, IFN-β1a IM: Interferon beta-1a intramuscular, GA: glatiramer acetate, IFN-β1b: Interferon beta-1b.

The number of patients whose IMT treatment was continued or discontinued is shown in table 2. When the number of patients whose treatment was discontinued and continued, Chi-square test revealed no significant difference among treatment groups. The rate of continuation of treatment in IFN-β1a SC, IFN-β1a IM, GA and IFN-β1b groups were %27.4, %27.1, %31.3, and %19.0, respectively. In patients whose treatment was discontinued, there was no significant difference in terms of duration of drug use. The duration of discontinuation of treatment in IFN-β1a SC, IFN-β1a IM, GA and IFN-β1b groups were 4.33±4.61, 4.78±4.48, 4.02±4.44, and 4.51±4.42 years respectively.

Table 2. *Number of patients continuing/discontinuing IMTs treatment and the duration of IMTs treatment.*

IMT	Total IMT n (%)	Continuing IMT n (%)	Discontinuing IMT n (%)	Duration of IMT (years) Mean ± SD
IFN-β1a SC	423 (100)	116 (27,40)	308 (72,60)	4.33 ± 4.61
IFN-β1a IM	384 (100)	104 (27,10)	280 (72,90)	4,78 ± 4.48
GA	383 (100)	120 (31,30)	263 (68,70)	4.02 ± 4.44
IFN-β1b	274 (100)	52 (19,00)	222 (81,00)	4.51 ± 4.42

IMT: Immunomodulatory therapy, IFN-β1a SC: Interferon beta-1a subcutaneous, IFN-β1a IM:

Interferon beta-1a intramuscular, GA: glatiramer acetate, IFN-β1b: Interferon beta-1b.

Table 3 shows reasons for discontinuation of treatment. It was observed that treatment was discontinued most frequently due to increase in disease progression-disability. This was followed by side effects, increased frequency of relapses, patient request, improvement in imaging findings, pregnancy status and other reasons.

Table 3. *Reasons for Discontinuing IMTs.*

IMT	Total	Disease progression	Side effects	Relapse frequency	Patient demand	MRI activity	Pregnancy	Others	Unknown
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
IFN-β1a SC	308 (100)	62 (20,13)	63 (20,45)	22 (7,14)	22 (7,14)	19 (6,17)	20 (6,49)	31 (10,06)	69 (22,40)
IFN-β1a IM	280 (100)	55 (19,64)	33 (11,79)	16 (5,71)	29 (10,36)	25 (8,93)	12 (4,29)	45 (16,07)	65 (23,21)
GA	263 (100)	74 (28,14)	46 (17,49)	19 (7,22)	11 (4,18)	13 (4,94)	4 (1,52)	40 (15,20)	56 (21,29)
IFN-β1b	222 (100)	53 (23,87)	44 (19,82)	15 (6,76)	15 (6,76)	14 (6,31)	4 (1,80)	38 (17,129	39 (17,57)

IMT: Immunomodulatory therapy, IFN-β1a SC: Interferon beta-1a subcutaneous, IFN-β1a IM: Interferon beta-1a intramuscular, GA: glatiramer acetate, IFN-β1b: Interferon beta-1b. MRI: magnetic resonance imaging

Discussion

In the last 20 years, there have been rapid developments in the treatment of MS disease. Although the disease cannot be completely cured, the number of relapses can be reduced, the increase in disease progression and brain atrophy can be prevented with the current drugs [2]. Apart from these parameters, *no evidence of disease activity* (NEDA) [4] and progression independent of relapse activity (PIRA) [5] concepts have come into prominence. As in previous years, waiting for a long time in low-efficacy treatments is replaced by starting high-effective treatments as soon as possible [6,7]. IMTs used as injections are still used and the effects that expected from IMTs are increasing day by day in the treatment of MS.

There are not major safety problems for the first-line IMTs used as injections [2]. Thanks to the experience accumulated over many years, almost all the side effects that may occur during the use of these treatments have been observed and management strategies have been determined.

However, it is very difficult to cope with the side effects and to manage the ineffectiveness-disease progression state. Our study revealed that the treatments used in this way were most frequently discontinued due to disease progression and side effects. This result is in parallel with the current MS treatment strategies.

The interesting aspect of our study is that gender distribution, age and disease duration are similar in all four IMTs groups. In addition, a similar duration of treatment was observed in all treatment groups. The fact that IFN-β1a IM treatment, which provides lower disease activity control than other injection treatments, has similar findings with other treatments, may possibly be related to the initiation of the patient group with lower activity. For preventing disease progression, the most effective strategy applied today is known as switching to a high-efficiency treatment rather than switching within the first-line treatments [6]. From this point of view, it can be said that this is the most obvious reason for reducing the use of first-line injection treatments.

Side effects are another problem for IMTs injection treatments. Patient compliance has a great impact on treatment effectiveness [8,9]. Correct application of IMDs by patients is of great importance in terms of avoiding side effects. Minor changes in the way of the administration of the IMTs may improve compliance [10, 11]. In this respect, it is very important to give injection trainings to patients by MS professionals. The occurrence of side effects, which was the second most common reason of discontinuation in our study, can be the sign of this reason. The best way to optimize success in MS treatment is through the appropriate administration of treatments that meet the NEDA criteria. For this reason, it is necessary to consider the parameters such as efficacy, reliability, patient compliance [2, 12]. Although we can say that the problem of safety for first-line injection treatments has been overcome, efficacy and management of side effects are still among the most basic problems.

Apart from the inability to control the disease activity, it is seen that the treatments are also discontinued for patient request and pregnancy planning. For MS patients with pregnancy planning, first-line IMTs appear to be safe compared to other treatment options [13]. Although this can be seen as an advantageous situation, the discontinuation of the treatment with the patient request approaching 10 percent should not be ignored. It is very important to evaluate this pregnancy planning patient group in more detail, to reveal the situation that caused the discontinuation of the treatment and to reorganize it in an appropriate way.

Conclusion

Similar results for IFN and GA treatments indicate that the most common reasons of discontinuation of IMTs are disease progression and side effects. For optimal MS treatment, individualized patient-specific approaches should be applied. From this point of view, first-line injection treatments can be continued to be used, considering efficacy, safety and side effects.

Conflict of interest

The authors declare no conflict of interest.

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International Archives of Medical Research 14:1 (2022) 13-19

ORIGINAL RESEARCH PAPER

Multiple Myeloma; Experience of a Center

Received Date: 19.04.2022, Accepted Date: 07.05.2022

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Özet:

Amaç: *Multıple myelom(MM) tanısı konulmuş olan hastaların tanı anındaki demografik özellikleri, laboratuvar parametreleri, verilen tedavileri ve tedavi yanıtları toplumlar arası farklılık göstermektedir. Multple myelom hastalarının bu verilerini araştırmayı ve literatür verileriyle karşılaştırmayı hedefledik.*

Materyal Metot: *Bu çalışmada 1 Ocak 2010-31 Ocak 2019 tarihleri arasında ..... Üniversitesi tıp fakültesi iç hastalıkları hematoloji kliniğinde MM tanısı konulmuş 272 hastanın verileri retrospektif olarak incelendi. Çalışmaya alınan hastaların tanı anındaki genel özellikleri, laboratuvar değerleri, tedavi seçenekleri, tedavi yanıtları, ortalama ve ortanca sağkalım süreleri ve mortalite nedenleri araştırıldı.*

Bulgular: *Multıple myelom hastalarımızın alt tip analizlerinde hastaların 124'ü(%45,6) ıgG, 50'si(%18,4) ıgA, 59'u(%21,7) hafif zincir, 21'i(%7,7) plazmasitom, 4'ü(%1,5) ıgM, 3'ü(%1,1) plazma hücre lösemisi, 11'i(%4) de nonsekretuvar myelom olarak bulundu. 77 hastaya otolog hematopoetik kök hücre nakli (OHKHN) yapıldı. OHKHN yapılan hastalarda ortalama yaşam süresi 68 ay iken OHKHN yapılmayan hastalarda bu süre 42 ay olarak tespit edildi (p<0,001). En sık mortalite sebeblerini enfeksiyonlar (%55), tromboembolik olaylar (%22), hemorajik kompikasyonlar ve hastaların komorbid durumları (%22) oluşturdu.*

Sonuç: *Myelom tanımlayıcı olayların oranları, tedavi yanıt oranları, sağkalım süreleri, OHKHN yapılan hastalardaki sağkalım süreleri ve mortalite nedenleri literatür verileriyle benzer bulundu. Tedavi yanıt oranları ve ortalama sağkalım sürelerinin yeni ajanların çıkmasıyla arttığını görmekteyiz.*

Anahtar Kelimeler: *Myelom, New agents, Transplantation*

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Abstract:

Objective: *Demographic characteristics, laboratory parameters, applied treatments, and treatment responses of patients diagnosed with multiple myeloma (MM) at the time of diagnosis vary between communities. We aimed to investigate this data of Multiple Myeloma patients and compare it with literature data.*

Material Method: *In this study, we retrospectively examined data of 272 patients diagnosed with MM between January 1st, 2010, and January 31st, 2019 in ..... University Faculty of Medicine Internal Medicine Hematology Clinic. At the time of diagnosis, general characteristics, laboratory values, treatment options, treatment responses, mean and median survival times, and causes of mortality of the participated patients in the study were investigated.*

Results: *We found that 124 (45.6%) patients had IgG, 50 patients had (18.4%) ıgA, 59 patients had (21.7%) light chain, 21 patients had (7.7%) plasmacytoma, four patients had (1.5%) ıgM, three patients had (1.1%) plasma cell leukemia, and 11 patients had (4%) non-secretory myeloma. 77 patients underwent autologous hematopoietic stem cell transplantation (AHSCT). The average life expectancy in patients with AHSCTwas 68 months, while in patients without AHSCT, this period was determined as 42 months ($p<0.001$).*

Conclusion: *We see that treatment response rates and average survival times increase with the introduction of new agents.*

Key words: *Myelom, New agents, Transplantation*

Introduction

Multiple myeloma (MM) is a hematological disorder characterized by the proliferation of malignant plasma cells in the bone marrow. Plasma cells produce abnormal monoclonal paraprotein and/or immunoglobulin light chains, causing organ damage[1]. At the time of diagnosis, 20% of patients experience kidney failure, which is also of prognostic importance[2]. Anemia (hb<10 g/dl) occurs in 40-72% of patients[3]. 66% of patients with multiple myeloma have a bone event (osteolytic bone lesions, bone fractures, and osteoporosis). The average life expectancy with traditional chemotherapy regimens is 3-4 years, while with autologous hematopoietic stem cell transplantation, this period has increased to 5-7 years. The life expectancy of 5 years is 46%[4]. Immune paralysis is the main cause of frequent and severe infections in myeloma. It is also the biggest cause of mortality[5]. Other causes of mortality are treatment-related toxicity and thrombosis, bleeding, and amyloidosis in patients diagnosed with multiple myeloma[3,5].

The objective of this study conducted on 272 patients diagnosed with MM at adult hematology clinic is to investigate the demographic characteristics of patients such as age, gender at the time of diagnosis, their hemogram and biochemical parameters, presence of bone cases, whether they have or have not received radiation therapy, which type of myeloma was diagnosed, whether AHSCT performed or not, patients' mean and median survival time diagnosed with multiple myeloma and mortality causes.

Material and Methods

This study included 272 patients older than 18 who were diagnosed with MM between January 1st, 2010 and January 31st, 2019 in Dicle University Faculty of Medicine Internal Medicine Hematology Clinic and whose data can be accessed.

The 2010 International Myeloma Working Group (IMWG) diagnostic criteria were applied to patients diagnosed before 2015, and the updated IMWG diagnostic criteria as of 2014 were applied to patients diagnosed in 2015 and after. Demographic characteristics of patients diagnosed with MM at the time of diagnosis were investigated, their values of hemoglobin (Hb), platelet (plt), white blood cell (WBC), urea, creatinine (cr), calcium (ca), total protein, globulin, the presence of bone cases, myeloma subtypes, treatment responses, life expectancy, and causes of mortality were investigated using the hospital system.

In this study, the prevalence of the disease, the age, the female-male ratio, the rates of events descriptive at myeloma diagnosis, except for anemia, and the presence of bi-cytopenia, pancytopenia; their total protein and globulin values, the sub-type of myeloma, the sequence of their treatment, causes of mortality, and survival were evaluated. Comparing the life expectancy of patients with and without AHSCT, the treatment response rates in stages and the causes of mortality were reviewed.

The Dicle University Faculty approved this thesis of Medicine Non-interventional Clinical Research Ethics Committee's Decision No. 196 dated 06.06.2018.

***Statistical Analysis**:* Statistical analysis of the results obtained in the study was performed using the statistical software package SPSS (Statistical Package for the Social Sciences) 18.0. Descriptive statistics amongst the continuous variables focused on were expressed as mean ± standard deviation, minimum and maximum value, while categorical variables were expressed as numbers and percentages. Chi-square test was also used in the analysis of categorical variables (such as gender, bone involvement, renal failure, hypercalcemia, anemia). Overall survival, intra-group

survival, and 5-year life expectancy were investigated using the Kaplan-Meier test. In these tests, the value of p (probability) less than 0.05 was considered to be statistically significant.

Result

The median age of 272 patients admitted to ..... University Hospital and diagnosed with MM was 64 (24-94), and the average age of disease incidence was 62. Out of the patients, 159 (58.5%) were male, and 113 (41.5%) were female. The number of patients under 40 years of age was 13 (4.8%), the number of patients over 65 years of age was 125 (45.9%), the number of patients between 40-65 years of age was 134 (49.3%), and the ratio of men and women was 1,4/1 (Table 1).

Table 1. *Age and Gender distributions of patients at the time of admission*

Number of male patients	159(%58,5)
Number of female patients	113(%41,5)
Male / female ratio	1,4/1
Number of patients under 40	13(%4,8)
Number of patients aged between 40-65	134(%49,3)
Number of patients over 65	125(%45,9)
Average age of patients	62±11,6
Average age of male patients	59,9±11,7
Average age of female patients	65,1±10,9
Median age (min-max)	64(24-94)

Lab values at the time of diagnosis were analyzed. 121 (44.5%) patients with Hb<10 gr/dl, 37 (13.6%) with wbc<4.5 10^3/uL and 30 (11%) with plt<100 10^3/uL were determined. 46 (16.9%) patients with calcium>11 mg/dl and 54 (19.9%) patients with creatinine>2 mg/dl were determined. 172 (63%) of patients were admitted with a bone case (lytic lesion, pathological fracture, osteoporosis). The most commonly seen bone involvement was vertebral involvement with 111 patients. 100 patients had no bone involvement, while 26 (9.6%) patients had bone involvement in more than one location. 65 of 172 patients with bone involvement underwent radiation therapy in addition to chemotherapy.

124 (45.6%) of the patients had IgG, 50 (18.4%) of the patients had IgA, 59 (21.7%) of the patients had a light chain, 21 (7.7%) of the patients had plasmacytoma, 4 (1.5%) of the patients had IgM, 3 (1.1%) of the patients had plasma cell leukemia (PCL), and 11 (4%) of the patients had non-secretory myeloma when multiple myeloma subtype analysis was performed.

In patients who were not treated employing AHSCT, the median life span was 35 months (standard deviation:2,3 CI:30-400), while in the group of patients who had AHSCT, the median life span was not found (p<0.001). In the AHSCT group, the median survival time was significantly longer than

in the group without AHSCT. The overall 5-year survival rate of patients was found to be 35%. The best 5-year survival rate was 63% in patients with AHSCT, while this rate was 24% in patients without AHSCT.

In survival analyses according to MM subgroups, the best median survival was found in IgG-type myeloma, while the worst survival was found in plasma cell leukemia (Table-2).

Table 2. *Median and Average survival times by MM subtype*

subtype	median survival time	95% CI (confidence interval)	average survival-time	95% CI (confidence interval)
Ig G	52,5±5,9	40,9-64,1	54,2±4,4	45,6-62,9
Ig A	40,2±9,4	21,7-58,7	41,2±4,4	32,5-49,9
Kappa	48,7±17	15,4-82,1	43,3±6,4	30,6-55,4
Lambda	42,4±14,3	14,2-70,6	45,8±6	34-57,7
Plasmacytoma	40,8±3,4	34,1-47,6	50,4±8,3	34,2-66,7
Ig M	49,1±16,7	0-76	49,1±16,7	16,2-82
PCL	7,3±4,1	0-15,4	8,1±2,9	2,3-13,8
Non-secretory	44,2±7,8	28,9-59,5	44,1±9	26,4-61,8

In our study, 107 of 272 patients died. The most common causes of death were infection, thrombotic and hemorrhagic complications, and patients' existing comorbid conditions. When we reviewed co-morbid conditions, 5 patients had simultaneous advanced heart failure (EF<35%), 3 patients had amyloidosis and heart failure, and 6 patients had COPD.

Discussion

Multiple myeloma is known as an advanced age disease, and it is relatively less common in young people and has male dominance[6]. In a study involving patients from the United States, Germany, Canada, and the United Kingdom, the average age of occurrence was 67, and the ratio of men and women was 1,5/1[7]. In our study, 272 patients had a median age of 64(24-94) and an average age of 62. Out of the patients, 159 (58.5%) were men and 113 (41.5%) were women, the male/female ratio was high in old age and men, similar to 1,4/1 studies.

A multi-center study conducted in South Korea showed a bone involvement rate of 60.2%, anemia rate of 60.7%, and acute kidney damage rate of 23.4%, hypercalcemia rate of 16.7%[8]. The rates of hypercalcemia (16.9%), acute kidney injury (19.9%), bone involvement (63%), and anemia (78.7%) observed in our patients were similar to this study.

In a study, the most common subtype of myeloma was IgG and then light chain and IgA, respectively, while the least observed ones were IgD and non-secretory type of myeloma[9]. When

the subtype analysis was performed, IgG 45.6%, IgA 18.4%, light chain 21.7%, plasmacytoma 7.7%, IgM 1.5%, plasma cell leukemia 1.1%, and non-secretory myeloma 4% were found. Despite high-dose chemotherapy and bone marrow transplantation in plasma cell leukemia, response rates are still meager, and the prognosis is poor[10]. In our study, the lowest median life expectancy (7.3±4.1 months; CI:0-15,4) the highest median life expectancy (52.5±5.9; CI: 40.9-64.1) was observed in plasma cell leukemia in the IgG subtype.

The total response rate (partial response, minimal response, excellent partial response, stable disease) in VCD (bortezomib, cyclophosphamide, dexamethasone) treatment ranges from 80-90%, while the total response rate ranges from 46-52%[11]. In our study, the total response rate of patients receiving VCD treatment in primary care was found as 58.5%.

In a study conducted by Emilie et al., the AHSCT treatment response was 73%[12]. This rate was 76% in our study. The average and median life expectancy in patients with AHSCT was significantly higher than in the group without AHSCT. 5-year survival rate was 63% in patients with AHSCT, while this rate was 24% in patients without AHSCT.

Conclusion: The median and average survival times were extended for the newly diagnosed MM patient with all the improvements in treatment. AHSCT is seen as the most effective treatment option[13]. For this reason, it is crucial to evaluate the MM patient for AHSCT and apply treatment in this direction. Bone involvement is the most common form of admission. For this reason, it is essential to bring MM to mind in patients who have complaints of bone pain or musculoskeletal system. Mortality is most commonly associated with infectious and thrombosis, and it is highly vital that administering anticoagulant or antiagregant and prophylactic antiviral, antifungal and antibacterial treatments to patients with risk factors at all stages of treatment and follow-up.

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