



maltepe üniversitesi
istanbul
TIP FAKÜLTESİ HASTANELERİ

maltepe tıp dergisi
maltepe **medical journal**



EDİTÖRDEN

Maltepe Tıp Dergisi yayın hayatına 2009 yılında başlamış olan Maltepe Üniversitesi'nin resmi bilimsel yayın organıdır ve yayıncısı T.C. Maltepe Üniversitesi'dir. Nisan, Ağustos ve Aralık olmak üzere yılda üç sayı olarak yayımlanır.

Maltepe Tıp Dergisi bünyesinde Tıp alanının bütün dalları ile ilgili klinik ve deneysel çalışmalara dayalı orijinal araştırma makaleleri, derlemeler, orijinal olgu sunumları, editöre mektup ve teknik notlar yayınlanmaktadır. Index Copernicus International, Academindex, ASOS İndeks, SOBIAD Atıf dizini, IDEAL ONLINE ve TurkMedline olmak üzere ulusal ve uluslararası atıf dizinlerinde taranmakta olup elektronik ortamda basılan çift kör ulusal hakemli bir dergidir.

Maltepe Tıp Dergisi'nin siz değerli okuyuculara ulaşması için bize destek olan T.C. Maltepe Üniversitesi Rektörü Sayın Prof. Dr. Edibe Sözen Hocamıza teşekkür ediyorum. Bir teşekkür de yoğun emek gerektiren bilimsel çalışmalarını dergimize gönderen yazarlarımıza, bu çalışmaların literatüre katkı sağlayacak bilimsel forma dönüşmesi için deneyimlerini paylaşan hakemlerimize ve aylar süren yoğun tempoda çalışıp zamanında sayılarımızı çıkaran dergi ekibimizdir.

Yeni sayımızın alanımıza ve literatüre katkı sağlaması dileği ile.

Doç. Dr. Feride Sinem AKGÜN

The impact of COVID-19 pandemic on recommended adult vaccination in the elderly: A hospital-based study

COVID-19 pandemisinin önerilen erişkin aşılamalarına etkisi: Hastane temelli çalışma

Cemile Karaçepiş¹, Hacer Hicran Mutlu², Hasan Hüseyin Mutlu², Ayşe Gülek¹

¹Department of Family Medicine, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

²Department of Medical Education, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

Submitted Date: 21 January 2024, Accepted Date: 28 August 2024

Correspondence: Hacer Hicran Mutlu
Department of Family Medicine; Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey
e-mail: hicranbeyca@hotmail.com

ORCID ID: CK [0000-0002-1865-7305](https://orcid.org/0000-0002-1865-7305)
HHM [0000-0003-3712-0068](https://orcid.org/0000-0003-3712-0068)
HHM [0000-0001-8947-711X](https://orcid.org/0000-0001-8947-711X)
AG [0000-0003-0196-4111](https://orcid.org/0000-0003-0196-4111)

SUMMARY

Aim: With the COVID-19 pandemic, significant changes have occurred all over the world and in Turkey. Recommended adult vaccination practices are one of them. This study aims to compare the adult vaccination rates and awareness before and after the COVID-19 pandemic.

Material and Methods: Sociodemographic characteristics (age, gender, marital status, education status, comorbidities), vaccines performed in adulthood, and reasons for getting vaccinated and avoiding vaccines before and during the pandemic were asked to the responders. The results were compared with the data of the study which was performed between 31.01.2017-01.06.2017 in the same outpatient clinic of the same hospital were used with permission of all the authors.

Results: It was observed that pneumococcal (9.9% vs 56.5 %) ($p<0,001$), influenza (33.9 % vs 47.7 %) ($p=0,004$), tetanus (1.3 % vs 20.7 %) ($p<0,001$) and hepatitis B (0.7 % vs 4.8 %) ($p=0,04$). Vaccination rates significantly increased during pandemic compared to the period before the pandemic.

Conclusion: The adult vaccination coverage was insufficient, on the other hand with the pandemic particularly pneumococcal vaccination coverage has increased among adults. It was considered that traditional and social media had an important role in this increase.

Keywords: COVID-19 pandemics, immunization schedule, mass media, social media, vaccination, vaccine hesitancy

ÖZET

Amaç: COVID-19 salgınıyla birlikte tüm dünyada ve Türkiye'de önemli değişiklikler meydana geldi. Önerilen yetişkin aşılamaya uygulamaları da bunlardan biridir. Bu çalışma, COVID-19 salgını öncesi ve sonrası yetişkinlerde aşılamaya oranlarını ve farkındalıklarını karşılaştırmayı amaçlamaktadır.

Materyal ve Metodlar: Yanıt verenlere sosyodemografik özellikler (yaş, cinsiyet, medeni durum, eğitim durumu, yandaş hastalıklar), yetişkinlikte yapılan aşılarda, pandemi öncesi ve pandemi sırasında aşı yaptırmama ve aşılardan kaçınma nedenleri soruldu. Sonuçlar tüm yazarların izni alınarak aynı hastanenin aynı polikliniğinde 31.01.2017-01.06.2017 tarihleri arasında gerçekleştirilen çalışmanın verileriyle karşılaştırıldı.

Bulgular: Pnömonokok (%9,9 vs %56,5) ($p<0,001$), influenza (%33,9 vs %47,7) ($p=0,004$), tetanoz (%1,3 vs %20,7) ($p<0,001$) ve hepatit B (%0,7 vs %4,8) ($p=0,04$) olduğu gözlemlendi. Aşılanma oranlarında pandemi öncesi döneme göre pandemi döneminde anlamlı artış görüldü.

Sonuç: Erişkin aşı kapsamı yetersiz olmakla birlikte, pandemiyle birlikte erişkinlerde özellikle pnömonokok aşı kapsamı artmıştır. Bu artışta geleneksel ve sosyal medyanın önemli bir rolü olduğu değerlendirildi.

Anahtar kelimeler: Aşılamaya, aşı karşıtlığı, aşı takvimi, COVID-19 pandemisi, geleneksel medya, sosyal medya

INTRODUCTION

Novel Coronavirus Disease (COVID-19) is a virus that was first detected on January 13, 2020, and spread from person to person in a group of patients who developed respiratory symptoms (fever, cough, shortness of breath) in Wuhan Province, China, towards the end of December 2019 (1). In humans, several coronaviruses have been found to cause respiratory infections, ranging from common cold to much more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The severe acute respiratory syndrome related coronavirus (SARS-CoV-2) is the causative agent of the New Coronavirus Disease (2). The first COVID-19 case detected in Turkey was announced by the Ministry of Health on March 10, 2020, and the first death due to the virus in our country occurred on March 15, 2020. The Ministry of Health announced on April 1, 2020, that the coronavirus cases had spread all over Turkey (3).

After the COVID-19 pandemic, significant changes have occurred all over the world and in our country. A number of factors played a role in the limitation to accessing healthcare of elderly people which led to a deterioration of their chronic diseases. The home quarantine processes and the burden on the healthcare system are the factors that restrained them from going to the hospitals. On the other hand, they felt the need to take many precautions, which they learned through traditional and social media, for fear of having COVID-19 and anxiety of having severe COVID-19. The spread of the perception that the pneumococcal vaccine prevents COVID-19 was one of them (4).

Aging is the process of reaching the end of life expectancy as a result of the decrease in life functions at the level of organs, tissues, cells, and genes in the life process that begins with the birth of a person. According to the World Health Organization (WHO), the aging process begins at the age of 65 (5). Infectious diseases are an important cause of morbidity and mortality in elderly individuals who have significant comorbidities and who are naturally immune suppressed (6). Vaccination is still the most effective and cost-efficient, medical therapy against infectious diseases. Providing scheduled immunizations can protect elderly individuals and communities from vaccine-preventable diseases (7). After the health reform in our country, it has been reported that childhood vaccination in primary care has reached 98%. However, the same success has not been demonstrated with elderly vaccination yet (5). In the light of these statements, we aimed to compare the adult vaccination rates, awareness, and reasons for avoiding getting vaccinated before and during the pandemic, who applied to the family medicine outpatient clinic of our hospital, particularly in individuals over 65 years of age who would be easily protected from the morbidity and mortality of infectious diseases by vaccination.

The primary outcome of this study was to evaluate the impact of the COVID-19 pandemic on adult vaccination in elderly people. The secondary outcome was the determination of vaccination coverage and the factors affecting it.

MATERIAL AND METHODS

Participants

All of the patients who consecutively applied to Family Medicine outpatient clinics between 01.11.2021-01.01.2022 in a tertiary hospital in Istanbul who met inclusion criteria were recruited in the study. The inclusion criteria were being over 65 years old and volunteering for the study.

Data Collection

A questionnaire was developed by the researchers within the scope of the research to collect some demographic information and the vaccination status of the responders. Sociodemographic characteristics (age, gender, marital status, education status, comorbidities), vaccines performed in adulthood, and reasons for getting vaccinated and avoiding vaccines before and during the pandemic were asked in the questionnaire.

As pre-pandemic data, the data of Mutlu et al. study (5) who is one of the researchers of the present study, in which vaccination rates and awareness were measured in individuals over the age of 65, between 31.01.2017-01.06.2017 in the same outpatient clinic of the same hospital were used with permission of all the authors.

Ethical Approval

The study was performed in accordance with the Declaration of Helsinki and was approved by Istanbul Medeniyet University Göztepe Research and Training Hospital Ethical Committee (2021/0532) on 27.10.2021.

Statistical Analysis

For the descriptive analysis of the study, a database was created in the SPSS 25.0 program and the frequency, percentage, mean, and standard deviation values of the data were calculated. $p < 0.05$ was considered significant in all analyses.

Normally distributed data were shown as mean \pm SD and the data that were not normally distributed were presented as median, minimum and maximum values. Significant differences of normally distributed data were assessed using a t-test and significant differences of not normally distributed data were analyzed using the Mann-Whitney U test. Categorical data were expressed as percentages.

RESULTS

52.6% of the participants were female and the mean age

of them was 72.35±5.31 years. The other sociodemographic characteristics and co-morbidities of the study population are presented in Table 1. The most prevalent comorbidity was hypertension (53.5%) and diabetes mellitus (30.3%).

Table 1. The sociodemographic characteristics and co-morbidities of the participants

		N (310)	%	
Age	(mean±SD) (min-max)	72,35±5,31	(65- 91)	
Gender	Female	163	52,6	
	Male	147	47,4	
Marital status	Married	207	66,8	
	Single	17	5,5	
	Divorced/widow	86	27,7	
	illiterate	29	9,4	
Educational status	Literate	13	4,2	
	Primary school	103	33,2	
	Middle school	30	9,7	
	High school	62	20,0	
Having social insurance	University	73	23,5	
	Having social insurance	295	95,2	
	Having chronic disease	Having chronic disease	263	84,8
		Diabetes mellitus	94	30,3
Hypertension		166	53,5	
Chronic lung disease		26	8,4	
Chronic cardiovascular disease		79	25,5	
Chronic renal disease		15	4,8	
Chronic liver disease		6	1,9	
Any other chronic disease		63	20,3	

The adult vaccination coverage except for the COVID-19 vaccine was 61% during the pandemic and COVID-19 vaccination coverage was 77.4% among our sample. Pneumococcal, influenza, tetanus, hepatitis B, and meningococcal vaccination coverage were 56.5%, 47.7%, 20.6%, 4.8%, and 3.9% respectively. None of the participants were vaccinated against Hepatitis A, measles, mumps and rubella (MMR), or Herpes zoster (Table 2).

The reasons for following adult vaccination recommendations before the COVID-19 pandemic were asked to the participants. 58.2% of the responders declared that they were recommended by a physician and 23.3% of them reported that it was their self-decision. The percentage of those who were affected by traditional and social media was relatively low (10.3%) (Figure 1). The reasons for the above-mentioned issues were also asked during the COVID-19 pandemic and are presented in Figure 1. It is apparent from this figure that the percentages of recommendation by a physician and self-decision had

markedly reduced during pandemics, on the other hand, the rate of the participants that heard about the necessity of adult vaccination from traditional and social media had evidently increased.

Table 2. The vaccination rates of the participants

	N	%
Adult vaccination rate during the pandemic except for COVID-19	189	61.0
Total adult vaccination rate (before or during the pandemic)	240	77.4
Pneumococcal vaccination rate	175	56.5
Influenza vaccination rate	148	47.7
Tetanus vaccination rate	64	20.6
Hepatitis B vaccination rate	15	4.8
Meningococcal vaccination rate	12	3.9
Hepatitis A vaccination rate	0	0.0
MMR vaccination rate	0	0.0
Herpes zoster vaccination rate	0	0.0
Total	310	100.0

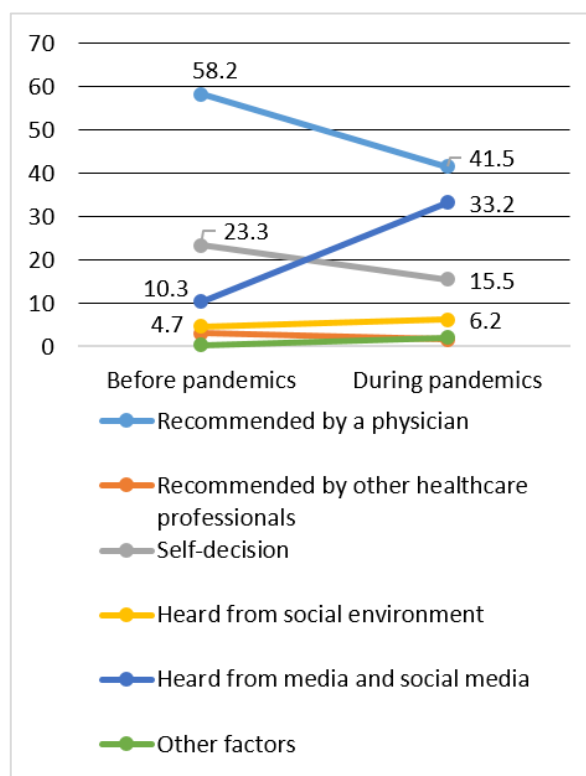


Figure 1. The reasons for following adult vaccination recommendations

The barriers to adult vaccinations were also asked. The majority of the responders reported that they were not aware of vaccination is a necessity (48.6%), 19.3% of the sample believed that a healthy person did not need to be

vaccinated and 14.7% of them were anxious about the side effects of the vaccines.

When the barriers to adult vaccination during pandemics were investigated it was clearly observed that the percentage of responders who reported that they were not aware of vaccination is a necessity had decreased (Figure 2).

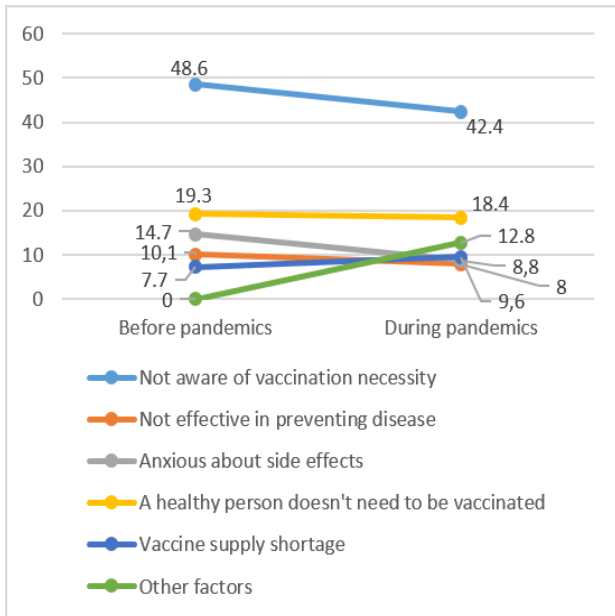


Figure 2. The barriers to adult vaccination

Pneumococcal and influenza vaccines were the most administered vaccines during COVID-19 pandemics (Figure 3).

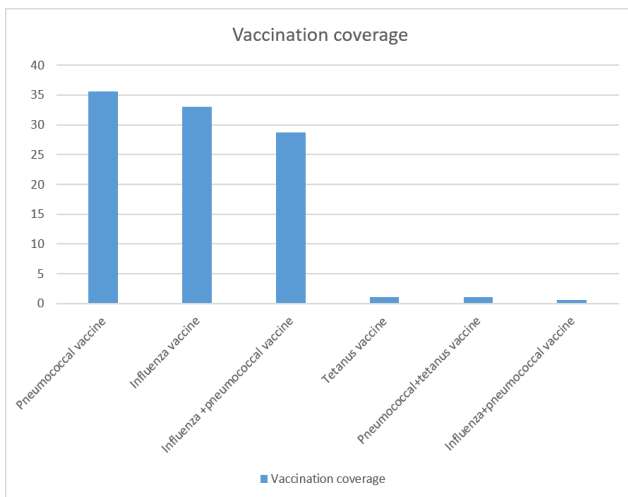


Figure 3. Adult vaccination coverage during the COVID-19 pandemic

No association was determined between pneumococcal vaccination rates and sociodemographic characteristics

and co-morbidities. The influenza vaccination rates were higher in males, married individuals, and patients with chronic heart disease (Table 3).

Table 3. The relationship between sociodemographic characteristics and influenza and pneumococcal vaccination status

		Influenza vaccination status		p	Pneumococcal vaccination status		p
		Yes	No		Yes	No	
Age		72.72±5	72.02	0.366	72.40±	72.18±5	0.621
Gender	Female	.63	±4.99	0.014	5.31	.37	0.385
	Male	(41.1)	(58.9)		(75.5)	(24.5)	
Marital status	Married	81	66	0.027	117	30	44 (21.3) 26 (25.2)
	Single	(55.1)	(44.9)		(79.6)	(20.4)	
	illiterate	108	99		163 (78.7)	77 (74.8)	
Educational status	Primary+middle school	40	63	0.151	27	15	0.080
	High school+university	(38.8)	(61.2)		(64.3)	(35.7)	
	Primary+middle school	15	27		(64.3)	(35.7)	
Having social insurance	Primary+middle school	62	71	0.932	104	29	0.698
	High school+university	(46.6)	(53.4)		(78.2)	(21.8)	
Co-morbidities	High school+university	71	64	0.889	109	26	0.599
	Chronic lung disease	(52.6)	(4.4)		(80.7)	(19.3)	
Diabetes Mellitus	Chronic lung disease	141	154	0.308	229	66 (224)	0.698
	Chronic heart disease	(47.8)	(52.2)		(77.6)		
Hypertension	Chronic heart disease	126	137	0.393	205	58	0.599
	Chronic renal disease	(47.9)	(52.1)		(77.9)	(22.1)	
Chronic lung disease	Chronic renal disease	49	45	0.289	76	18	0.340
	Chronic heart disease	(52.1)	(47.9)		(80.9)	(19.1)	
Chronic heart disease	Chronic heart disease	83	83	0.001	132	34 (205)	0.343
	Chronic renal disease	(50.0)	(5.0)		(79.5)		
Chronic renal disease	Chronic renal disease	15	11	0.231	20	6 (23.1)	0.950
	Chronic heart disease	(57.7)	(42.3)		(76.9)		
Chronic heart disease	Chronic heart disease	50	29	0.001	65	14	0.231
	Chronic renal disease	(63.3)	(36.7)		(82.3)	(17.7)	
Chronic renal disease	Chronic renal disease	7 (46.7)	8		14	1 (6.7)	
	Chronic heart disease	(53.3)	(93.3)				

COVID-19 vaccination coverage among our sample was also investigated in the current study. The percentage of the participants who were vaccinated with any of the COVID-19 vaccines was 99.4%. The distribution of COVID-19 vaccine percentages among our sample is shown in Figure 4. 80% of the responders had been vaccinated with two doses of inactivated COVID-19 vaccine (Sinovac). The rate of those who were vaccinated with two doses of mRNA COVID-19 vaccine (BioNtech) was 38.1%.

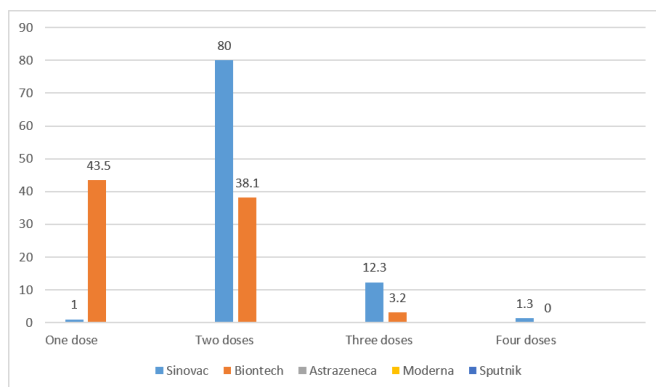


Figure 4. The distribution of COVID-19 vaccine percentages among our sample

When vaccination rates before and during the pandemic were compared, it was observed that pneumococcal, influenza, tetanus, and hepatitis B vaccination rates significantly increased during the pandemic compared to the period before the pandemic.

DISCUSSION

The results of the study showed that almost all of the participants were vaccinated at least with one dose of vaccine against COVID-19. The most striking finding of this study was the increase in particularly pneumococcal vaccination coverage during the pandemic in adult vaccination.

A Center for Disease Control and Prevention (CDC) report declared influenza, pneumococcal, herpes zoster, tetanus, hepatitis B, and hepatitis A vaccination coverage respectively as 61%, 69%, 39.5%, 22.2% and 6.2% in the elderly population who were ≥ 65 years. These rates are quite higher than our results except for tetanus vaccination coverage which was similar to our results. This result may be due to the fact that the individuals are vaccinated against tetanus in case of an injury or an animal bite occurs beyond the periodical vaccinations (8). In a study conducted in Denmark with elderly individuals influenza vaccination coverage was lower (41%) than ours. The studies from China reported that the vaccination coverage of the elderly with influenza ve pneumococcal vaccines is much more lower than the results in the literature. Influenza and pneumococcal vaccination coverage in elderly individuals was 7.3% and 0.7%, respectively (9,10). Another study reported that pneumococcal vaccination coverage in persons >65 years old was 49.5% which is again lower than our pneumococcal vaccination coverage (11). The pneumococcal vaccination coverage (56%) of > 65 years old people in Australia was similar to our results, however, influenza vaccination coverage differed from our findings. The influenza vaccination rates were higher (74.8%) than the current study's finding like the study conducted in Greece (12). In this study, the influenza

vaccination coverage was 83%, and pneumococcal vaccination coverage was 49.7% (13).

Herpes zoster vaccination coverage was more than our findings though not enough yet in various studies (13,14). According to a CDC report the herpes zoster vaccination coverage was 34.5% which is better than in European countries (8). In the present study, not a single person was vaccinated against herpes zoster because we don't have a herpes zoster vaccine in our country. In the aforementioned studies conducted in Italy and Greece tetanus or tetanus, diphtheria, and pertussis (Tdap) and hepatitis B vaccination coverage was lower than our findings (13,14). This result may be due to the fact that the present study was conducted during the pandemic and the most important finding of the present study was that, it was observed that the awareness for adult vaccination increased with the pandemic.

The findings about the relationship between sociodemographic factors and influenza and pneumococcal vaccination are conflicting in the literature. In a review where many studies from different countries were collected, the influenza vaccination rate increased with age and the older female gender was more vaccinated (15). Another study declared that females were more vaccinated against pneumococcal (11). The study investigating the racial and socioeconomic disparities in adult vaccination found an association with low educational status and adult vaccination coverage (16). Hellfritsch et al reported that the predictors of influenza vaccination in adults were age, having heart and vascular disease, chronic pulmonary disease, and diabetes. There was no difference in terms of gender and educational status in this study (17). Heart and pulmonary disease were found to be predictors of pneumococcal vaccination among Australian adults (18). In our study no association was found between pneumococcal vaccination and sociodemographic factors, on the other hand, male gender, being married, and having heart disease was the predictors of influenza vaccination. In Turkey, while the pneumococcal vaccine could be easily supplied during the pandemic, the influenza vaccine was limited to those with special conditions which having a chronic ischemic heart disease was one of them. Men could have been more vaccinated against influenza because of being a risk factor for chronic ischemic heart disease.

The reasons for following adult vaccination recommendations before and during the pandemic were also asked to the responders in the current study. The doctor and healthcare professionals' recommendations were the most reasons for following adult vaccination recommendations in this study which is in line with Gürsoy et al's study conducted in another region in Turkey (19). The advice of doctors and healthcare professionals has been shown to be the most important factor that promotes vaccination in the elderly (5,20-22). Therefore, it

is important to recommend vaccination to elderly individuals at every healthcare professional visit. In the literature, most of the studies claimed that unawareness of necessity was the most frequent barrier to vaccination likewise the current study's findings (1,5,9,19,23). Hence, it is important to increase awareness of adult vaccination among the elderly to promote vaccination.

Another interesting finding in the present study is the impact of traditional and social media on vaccination. The percentage of participants that were recommended for vaccination by a doctor had evidently decreased, on the other hand, the rate of participants that heard about the necessity of adult vaccination from traditional and social media had evidently increased during the pandemic. During the pandemic, public exposure to health communication from traditional and social media has risen due to both lockdowns and coronaphobia, by contrast, direct communication between patients and healthcare

providers had reduced (4). Therefore, traditional and social media became a tool for seeking information about healthcare and this information played an important role in vaccination decision-making (24). While traditional media pursued a pro-vaccine approach, some social media sources had antivaccine content (25). Meanwhile, there was also misinformation that every person should be vaccinated against pneumococcal for protection from catching COVID-19. Our data showed this misinformation has achieved its purpose. The most striking result of this study was the increase of pneumococcal vaccination coverage from 9.9% to 56.5% during the pandemic. On the other hand, some increase has been seen in influenza vaccination rates supporting other findings in the literature (26-31), but this increment is not as dramatic as with the pneumococcal vaccine.

Another important finding of our study was the high levels of COVID vaccination coverage. The vaccination coverage with any COVID-19 vaccines was 99.4% in our sample. The percentage of the participant that has vaccinated with two doses of inactivated COVID-19 vaccine (Sinovac) was 80%, on the other hand, 38.1% of the responders were vaccinated with two doses of mRNA COVID-19 vaccine (BioNtech). These percentages are quite higher than the average coverage of Turkey which is 63% within the dates that the study was conducted (32). Our findings were also higher than the study's findings performed in China. This study declared that the COVID-19 vaccination coverage was 73.6% and the coverage was increased to 82.2% when the vaccines became free (33).

The current study has a few limitations. First, it is a single-center hospital-based study. Second, the vaccination coverage has obtained with self-report questionnaires. Third, the sample size is relatively low.

In our study, it was revealed that adult vaccination

coverage was insufficient in adults over 65 years of age before the pandemic and adult vaccination coverage increased during the pandemic. It was shown that this increase was particularly evident in pneumococcal vaccination. It was thought that this significant increase may be due to misinformation in traditional and social media that pneumococcal vaccination can protect individuals from catching COVID. As a result, with the right information, traditional and social media can have important implications for increasing vaccination rates, as with improving many health issues.

Author Contributions: Working Concept/Design: HHM, Data Collection: CK, AG, Data Analysis / Interpretation: HHM, HHM, Text Draft: CK, AG, Critical Review of Content: HHM, HHM, AG, Final Approval and Responsibility: CK, HHM, HHM

Conflict of Interest: The authors state that there is no conflict of interest regarding this manuscript.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Balcı UG, Şimşek Y, Öngel K. Level of knowledge and attitude of the patients older than 65 years about pneumococcal vaccine. *J Heal Sci.* 2015;3:113-116.
- Krammer F. SARS-CoV-2 vaccines in development. *Nature.* 2020;586(7830):516-527.
- Akdi Y, Emre Karamanoğlu Y, Ünlü KD, Baş C. Identifying the cycles in COVID-19 infection: the case of Turkey. *J Appl Stat.* 2022;1-13.
- Puri N, Coomes EA, Haghbayan H, Gunaratne K. Social media and vaccine hesitancy: new updates for the era of COVID-19 and globalized infectious diseases. *Hum Vaccin Immunother.* 2020;16(11):2586-2593.
- Mutlu HH, Coşkun FO, Sargın M. Aile hekimliği polikliniğine başvuran 65 yaş ve üstü kişilerde aşılama sıklığı ve farkındalığı. *Ankara Med J.* 2018;18(1):1-13.
- Yılmaz T, Yılmaz TE, Ceyhan Ş, Kasım I, Abdülkadir K, Odabaş ÖK, et al. Evde sağlık hizmetleri birimine kayıtlı geriatrik hastaların influenza ve pnömokok aşısı ile aşılama durumları ve doktor önerisinin etkisi. *Ankara Med J.* 2018;18(3):391-401.
- de Gomensoro E, Del Giudice G, Doherty TM. Challenges in adult vaccination. *Ann Med.* 2018;50(3):181-192.
- Report MW. Surveillance of Vaccination Coverage Among Adult Populations — United States , 2018. 2021;70(3).
- Yan S, Wang Y, Zhu W, Zhang L, Gu H, Liu D, et al. Barriers to influenza vaccination among different populations in Shanghai. *Hum Vaccin Immunother.* 2021;17(5):1403-1411.
- Liu Y, Xu Y, Wang J, Che X, Gu W, Du J, et al. Vaccination pattern of the 23-valent pneumococcal polysaccharide vaccine (PPV23) in Hangzhou, China: A coverage and adverse events following immunization of different age

- groups. *Hum Vaccin Immunother.* 2021;17(1):157-161.
- 11.Sabapathy D, Strong D, Myers R, Li B, Quan H. Pneumococcal vaccination of the elderly during visits to acute care providers: Who are vaccinated? *Prev Med (Baltim).* 2014;62:155-160.
- 12.Dyda A, Karki S, Hayen A, MacIntyre CR, Menzies R, Banks E, et al. Influenza and pneumococcal vaccination in Australian adults: a systematic review of coverage and factors associated with uptake. *BMC Infect Dis.* 2016;16(1):1-15.
- 13.Papagiannis D, Rachiotis G, Mariolis A, Zafiriou E, Gourgoulanis KI. Vaccination coverage of the elderly in Greece: a cross-sectional nationwide study. *Can J Infect Dis Med Microbiol.* 2020;2020:5459793.
- 14.Veronese N, Vassallo G, Armata M, Cilona L, Casalicchio S, Masnata R, et al. Multidimensional Frailty and Vaccinations in Older People: A Cross-Sectional Study. *Vaccines.* 2022;10(4):555.
- 15.Kini A, Morgan R, Kuo H, Shea P, Shapiro J, Leng SX, et al. Differences and disparities in seasonal influenza vaccine, acceptance, adverse reactions, and coverage by age, sex, gender, and race. *Vaccine.* 2022;40(11):1643-1654.
- 16.Kawai K, Kawai AT. Racial/ethnic and socioeconomic disparities in adult vaccination coverage. *Am J Prev Med.* 2021;61(4):465-473.
- 17.Hellfritzsch M, Thomsen RW, Baggesen LM, Larsen FB, Sørensen HT, Christiansen CF. Lifestyle, socioeconomic characteristics, and medical history of elderly persons who receive seasonal influenza vaccination in a tax-supported healthcare system. *Vaccine.* 2017;35(18):2396-2403.
- 18.Trent MJ, Salmon DA, MacIntyre CR. Predictors of pneumococcal vaccination among Australian adults at high risk of pneumococcal disease. *Vaccine.* 2022;40(8):1152-1161.
- 19.Yalçın Gürsoy M, Tanrıverdi G, Özsezer G, Chousko Mehmet F. Vaccination coverage and related factors among the elderly: A cross-sectional study from Turkey. *Public Health Nurs.* 2022;39(2):390-397.
- 20.Dardalas I, Pourzitaki C, Manomenidis G, Malliou F, Galanis P, Papazisis G, et al. Predictors of influenza vaccination among elderly: a cross-sectional survey in Greece. *Aging Clin Exp Res.* 2020;32(9):1821-1828.
- 21.Higuchi M, Narumoto K, Goto T, Inoue M. Correlation between family physician's direct advice and pneumococcal vaccination intention and behavior among the elderly in Japan: a cross-sectional study. *BMC Fam Pract.* 2018;19(1):1-11.
- 22.Qendro T, de la Torre ML, Panopalis P, Hazel E, Ward BJ, Colmegna I, et al. Suboptimal immunization coverage among Canadian rheumatology patients in routine clinical care. *J Rheumatol.* 2020;47(5):770-778.
- 23.Uzuner A, Arabacı Ş, Yücel Aİ, Kocatürk AC, Kaynar E, Khan A. Knowledge, attitude and behaviors of adults about adulthood immunization. *TJFMPC.* 2018;12(3):215-225.
- 24.Zimand-sheiner D, Kol O, Frydman S. To Be (Vaccinated) or Not to Be : The Effect of Media Exposure , Institutional Trust , and Incentives on Attitudes toward COVID-19 Vaccination. 2021;18(24):12894.
- 25.Viswanath K, Bekalu M, Dhawan D, Pinnamaneni R, Lang J, Mcloud R. Individual and social determinants of COVID-19 vaccine uptake. 2021;1-10.
- 26.Kong G, Lim N-A, Chin YH, Ng YPM, Amin Z. Effect of COVID-19 Pandemic on Influenza Vaccination Intention: A Meta-Analysis and Systematic Review. *Vaccines.* 2022;10(4):606.
- 27.Gallant AJ, Nicholls LAB, Rasmussen S, Cogan N, Young D, Williams L. Changes in attitudes to vaccination as a result of the COVID-19 pandemic: A longitudinal study of older adults in the UK. *PLoS One.* 2021;16(12):e0261844.
- 28.Aşılari E, Bilgi H, Davranışları T, Bachtiger P, Adamson A, Peters NS, et al. Social media and vaccine hesitancy: new updates for the era of COVID-19 and globalized infectious diseases. *Ankara Med J [Internet].* 2020;17(3):155-160.
- 29.Zingel R, Beinker P, Kostev K. The Impact of the COVID-19 Pandemic on Immunization Rates for Preventable Diseases in Primary Care and Pediatric Practices in Germany. *Dtsch Arztebl Int.* 2022;119(11):195.
- 30.Bachtiger P, Adamson A, Chow J-J, Sisodia R, Quint JK, Peters NS. The impact of the COVID-19 pandemic on the uptake of influenza vaccine: UK-wide observational study. *JMIR public Heal Surveill.* 2021;7(4):e26734.
- 31.Domnich A, Cambiaggi M, Vasco A, Maraniello L, Ansaldi F, Baldo V, et al. Attitudes and beliefs on influenza vaccination during the COVID-19 pandemic: Results from a representative Italian survey. *Vaccines.* 2020;8(4):711.
- 32.HASUDER Bulaşıcı Hastalıklar Grubu. COVID-19 PANDEMİSİNDE GÜNCEL DURUM VE ÖNERİLER [Internet]. Available from: <https://hasuder.org.tr/wp-content/uploads/HASUDER-COVID-19-RAPORU.pdf>
- 33.Liu R, Zhang Y, Nicholas S, Leng A, Maitland E, Wang J. COVID-19 vaccination willingness among Chinese adults under the free vaccination policy. *Vaccines.* 2021;9(3):292.

Rare ovarian granulosa tumors: A retrospective analysis

Nadir over granüloza tümörleri: Retrospektif bir analiz

Ayşe Konaç¹, H. Serpil Bozkurt²

¹Gelisim University, School of Health Sciences, Istanbul, Turkey

²Private Practice, Istanbul, Turkey

Correspondence: Ayşe Konaç

Gelisim University, School of Health Sciences, Istanbul, Turkey

e-mail: akonac@gelisim.edu.tr

ORCID ID: AK 0000-0002-9119-3332

HSB 0009-0002-5502-6825

Submitted Date: 6 May 2024, Accepted Date: 8 August 2024

SUMMARY

Aim: Granulosa cell tumors (GCTs) of the ovary, representing 5-8% of all ovarian cancers, are a rare subtype of sex cord-stromal tumors. These tumors are generally low-grade malignancies with a favorable prognosis. However, clinical presentation and outcomes can vary widely among patients. This study analyzes the clinical and pathological characteristics of GCTs in 17 patients diagnosed within a cohort of 596 individuals evaluated at our institution.

Material and Methods: We retrospectively reviewed clinical data from 596 patients treated between January 2017 and February 2023. Seventeen patients diagnosed with ovarian granulosa cell tumors were selected for detailed analysis. Data included age, menopausal status, symptoms, radiological findings, serum CA-125 levels, FIGO stage, surgical interventions, adjuvant therapies, and follow-up outcomes.

Results: The patients' ages ranged from 39 to 64 years (median 47, mean 50.41), with 52.9% premenopausal. Common symptoms were abdominal mass (82.4%), dysmenorrhea (29.4%), abdominal pain (17.6%), and cervical lymphadenopathy (70.6%). Radiological imaging showed cystic masses in 41.17% and mixed cystic-solid components in 17.64% of cases. Tumor sizes averaged 7 cm (range 2-20 cm). Elevated CA-125 was observed in 47.1%. No recurrences or metastases were detected during follow-up.

Conclusion: GCTs of the ovary generally have a favorable prognosis with low recurrence rates. This study highlights the importance of a multidisciplinary approach and individualized surgical intervention. Further research is necessary to enhance understanding and management of these tumors.

Keywords: Chemotherapy, ovarian granulosa cell tumour, ovarian tumors, prognostic factors

ÖZET

Amaç: Overin granüloza hücreli tümörleri (GHT'ler), tüm over kanserlerinin %5-8'ini oluşturan nadir bir seks kord-stromal tümör alt tipidir. Bu tümörler genellikle düşük dereceli maligniteler olup, iyi bir prognoz ile ilişkilidir. Ancak, klinik prezentasyon ve sonuçlar hastalar arasında geniş bir yelpazede değişiklik gösterebilmektedir. Bu çalışma, kurumumuzda değerlendirilen 596 bireyden teşhis edilen 17 hastada GHT'lerin klinik ve patolojik özelliklerini analiz etmeyi amaçlamaktadır.

Materyal ve Metodlar: Ocak 2017 ile Şubat 2023 tarihleri arasında tedavi edilen 596 hastanın klinik verileri retrospektif olarak incelendi. Over granüloza hücreli tümörü teşhisi konulan 17 hasta ayrıntılı analiz için seçildi. Veriler yaş, menopoz durumu, semptomlar, radyolojik bulgular, serum CA-125 seviyeleri, FIGO evresi, cerrahi müdahaleler, adjuvan tedaviler ve takip sonuçlarını içermektedir.

Bulgular: Hastaların yaşları 39 ile 64 arasında değişmekte olup, ortanca yaş 47, ortalama yaş ise 50,41 idi ve hastaların %52,9'u premenopozal idi. Yaygın semptomlar abdominal kitle (%82,4), dismenore (%29,4), abdominal ağrı (%17,6) ve servikal lenfadenopati (%70,6) idi. Radyolojik görüntüleme, hastaların %41,17'sinde kistik kitleler ve %17,64'ünde karışık kistik-solid komponentler gösterdi. Tümör boyutları ortalama 7 cm olup (2-20 cm arası), hastaların %47,1'inde yüksek CA-125 seviyeleri gözlemlendi. Takip süresince nüks veya metastaz tespit edilmedi.

Sonuç: Over granüloza hücreli tümörleri genel olarak düşük nüks oranları ile iyi bir prognoza sahiptir. Bu çalışma, multidisipliner yaklaşımın ve bireyselleştirilmiş cerrahi müdahalenin önemini vurgulamaktadır. Bu tümörlerin yönetimi ve anlaşılmasını iyileştirmek için daha fazla araştırmaya ihtiyaç vardır.

Anahtar kelimeler: Kemoterapi, over granüloza hücreli tümörü, over tümörleri, prognostik faktörler

INTRODUCTION

Ovarian cancer, a predominant cause of mortality from gynecological malignancies worldwide, exhibits a variety of subtypes, each distinguished by unique cellular origins and pathological features. Among these, Granulosa cell tumors (GCTs) are particularly notable for their rarity and distinctive origin. Accounting for approximately 5-8% of all ovarian cancers, GCTs fall under the category of sex cord-stromal tumors. Unlike the commonly encountered ovarian epithelial tumors that originate from the epithelial cells on the ovarian surface, GCTs develop from sex cord-stromal tissue, which is crucial for hormone production and structural support of the ovaries. This origin lends GCTs distinct clinical behaviors and generally more favorable prognostic outcomes, often manifesting as low-grade malignancies.

Ovarian GCTs are characterized by a prolonged natural history and a propensity to recur years after initial treatment. They frequently present with symptoms induced by estradiol secretion, such as vaginal bleeding or, in younger patients, precocious puberty. In some cases, tumor rupture may lead to abdominal pain and hemoperitoneum. Typically, a pelvic mass is identified during physical examination, which is further investigated using imaging techniques to confirm the diagnosis. Surgical intervention is pivotal in the initial management of GCTs, serving dual purposes: providing a definitive histological diagnosis and allowing for appropriate cancer staging and debulking. This surgical approach not only facilitates the removal of tumor mass but also critically impacts the long-term management strategy, aiming to minimize the likelihood of recurrence and optimize patient outcomes (1-3).

Ovarian cancer remains a significant challenge in gynecological oncology, with various subtypes that present distinct pathological and clinical profiles. Among these, GCTs of the ovary are particularly noteworthy due to their unique characteristics and long natural history. Historical context is crucial in understanding these tumors: GCTs of the ovary were first described by Rokitsansky in 1855, marking the initial recognition of this rare and distinct subtype of ovarian tumors. GCTs are extremely uncommon, constituting a minority of ovarian tumors, and are often described in terms of their indolent progression and potential for late recurrence (4).

Historical data, notably from a seminal study conducted by Fox, H, Agrawal, K, & Langley, FA. in 1975 (5), has been pivotal in shaping our understanding of GCTs. Their research, which analyzed 92 cases of ovarian GCTs, highlighted several key prognostic factors that influence outcomes in patients. They found that factors such as age over 40 at diagnosis, presentation with abdominal symptoms, presence of a palpable mass, large solid tumors, bilateral tumors, extraovarian spread, and

numerous mitotic figures are indicative of a poorer prognosis. These findings underscore the malignant potential of GCTs and suggest that even tumors that appear to be low-grade can have significant long-term implications for patient survival. Their study also demonstrated the importance of considering all GCTs as potentially malignant due to their ability to cause death related to the tumor within 20 years in approximately half of the cases if left untreated. This underscores the necessity for vigilant long-term follow-up and management strategies tailored to mitigate these risks. The insights from Fox et al. (5) have provided a foundation for subsequent research and are crucial for informing current clinical practices, which emphasize early detection and comprehensive management to improve outcomes for patients diagnosed with this rare but significant subtype of ovarian cancer (5).

GCTs are often hormone-producing, which contributes to their early presentation and detection compared to other epithelial ovarian cancers, usually diagnosed at an advanced stage. The juvenile form of GCT may present in young girls, allowing for conservative management options such as unilateral salpingo-oophorectomy, given that 95% of these tumors are unilateral. Surgical resection remains the treatment of choice, with the extent of initial staging laparotomy being a key determinant in assessing the risk of recurrence. Prognostically, factors such as advanced stage, tumor size greater than 5 cm, high mitotic index (greater than 10 per high power field), nuclear atypia, and the absence of Call-Exner bodies are associated with poorer outcomes. These tumors are also characterized by their potential for late recurrences, necessitating prolonged follow-up. Tumor markers such as inhibin and estradiol are valuable during follow-up for detecting recurrences. While chemotherapy, radiotherapy, and hormone replacement therapy play limited roles in initial treatment, they may be considered in cases of recurrence. With optimal management, patients with GCTs can achieve better survival rates compared to those with other forms of ovarian malignancies (6,7).

Studying GCTs is imperative due to their distinct clinical and pathological features, which significantly impact management strategies and patient outcomes. Despite their relatively benign course, the presentation, response to treatments, and long-term outcomes of GCTs can vary widely, presenting challenges in clinical management and prognosis. The rarity of these tumors contributes to a limited understanding within the medical community, often leading to generalized treatment approaches that may not be optimal for all patients. Therefore, a deeper exploration into the nuances of GCTs is crucial for developing tailored therapeutic strategies that address their unique aspects effectively.

MATERIAL AND METHODS

This retrospective study was conducted at the Istanbul Training and Research Hospital, a tertiary care center with a comprehensive cancer treatment facility. The study encompasses a period from January 2017 to February 2023, during which patient data were collected and analyzed to assess the clinical and pathological characteristics of ovarian granulosa cell tumors.

Patients included in this study were specifically those diagnosed with ovarian granulosa cell tumors, as confirmed by histopathological analysis during the study period. The selection process involved reviewing the hospital's cancer registry and patient medical records to identify cases that met the diagnostic criteria for GCTs. From a broader cohort of 596 patients evaluated for various conditions, 17 were identified and confirmed to have ovarian granulosa cell tumors based on these criteria.

Comprehensive data extraction was performed from electronic medical records. The collected data included age at diagnosis, menopausal status, initial symptoms, and detailed information on radiological and surgical findings. Additionally, serum CA-125 levels at presentation, FIGO stage at diagnosis, type of surgical intervention, and the administration of any adjuvant therapy (chemotherapy or radiation) were meticulously recorded. Follow-up data, capturing recurrence rates and long-term complications, were also included.

Data were analyzed using descriptive and inferential statistics to explore associations between clinical variables and patient outcomes. Kaplan-Meier survival analysis was conducted to estimate the prognosis, and Cox regression models were employed to identify predictors of survival and recurrence. All statistical analyses were performed using SPSS software (version 26.0, IBM Corp.).

In cases where data were missing or incomplete, multiple imputation techniques were applied to estimate missing values, ensuring the robustness of the statistical analysis and minimizing bias. The proportion of missing data and the impact of imputation on the study results were assessed and reported.

The study protocol was reviewed and approved by the Ethics Committee of Istanbul Training and Research Hospital. The study was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

All patient data were anonymized and de-identified prior to analysis to protect confidentiality. Access to the data was restricted to the research team, and all electronic data were secured with password-protected access to ensure that patient information was safeguarded throughout the study.

RESULTS

The research encompassed a cohort of seventeen individuals who had been clinically diagnosed with ovarian granulosa cell tumors. These participants presented a diverse age range spanning from 39 to 64 years (Figure 1). Statistical analysis of the age distribution revealed that the median age at which the diagnosis was confirmed stood at 47 years. Additionally, the calculated mean age of the study participants was approximately 50.41 years. This age-related data is crucial as it provides insights into the typical age window during which these tumors are most likely to be diagnosed, suggesting a potentially heightened risk in the perimenopausal and early postmenopausal phases of a woman's life. Such information is essential for developing age-specific screening strategies and improving the understanding of the epidemiology of ovarian granulosa cell tumors.

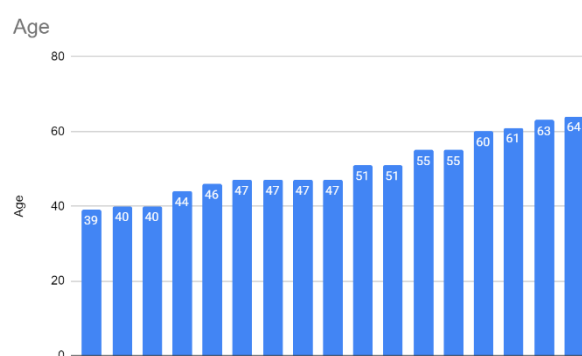


Figure 1. Age Distribution

According to the extensive retrospective study conducted at Istanbul Training and Research Hospital, which reviewed clinical data from 596 patients between January 2017 and February 2023, it was determined that 52.9% of the patients were premenopausal at the time of their diagnosis with ovarian granulosa cell tumors. Furthermore, 35.3% of these patients were classified as postmenopausal, based on the data extracted from a subset of 17 specifically diagnosed cases (Figure 2). In the same study, 29.4% of the patients reported experiencing dysmenorrhea, and 17.6% presented with abdominal pain. This detailed data collection included age at diagnosis, menopausal status, initial symptoms, radiological findings, serum CA-125 levels, and FIGO staging at the time of diagnosis. Additionally, the types of surgical interventions performed—ranging from unilateral salpingo-oophorectomy to more extensive procedures such as total abdominal hysterectomy and bilateral salpingo-oophorectomy—were thoroughly documented. The study also noted any adjuvant therapies employed, such as chemotherapy or radiation, and systematically collected follow-up data to monitor outcomes including recurrence rates and long-term complications. This comprehensive analysis aids in understanding the demographic and clinical

characteristics of patients affected by this specific type of ovarian tumor.

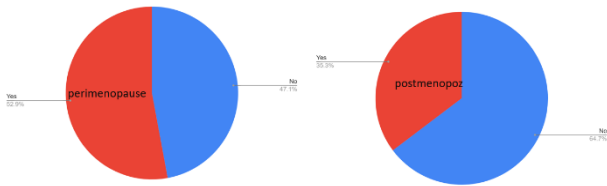


Figure 2. Perimenopause and Postmenopoz Status

Within the scope of the study, it was observed that 52.9% of the patients exhibited normal tumor marker values at the time of diagnosis. Conversely, 47.1% of the patients demonstrated elevated levels of the serum tumor marker CA-125, indicative of potential malignant activity. These findings underscore the variability in tumor marker expressions among patients diagnosed with ovarian granulosa cell tumors and highlight the importance of CA-125 as a diagnostic tool in assessing the presence and extent of the disease (Figure 3).

Tumour Marker Values

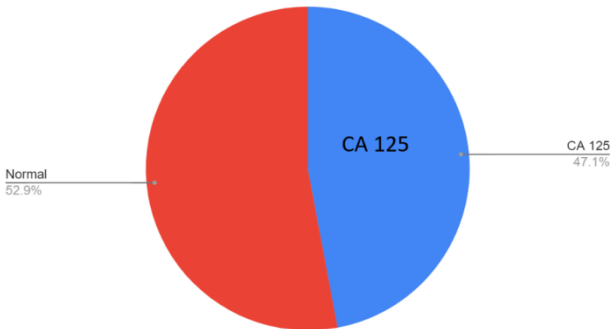


Figure 3. Tumour Marker Values

In the referenced study, 17.6% of the patients were found to have an abdominal mass, while a significant 70.6% exhibited cervical lymphadenopathy (LAP) at the time of diagnosis. These statistics highlight the prevalence of physical manifestations associated with the condition being investigated (Figure 4).

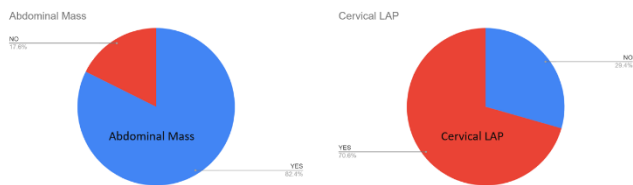


Figure 4. Abdominal Mass and Cervical LAP Status

In the detailed analysis of the study, cystic masses were identified in 41.17% of the patients, indicating a common presentation of the condition within the cohort.

Additionally, mixed cystic-solid components were

observed in 17.64% of the patients, showcasing the diversity in tumor characteristics. The average tumor size noted across the cohort was 7 cm, with a range spanning from 2 cm to 20 cm, highlighting the variability in the size of the tumors at the time of diagnosis. To further illustrate these findings, two photographs depicting examples of the tumors identified have been included in this article, providing visual evidence of the diverse manifestations observed in this study (Figure 5-6).



Figure 5. Illustrative Examples of Ovarian Granulosa Cell Tumors

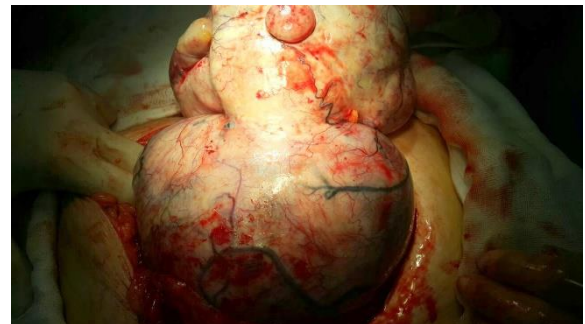


Figure 6. Illustrative Examples of Ovarian Granulosa Cell Tumors

DISCUSSION

The comparison between our study and the study conducted by Dridi et al. (8) provides an intriguing insight into the presentation and characteristics of adult granulosa cell tumors (AGCT) across different patient populations. Our study included patients ranging in age from 39 to 64 years, with a median age of 47 and a mean age of 50.41, indicating a somewhat younger demographic compared to Dridi et al., where the mean age was 53 years with a range of 35 to 73 years. About 52.9% of our patients were premenopausal at diagnosis, highlighting a younger onset of disease compared to Dridi et al.'s cohort, which included a higher likelihood of postmenopausal symptoms, as

indicated by the 32% incidence of postmenopausal bleeding. Abdominal masses were prominent in both studies, observed in 82.4% of our patients and 61% in Dridi et al.'s study. The presence of abdominal pain and other symptoms such as cervical lymphadenopathy (70.6% in our study) underscores the aggressive nature of some tumors or more advanced disease at presentation in our cohort. Dridi et al. did not report on cervical lymphadenopathy, which could suggest different diagnostic or reporting practices.

Radiological findings in our study indicated that 41.17% of patients had cystic masses and 17.64% had mixed cystic-solid components, whereas Dridi et al. reported a higher prevalence of cystic unilateral masses (80%). The size of the tumors also varied significantly, with our average tumor size being smaller at 7 cm (ranging from 2 to 20 cm) compared to Dridi et al.'s median size of 20 cm (ranging from 4 to 33 cm). This difference might reflect varying stages of disease progression or differences in the timing of diagnosis. Elevated levels of the serum tumor marker CA-125 were observed in 47.1% of our patients, closely aligning with the 42% reported by Dridi et al. This similarity indicates the consistent role of CA-125 as a marker for disease in AGCT, despite differences in other tumor characteristics and demographics (8).

Our study did not note any instances of recurrence or metastasis during the follow-up period, suggesting either a less aggressive form of the disease or effective management strategies. In contrast, the absence of similar long-term outcome data from Dridi et al. makes it difficult to compare the effectiveness of treatments or disease progression comprehensively.

When comparing our study with the research conducted by Seagle et al. (9), several points of alignment can be observed, specifically regarding the clinical presentation and diagnostic findings of ovarian granulosa cell tumors. Our patients ranged in age from 39 to 64 years with a median age of 47 and a mean age of 50.41, which is somewhat younger compared to the median age of 53 years reported by Seagle et al. This discrepancy might reflect different population demographics or potentially earlier diagnosis in our cohort. In our study, the average tumor size was 7 cm, ranging from 2 to 20 cm, which is smaller compared to the median tumor size of 9.0 cm reported by Seagle et al. The range in both studies, however, indicates a variability in tumor size at diagnosis, which could be influenced by the timing of diagnosis or the aggressiveness of the tumor subtype.

When comparing the findings from our study with the clinical data reported from the National Institute of Oncology in Rabat, Morocco, we can observe some similarities and distinctions regarding patient demographics, clinical presentations, and tumor characteristics (10). Our study had a median age of 47

years with a range from 39 to 64 years, indicating a younger patient demographic compared to the median age of 53 years reported in Sekkate et al. (10) study. This difference may suggest variations in the age of onset or diagnosis across different populations. The most common presenting symptoms in our cohort included abdominal mass (82.4%), dysmenorrhea (29.4%), abdominal pain (17.6%), and cervical lymphadenopathy (70.6%). In contrast, the Rabat study highlighted abdominal pain and vaginal bleeding as the most prevalent symptoms. This suggests differences in the clinical manifestations of granulosa cell tumors, which could be influenced by tumor location, size, or progression at the time of diagnosis. Our average tumor size was notably smaller, at 7 cm (ranging from 2 to 20 cm), compared to the mean tumor size of 14 cm in the Rabat study. The larger tumor sizes reported in Rabat could reflect later stages of detection or possibly different growth patterns of the tumors in their patient population.

The study by Khosla et al. (11) presents data on ovarian granulosa cell tumors that complement our findings, enhancing our understanding of the disease. They reported a median age of 50 years, ranging from 17 to 71 years, which is similar to our reported median age of 47 years and range of 39 to 64 years. This similarity in age distribution underscores the common age group affected by this disease. Both studies indicate a predominance of middle-aged women, although Khosla et al.'s broader age range suggests a wider variability in the age at diagnosis. In terms of symptoms, while our study found that the most common presentations included abdominal mass (82.4%), dysmenorrhea (29.4%), abdominal pain (17.6%), and cervical lymphadenopathy (70.6%), Khosla et al. identified abdominal pain as the most prevalent symptom. This difference could be due to variations in tumor location, size, or the criteria used for symptom recording. The survival data from Khosla et al. are particularly notable. They reported estimated 5 and 10-year overall survival rates of 84.6% and 72.5%, respectively. Our study did not specify survival rates, but no instances of recurrence or metastasis were observed during the follow-up period, which could suggest favorable survival outcomes, potentially aligning with the high survival rates reported by Khosla et al.

LIMITATIONS

This study, while providing valuable insights into the clinical and pathological features of ovarian granulosa cell tumors, has several limitations that must be considered when interpreting the findings. One significant limitation is the small sample size of only 17 patients diagnosed with GCTs out of a larger cohort of 596 patients reviewed for various conditions. Although this number may seem small, it is important to acknowledge that GCTs are a very rare form of ovarian cancer. Consequently, a sample size of 17 patients is substantial and meaningful within this context,

as it provides a rare opportunity to study this specific tumor type in greater detail than typically possible. However, the limited number of GCT cases may not fully represent the broader population of patients with this type of tumor, potentially affecting the generalizability of the study results. Despite the small sample size, the study provides critical preliminary data that can inform future prospective studies and clinical trials. The rarity of GCTs emphasizes the importance of such focused studies, even with smaller cohorts, as they contribute significantly to the limited pool of research available on this tumor type. By highlighting the need for more comprehensive research with larger, more diverse populations, this study contributes to the foundational knowledge necessary for advancing the understanding and management of ovarian granulosa cell tumors.

CONCLUSION

The extensive retrospective analysis of ovarian GCTs presented in this study highlights several critical aspects of this rare subtype of ovarian cancer, emphasizing its distinctive clinical presentation, treatment response, and favorable prognostic outcomes. GCTs, while constituting a minor fraction of ovarian cancers, exhibit unique characteristics that necessitate specialized attention and management strategies, which were meticulously examined in our cohort of 17 patients within a larger dataset of 596 individuals assessed at Istanbul Training and Research Hospital.

Our findings underline that the median age of diagnosis stands at 47 years, with a notable predominance of premenopausal status at diagnosis (52.9%). The clinical manifestations, including a high prevalence of abdominal masses and significant instances of dysmenorrhea and abdominal pain, align with the hormonally active nature of these tumors. The variability in presentation, such as the presence of cervical lymphadenopathy in a substantial portion of patients (70.6%), calls for a nuanced understanding of the disease's pathology. Radiological assessments revealed a mix of cystic and solid tumor components, confirming the heterogeneous nature of GCTs. Notably, no instances of recurrence or metastasis were observed, which may reflect the typically indolent nature of GCTs but also underscores the efficacy of the surgical and adjuvant treatments employed. Our surgical approach, ranging from conservative surgeries to more radical interventions like total abdominal hysterectomy, was guided by the tumor characteristics and patient factors, emphasizing the importance of individualized treatment plans. The non-recurrence observed echoes the potential for successful long-term outcomes with appropriate management.

Comparisons with other studies such as those by Dridi et al. (8), Seagle et al. (9), and Sekkate et al (10), alongside the study by Khosla et al (11), provide broader validation of our

findings and highlight the global variability in GCT presentation and outcomes. These comparisons also stress the importance of early detection and tailored surgical management in improving prognosis and reducing the likelihood of late recurrences, which are characteristic of this tumor type.

This study significantly contributes to the ongoing discourse in gynecologic oncology by providing a deeper insight into the demographic and clinical dynamics of ovarian granulosa cell tumors. Our findings advocate for a multidisciplinary approach in the treatment of GCTs, incorporating patient-specific factors into decision-making to optimize outcomes. The favorable prognosis observed in our cohort, coupled with the low risk of recurrence, reaffirms the potential for positive outcomes with meticulous clinical and surgical management.

Future research should focus on longitudinal studies to further understand the long-term survival and quality of life of patients with GCTs, as well as exploring genetic and molecular aspects of the tumor to develop targeted therapies. Continued investigation into the unique pathological features of GCTs will enhance our ability to manage this rare but significant subtype of ovarian cancer effectively, aiming to maintain high survival rates and minimize adverse effects associated with treatment.

Author Contributions: Working Concept/Design: AK, Data Collection: AK, Data Analysis / Interpretation: AK, Text Draft: AK, Critical Review of Content: HSB, Supervision: HSB

Conflict of Interest: The authors state that there is no conflict of interest regarding this manuscript.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Gershenson DM. Management of early ovarian cancer: germ cell and sex cord-stromal tumors. *Gynecologic oncology*.1994;55(3):562-572.
- Carcangiu ML, Kurman RJ, Carcangiu ML, Herrington CS. WHO classification of tumours of female reproductive organs. International Agency for Research on Cancer. 2014.
- Pectasides D, Pectasides E, Psyri A. Granulosa cell tumor of the ovary. *Cancer treatment reviews*. 2008;34(1):1-12.
- Gittleman AM, Price AP, Coren C, Akhtar M, Donovan V, Katz DS. Radiology–pathology conference: juvenile granulosa cell tumor. *Clinical imaging*.2003;27(4):221-224.
- Fox H, Agrawal K, Langley FA. A clinicopathologic study of 92 cases of granulosa cell tumor of the ovary with special reference to the factors influencing prognosis. *Cancer*. 1975;35(1):231-241.

6. Geetha P, Nair MK. Granulosa cell tumours of the ovary. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2010;50(3):216-220.
7. Li J, Chu R, Chen Z, Meng J, Yao S, Song K, et al. Progress in the management of ovarian granulosa cell tumor: A review. *Acta Obstetrica et Gynecologica Scandinavica*. 2021;100(10):1771-1778.
8. Dridi M, Chraiet N, Batti R, Ayadi M, Mokrani A, Meddeb K, et al. Granulosa cell tumor of the ovary: a retrospective study of 31 cases and a review of the literature. *Int J Surg Oncol*. 2018;2018:4547892.
9. Seagle BLL, Ann P, Butler S, Shahabi S. Ovarian granulosa cell tumor: a National Cancer Database study. *Gynecologic oncology*. 2017;146(2):285-291.
10. Sekkate S, Kairouani M, Serji B, Tazi A, Mrabti H, Boutayeb S, et al. Ovarian granulosa cell tumors: a retrospective study of 27 cases and a review of the literature. *World journal of surgical oncology*. 2013;11:1-6.
11. Khosla D, Dimri K, Pandey AK, Mahajan R, Trehan R. Ovarian granulosa cell tumor: clinical features, treatment, outcome, and prognostic factors. *North American journal of medical sciences*. 2014;6(3):133.

Yargıtay kararları ışığında adli tıbbi açıdan intihara yönlendirme suçu; Bir kesitsel araştırma

In lighth of the decisions of the court of cassation, the crime of incitement to suicide from a medical perspective: A cross sectional study

Fatma Tuğba Erkman¹

¹Adli Tıp Kurumu Ankara Grup Başkanlığı Adli Tıp Şube Müdürlüğü, Ankara, Türkiye

Gönderim Tarihi: 21 Haziran 2024, Kabul Tarihi: 24 Ağustos 2024

İletişim: Fatma Tuğba Erkman

Adli Tıp Kurumu Ankara Grup Başkanlığı Adli Tıp Şube Müdürlüğü,

Ankara, Türkiye

e-mail: ftugbaates@gmail.com

ORCID ID: FTE [0000-0002-3486-657X](https://orcid.org/0000-0002-3486-657X)

ÖZET

Amaç: İntihar eylemi, kişinin kasıtlı olarak hayatına son vermesi olarak tanımlanmakla birlikte kanunlarda suç olarak tanımlanmamaktadır. Ancak intihar suç olarak tanımlanmasa dahi Türk Ceza Kanunu 84. maddesinde intihara yönlendirme davranışı suç olarak belirtilmiştir. İntihara yönlendirme suçunun birçok unsuru bir arada içermesi ve olayın oluş vasfı açısından olay yeri ve adli tıbbi muayene özellikleri nedeni ile kasten yaralama, eziyet, cebir ve tehdit yolu ile kişiyi intihara mecbur etme suçları ile ayırımının yapılması gerekmektedir.

Materyal ve Metodlar: Yargıtay'ın resmi internet sitesi "https://karararama.yargitay.gov.tr/YargitayBilgiBankasilsitemciWeb/" adresine girilerek "intihara yönlendirme", "intihara azmettirme", "intihar", "intihara teşvik" anahtar kelimeleri kullanılarak saptanan 23.01.2012-14.09.2022 tarihleri arasındaki tüm kararlarda intihara yönlendirme suçunun demografik ve adli tıbbi verileri incelenmiş ve suçun oluşumunda ve değerlendirilmesinde adli tıbbi açıdan önemli olan noktalar taranmıştır. Ulaşılan Yargıtay kararı içerisinde karar içerikleri, suç tipleri ve ilk derece mahkeme (yerel mahkeme) kararının bozulma gerekçeleri belirtilen 38 karar çalışmaya dâhil edildi.

Bulgular: Literatür verilerine göre en sık intihar yöntemi olarak ası kullanılmasına rağmen bizim çalışmamızda %37,5 oranla en sık intihar yöntemi ateşli silahtı. Yine ülkemizde yapılan çalışmalarda ölümlü sonuçlanan olgularda erkek cinsiyet üstünlüğü varken bizim çalışmamızda vakaların %71,45'ini kadınlar oluşturdu.

Sonuç: Suç vasfının ayırımı açısından ayrıntılı olay yeri incelemesi, özellikli vakalarda verbal otopsi, her iki taraf açısından da ayrıntılı psikiyatrik muayene, eşlik eden koşulların ayrıntılı olarak incelenmesi son derece kritiktir.

Anahtar Kelimeler: İntihara azmettirme, intihara teşvik, intihara yönlendirme

SUMMARY

Aim: Suicide is defined as the deliberate act of ending one's own life, and it is not considered a crime in many legal systems. However, even the incitement to suicide is defined as a criminal offense in Article 84 of the Turkish Penal Code. The differentiation between incitement to suicide and other offenses such as deliberate injury, torture, coercion, and threats is necessary due to various factors that encompass the incident's nature, the location of the incident, and the characteristics of forensic medical examination.

Material and Methods: The official website of the Court of Cassation is accessed "https://karararama.yargitay.gov.tr/YargitayBilgiBankasilsitemciWeb/" using keywords. An analysis was conducted on all decisions made between January 23, 2012 and September 14, 2022 related to the crime of incitement to suicide. The study examined demographic and forensic medical data, focusing on key aspects of the offense's occurrence and evaluation from a medical perspective.

Results: According to the literature, hanging is the most common method of suicide; however, in our study, firearms were the most frequent method, with a rate of 37.5%. Contrary to studies conducted in our country, where suicide cases resulting in death are more common among males, in our study, 71.45% of the victims were women.

Conclusion: For distinguishing the nature of the offense, a detailed examination of the incident location, specific cases involving post-mortem examinations, comprehensive psychiatric evaluations for both parties, and a thorough analysis of accompanying circumstances are of utmost importance.

Keywords: Abetting suicide, incitement to suicide, suicide aiding

GİRİŞ

İntihar son yıllarda azalma eğiliminde olsa dahi Dünya Sağlık Örgütü verilerine göre hala önde gelen bir küresel sağlık sorunudur (1). Çeşitli genetik, toksikolojik ve psikolojik nedenlerin sorumlu tutulduğu intihar davranışı Türk Ceza Kanunu'nda (TCK) suç olarak kabul edilmez ancak kişileri çeşitli sebeplerle ve yöntemlerle intihara yönlendirmek yasalarda kişinin yaşama hakkının korunması kapsamında suç olarak tanımlanmaktadır. TCK 84. Maddesin'de "1-Başkasını intihara azmettiren, teşvik eden, başkasının intihar kararını kuvvetlendiren ya da başkasının intiharına herhangi bir şekilde yardım eden kişi, iki yıldan beş yıla kadar hapis cezası ile cezalandırılır. 2- İntiharın gerçekleşmesi durumunda, kişi dört yıldan on yıla kadar hapis cezası ile cezalandırılır. 3- Başkalarını intihara alenen teşvik eden kişi, üç yıldan sekiz yıla kadar hapis cezası ile cezalandırılır. 4- İşlediği fiilin anlam ve sonuçlarını algılama yeteneği gelişmemiş olan veya ortadan kaldırılan kişileri intihara sevk edenlerle cebir veya tehdit kullanmak suretiyle kişileri intihara mecbur edenler, kasten öldürme suçundan sorumlu tutulurlar" şeklinde belirtilmiş olup bir başkasını intihara yönlendirme suçu birden çok unsuru bir arada içeren bir suç türüdür (Tablo 1).

Tablo 1. Türk Ceza Kanunu 84. maddesi

Türk Ceza Kanunu 84. Maddesi

1-Başkasını intihara azmettiren, teşvik eden, başkasının intihar kararını kuvvetlendiren ya da başkasının intiharına herhangi bir şekilde yardım eden kişi, iki yıldan beş yıla kadar hapis cezası ile cezalandırılır.

2- İntiharın gerçekleşmesi durumunda, kişi dört yıldan on yıla kadar hapis cezası ile cezalandırılır.

3- Başkalarını intihara alenen teşvik eden kişi, üç yıldan sekiz yıla kadar hapis cezası ile cezalandırılır.

4- İşlediği fiilin anlam ve sonuçlarını algılama yeteneği gelişmemiş olan veya ortadan kaldırılan kişileri intihara sevk edenlerle cebir veya tehdit kullanmak suretiyle kişileri intihara mecbur edenler, kasten öldürme suçundan sorumlu tutulurlar.

İntihar primer olarak suç olarak kabul edilmese de intihara yönlendirme suç olarak kabul edildiğinden intihar girişimi varlığında kişiden ayrıntılı anamnez alınması, intihar girişiminin ölümle sonuçlandığı vakalarda ayrıntılı olay yeri incelemesi, ölen kişinin yakınlarından alınacak detaylı psikiyatrik anamnez ve detaylı otopsi işlemi son derece önem arz eder.

Çalışmamızda Yargıtay kararları ışığında intihara yönlendirme suçunun demografik ve adli tıbbi verileri incelenmiş ve suçun oluşumunda ve değerlendirilmesinde adli tıbbi açıdan önemli olan noktalara dikkat çekilmiştir.

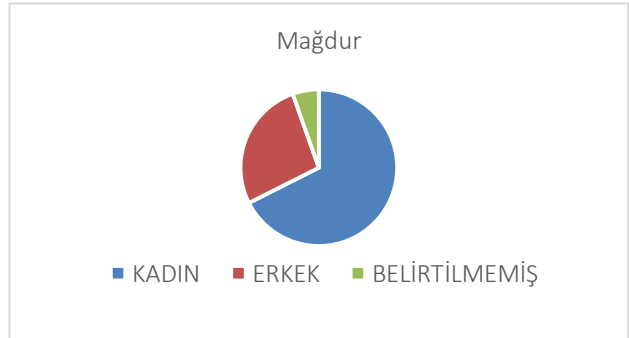
MATERYAL ve METODLAR

Yargıtay'ın resmi internet sitesi <https://karararama.yargitay.gov.tr/YargitayBilgiBankasilisTemciWeb/> adresine girilerek "intihara yönlendirme", "intihara azmettirme", "intihar", "intihara teşvik" anahtar kelimeleri kullanılarak saptanan 23.01.2012-14.09.2022 tarihleri arasındaki tüm kararlar tarandı. Ulaşılan Yargıtay kararı içerisinde karar içerikleri, suç tipleri ve ilk derece mahkeme (yerel mahkeme) kararının bozulma gerekçeleri belirtilen 38 karar çalışmaya dahil edildi. Dosya içeriği ile ilgili bilgilere ulaşılamayan kararlar dışlandı. Ulaşılan dosyalar intihar yöntemi, fail- mağdur cinsiyeti, bozma kararı gerekçeleri, olay yeri özellikleri, intihara yönlendiren kişi ile mağdur yakınlık derecesi, intihar sonucu ölüm gerçekleşip gerçekleşmemesi açısından incelendi. Bu çalışma internet araştırması niteliğinde olduğu için etik kurul izni alınmamış ancak çalışma kapsamında Helsinki Bildirgesi'ne kriterleri göz önünde bulundurulmuştur.

BULGULAR

Çalışmaya dahil edilen kararların incelemesi sonucunda intihara yönlendirme suçu mağdurlarının %71,45'ini kadınlar, %28,5'ini erkekler oluşturmaktaydı. İncelediğimiz dosyalarda iki olayın mağdurunun ve sanığının cinsiyeti bildirilmemişti. Zanlıların (n=37); %94,56'sını erkek, %5,4'ünü kadınlar oluşturdu (Tablo 2).

Tablo 2. Mağdur- Zanlı cinsiyet dağılım grafiği



İntihar girişimlerinin (n=37) %91,8'i ölümlle sonuçlanmış, %8,1'inde intihar sonucu ölüm meydana gelmemiştir. İntihar yöntemi olarak çalışmaya dahil edilen vakaların %37,5'i ateşli silah, %28,1'i ilaç-toksik madde, %18,7'i yüksekten düşme, %12,5'i ası yöntemi kullanmıştı (Tablo 3).

Tablo 3. İntihara yönlendirme suçu intihar yöntemleri

İntihar Yöntemi	N (%)
İlaç - Toksik Madde	9 (28,1)
Ası	4 (12,5)
Ateşli Silah	12 (37,5)
Yüksekten Düşme	6 (18,7)
Diğer/belirtilmemiş	6 (16,21)

Olay yeri incelemesinde %8,1'inde intihar notu varlığı belirtilmiş olup mağdur ile sanık arasındaki yakınlık açısından %51,3'ünde sanık eş ve ya partner iken, %10,8'inde üst soy, %5,4'ünde alt soy, %32,4'ünde arkadaş, tanıdık vb. kişiler idi (Tablo 4).

Tablo 4. İntihara yönlendiren kişi mağdur ilişki tablosu

İntihara Yönlendiren Kişi	N (%)
Partner-Eş	19 (51,3)
Üst soy	4 (10,8)
Alt Soy	2 (5,4)
Arkadaş vb.	12 (32,4)

Kararlar sonuçlarına göre incelendiğinde %18,9'unda yerel mahkeme kararı onanmış, onanan yerel mahkeme kararlarının 4'ünü intihara yönlendirme suçu olmadığı yönünde karar verilmiş olup, bozma kararı verilen 30 dosyanın 10'unda intihara yönlendirme suçu oluşmadığı, 3'ünde intihara yönlendirme suçu oluştuğu, 7'sinin yerel mahkemece dosyanın tekrar değerlendirilmesi gerektiği, 10'unda da suç vasfının değişimi nedeni ile bozma kararı verildiği belirtilmiştir (Tablo 5).

TARTIŞMA

İntihar Türk Dil Kurumuna göre kişinin yaşamına kendi iradesi ile son vermesi olarak tanımlanır. Dünya Sağlık Örgütü verilerine göre sıklığı azalmakla birlikte önde gelen küresel sağlık sorunlarından birisidir. Literatür verilerinde intihar yöntemi olarak %40-50 arasında değişen oranlarda en sık olarak ası yöntemi kullanıldığı belirtilmektedir (2,3). Bununla birlikte bizim çalışmamızda literatürden farklı olarak intihara yönlendirme suçu mağdurlarının muhtemelen öncesinde planlama gerekmemesi ve ulaşım kolaylığı nedeni ile en sık intihar yöntemleri sırası ile ateşli silah (%37,5), ilaç ve toksik madde maruziyeti (%28,1), yüksekten düşme (%18,7) olarak belirlenmiştir.

Tablo 5. Yargıtay Bozma Kararları ve gerekçeleri

Yargıtay Bozma Karar Gerekçeleri	n
İntihara yönlendirme kastı bulunmaması	2
Birlikte intihar etme kararı alınması	2
İntiharın gerçekleşmemesi	1
İntihara yönlendirme suçu unsurlarının oluşmaması	5
Yetersiz inceleme (otopsi bulguları, olay yeri kayıtları, intihar notu ve telefon kayıtlarının tekrar incelenmesi)	6
Yetkisiz mahkeme kararı verilmesi	1
Kasten öldürme suçunun intihara yönlendirme suçu olarak değerlendirilmesi,	3
İntihara yönlendirme suçunun intihara mecbur etme nedeni yöntemi ile kasten öldürme sayılması,	6
İntihara yönlendirme değil eziyet suçu olarak değerlendirilmesi gerektiği	1
İntihara yönlendirme suçu oluştuğu	3

Yine ülkemizde yapılan çalışmalarda ölümlle sonuçlanan intihar olgularında erkek cinsiyet çoğunlukta olmakla birlikte muhtemelen psikolojik dinamikler ve yönlendirilebilirlik göz önüne alındığında intihara yönlendirme suçu mağdurlarının %71,45 oranında kadınlar olduğu tespit edilmiştir (4).

Halen kadına yönelik şiddetin yaygın bir insan hakkı ihlali olduğu ve her 3 kadından 1'inin yaşamları boyunca tanıdıkları erkeklerin şiddetine maruz kaldığı ve kadınların en sık olarak partnerlerinden şiddet gördüğü literatürde bildirilmiştir (5). Psikolojik ve fiziksel şiddetin ileri bir boyutu olan intihara yönlendirme suçu zanlılarının da özellikle mağdurların büyük çoğunluğunun kadın olduğu göz önüne alındığında literatürle benzer şekilde %51,3 partner-eş, %14,8 üst soy, %5,4 alt soy ve %32,4 oranla arkadaş, tanıdık, iş arkadaşı vb. oluşturmaktadır.

İntihar etmek TCK'nda suç olarak düzenlenmemiş olmakla birlikte intihara yönlendirme suçu TCK m.84'de tanımlanmıştır (Tablo 1). TCK'nun 84. maddesinin gerekçesi, insanın yaşamını sürdürme içgüdüsüne rağmen belirli koşullar altında, algı yeteneğinin kaybı veya dayanılmaz acılar nedeniyle bireyin yaşamını sona erdirmeye yönünde bir irade ortaya koyabileceğini kabul etmektedir. Ancak bu iradenin hukuken geçerli sayılmaması nedeniyle, intihara teşvik veya yardım gibi eylemlerin cezalandırılabilir olduğu belirtilmiştir. Gerekçede, ahlaken tasvip edilmeyen intihar eyleminin cezai yaptırım gerektirmediği, buna karşılık başkasının intiharına neden olan fiillerin toplum düzeni ve birey hakları açısından tehlikeli olduğu vurgulanmaktadır. Hukuki olarak intihara yönlendirme suçu seçimlik suç olarak kabul edilip birden çok unsuru bir arada içermektedir (6). Bu unsurlardan birisi olan "intihara azmettirme" intihar düşüncesi olmayan kişide intihar

düşüncesi oluşturmak (7), “intihara teşvik” intihar fikri olan ancak tam olarak karar vermemiş kişiyi intihar etmeye yöneltmek, “intihar kararını kuvvetlendirme” intihar kararını vermiş olan kişinin bu kararını güçlendirmek, almış olduğu intihar kararını gerçekleştirmesi için motive etmek (7), “intihara herhangi bir şekilde yardım etme” ise intihara karar vermiş olan bir kimsenin intiharını kolaylaştırmaya yönelik her türlü hareket olarak sayılmaktadır (7). İntihara yönlendirme suçu intihar öncesinde, intihar sırasında, kişiye intihara azmettirme, teşvik etme, intihar kararını kuvvetlendirme veya intihara herhangi bir şekilde yardım etme şeklinde işlenebilir (6).

Yargıtay kararları incelendiğinde intihara yönlendirme suçu açısından gerçekleştirilen fiilin belirli bir ağırlıkta olması ve somut tehlike oluşturması ve suçu işleyen kişinin kastı gerektiği yönündedir. Yargıtay 1. Ceza Dairesi 2013/627K sayılı ve 13/11/2013 tarihli kararında failin intihara yönlendirme kastı olmadığından intihara yönlendirme suçu oluşmadığı belirtilmiştir. Yine suçun oluşması için herhangi bir şekilde mağdurun intihar fikrini eyleme geçirecek bir hareket gerçekleştirmesi gerekmektedir (8). Yargıtay 1. Ceza Dairesi 2018/4383K sayılı ve 25/10/2018 tarihli kararında intihar gerçekleşmediği için intihara yönlendirme suçu oluşmadığı vurgulanmıştır. Ancak suçun oluşumu açısından intihar sonucunda kişinin ölümün olmemesi aranan bir kriter olmayıp (7) Yargıtay kararlarında da intihara yönlendirme suçu nedeni ile intiharın ölümle sonuçlanmadığı ancak intiharın gerçekleştiği olgularda intihara yönlendirme suçu olduğu belirtilmiştir.

İntihara yönlendirme suçu olayın oluş vasfı, olay yeri özellikleri ve adli tıbbi bulgular açısından diğer suç unsurları ile karışabilmektedir. İntihara yönlendirme suçundan bahsedebilmek için fail, cebir veya tehdit yoluyla kişiyi intihara sevk etmemiş olmamalıdır, öyle ki cebir veya tehdittin eşlik etmesi durumunda kasten öldürme suçu meydana gelmektedir (8). Bu noktada Yargıtay kararları incelendiğinde kasten öldürme, cebir, tehdit, intihara yönlendirme suçlarının birbiri ile çok yakından ilişkili suçlar olduğu, %33 (n=10) oranla kararların bozma nedeni suç vasfının değişmesi olarak karşımıza çıkmaktadır. Suç vasfı değişen kararlar incelendiğinde olay yeri incelemelerinin yetersizliği, intihar notu/ses kaydı veya mesajlaşmaların dikkate alınmadığı, kişinin yapılan muayenesinde ve otopsisinde belirtilen farklı vasıftaki yaralanmaları dikkate alınmadığı gerekçesi ile intihara yönlendirme suçu olarak değerlendirilen 6 dosyanın cebir ve tehdit yolu ile intihara mecbur etme sureti ile kişilerin ölümüne sebep olanların TCK 81. madde kapsamında değerlendirilmesi gerektiği vurgulanmıştır.

SONUÇ

İntihara teşvik suçunun belirlenmesi adına ayrıntılı olay

yeri incelemesi, özellikli vakalarda verbal otopsi, her iki taraf açısından da ayrıntılı psikiyatrik muayene, eşlik eden koşulların ayrıntılı olarak incelenmesi son derece kritiktir. Özellikle çalışmamızda belirtildiği üzere aile içi şiddetin varlığı, kadın cinsiyet ve ikili intihar durumlarında ayrıntılı adli, tıbbi ve psikiyatrik muayene son derece elzemdir.

Yazar Katkıları: Çalışma Konsepti/Tasarımı: FTE, Veri Toplama: FTE, Veri Analizi /Yorumlama: FTE, Yazı Taslağı: FTE, İçeriğin Eleştirel İncelemesi: FTE, Son Onay ve Sorumluluk: FTE

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

KAYNAKLAR

- 1.W. H. Organization, «Suicide worldwide in 2019: global health estimates.» 2021.
- 2.Küçük H, Aksu A. Elazığ’da görülen intihar olgularının adli tıp açısından incelenmesi. Düşünen Adam. 2002;15(1):16-20.
- 3.Demir S, Eray M, Dereli AK, Acar K. Denizli’deki intihar ölümlerinin analizi: 10 yıllık retrospektif otopsi çalışması. Adli Tıp Bülteni. 2018;23(2):93-99.
- 4.Celbiş O, Özdemir B. Malatya Adli Tıp Grup Başkanlığı’nda 1999-2002 yılları arasında ölü muayene ve otopsileri yapılan intihar olguları. Journal of Turgut Ozal Medical Center. 2005; 12(3):173-176.
- 5.Ergönen AT, Biçen E, Ersoy G. «COVİD-19 salgınında ev içi şiddet.» Adli Tıp Bülteni. 2020;25(özel sayı):48-57.
- 6.Artuk ME. İntihar ve İntihara Yardım Suçu Üzerine Bir Deneme. Selçuk Üniversitesi Hukuk Fakültesi Dergisi. 1994;4(1-2):113-142.
- 7.Koca M. Üzülmez İ. Türk Ceza Hukuku Özel Hükümler 9. Baskı. Adalet Yayınevi. 2023.
- 8.Tulay ME. Türk Ceza Hukukunda İntihara Yönlendirme Suçu. Marmara Üniversitesi Hukuk Fakültesi Hukuk Araştırmaları Dergisi. 2020;26(2):814-837.

Renal Artery Variations with Clinical Significance: Multiple Renal Arteries and Their Coexistent Anatomical Abnormalities: A Cadaveric Study

Klinik Önemi Olan Renal Arter Varyasyonları: Çoklu Renal Arterler ve Eşlik Eden Anatomik Varyasyonlar: Bir Kadavra Çalışması

Hürriyet Çetinok^{1,2}

¹Department of Anatomy, Faculty of Medicine, Istanbul Atlas University, Istanbul, TURKEY

²Albert Einstein College of Medicine, Department of Anatomy and Structural Biology, Yeshiva University New York, USA

Correspondence: Hürriyet Çetinok

Department of Anatomy, Faculty of Medicine, Istanbul Atlas University, Istanbul, TURKEY

e-mail: hurriyet.cetinok@atlas.edu.tr

ORCID ID: HC [0000-0001-7083-966X](https://orcid.org/0000-0001-7083-966X)

Submitted Date: 7 August 2024, **Accepted Date:** 27 August 2024

SUMMARY

Aim: This cadaveric study aimed to identify the multiple renal arteries and evaluate their association with other anatomical abnormalities. The possible clinical consequences of more than one renal artery were analyzed.

Material and Methods: This study was carried out by accessing the Abdominal aorta (AA) from 20 American formalin-embalmed cadavers [12 males, 8 females, ages 50-96] donated to the C&DA Department of Albert Einstein College of Medicine. From the cadavers in the supine position, the branch points of the renal artery from the abdominal aorta on the right and left sides were checked to see if there was more than one. Renal artery (left side), celiac trunk, superior mesenteric artery, inferior mesenteric artery, and aortic bifurcation were measured in 3 ways: linear, longitudinal, and transverse. The obtained results were assessed using a comparative analysis with earlier research findings documented in the literature.

Results: Among the 20 cadavers included in the study, two of males, were found to have two renal arteries on the right side, and both of them are hiler arteries. These Multiple renal arteries were coexistent with splenomegaly, tortuosity of the abdominal aorta, and deviation of the vertebral column at the level of the 3rd lumbar vertebra. 94.7% of the cadavers exhibited normal renal arterial anatomy. The most common branching location of the main renal arteries and multiple renal arteries (MRA) were the find from the abdominal aorta.

Conclusion: Before surgical or radiological procedures in the anatomical region related to and adjacent to renal arteries, knowing the possible renal artery variations in the anatomy of the region is very important to reduce mortality and morbidity during surgical or interventional procedures. Knowing the anatomy of renal arteries and evaluating it radiologically will guide renal transplantation, hepatorenal surgery, interventional radiology, and nephrology the prevention and treatment of many conditions such as hypertension, and target organ damage them.

Keywords: Accessory renal artery, Multiple renal arteries, renal artery variations

ÖZET

Amaç: Bu kadavra çalışmasının amacı multipl renal arterleri tanımlamak ve aynı zamanda diğer anatomik anormallikler ile birlikteliğini değerlendirmektir. Birden fazla arteria renalis'in bulunmasının olası klinik sonuçları analiz edildi.

Materyal ve Metodlar: Bu çalışma, Albert Einstein College of Medicine C&DA Anabilim Dalı'na bağışlanan 20 Amerikan formalin fikse kadavradan [12 erkek, 8 kadın, yaşları 50-96] Aorta Abdominalis (AA)'e ulaşılarak gerçekleştirildi. Supin pozisyonundaki kadavralardan Arteria renalis'in sağ ve sol tarafta Aorta abdominalis'ten dallanma noktaları, birden fazla sayıda olup olmadıkları kontrol edildi. Arteria renalis(sol taraf), Truncus coeliacus, arteria(a.) mesenterica superior, a. mesenterica inferior, bifurcatio aorta arasındaki mesafeler, lineer, longitudinal ve transvers olmak üzere 3 şekilde ölçüldü. Elde edilen sonuçlar oranlanarak, literatürdeki önceki çalışmalarla kıyaslanarak değerlendirildi.

Bulgular: Çalışmaya alınan 20 kadavradan iki erkek cinsiyette, ikiside hiler arter olmak üzere sağ tarafta iki adet renal arter olduğu tespit edildi. Multiple renal arterlere, splenomagali, abdominal aorta da ondulan seyir, 3. Lumbal vertebra seviyesinde columna vertebralis'te deviasyon olduğu gözlemlendi. Hastaların %94,7'si normal renal arter anatomisine sahipti. Ana renal arterlerin ve ARA'nın en sık Aorta abdominalis'ten dallanıyordu.

Sonuç: Arteria renalis ile ilişkili ve komşuluğundaki Anatomik bölgedeki cerrahi veya radyolojik işlemler öncesinde bölge Anatomisindeki olası arteria renalis varyasyonlarının bilinmesi cerrahi veya girişimsel işlemler sırasındaki mortalite ve morbiditeyi azaltmakta çok önemlidir. Renal transplantasyon ve Hepatorenal cerrahi, girişimsel radyoloji, nefroloji başta olmak üzere A.(arteria) renalis anatomisinin bilinerek, radyolojik olarak değerlendirilmesi, hipertansiyon, hedef organ hasarı gibi pek çok kliniğin önlenmesi ve tedavisine kılavuz olacaktır.

Anahtar kelimeler: Aksesuar renal arter, multipl renal arter, a. renalis varyasyonları

INTRODUCTION

In the postconceptional ninth week, the kidneys achieve their adulthood position embryologically. When the kidneys reach their adult position, the blood procurement is made by the branches that arise from the cranial terminal of the abdominal aorta (AA), and the early branches atrophy (1, 2). Renal arteries are frequently at the plane of L1 and L2 vertebrae, the superior mesenteric artery is immediately below the inception. The left renal artery is generally located slightly upper than the right. The right renal artery is longer and goes under the inferior vena cava (3). Every renal artery inserts the hilum and is branched into anterior and posterior branches that supply the kidney parenchyma, then they are typically branched into four or more segmental branches (4). Several words, including "aberrant," "abnormal," "accessory," "additional," "extra," "supernumerary," and "supplementary," are used to describe to multiple renal arteries. Twenty to thirty percent of people have multiple renal arteries (MRA) (two in twenty-two, three in one to two percent, and four in 0.1%) (5). Variations in the number of renal arteries, particularly dual renal arteries, are the most frequently identified variant in addition to physical variations (6).

An embryological explanation for the existence of MRA was presented by Felix et al. in their work. Sampaio and Passos (13) divided the renal arteries into groups based on the portal of admission a branch of the aorta that penetrates the kidney in the hilum is called the Hilar artery. The kidney is penetrated by the Superior Polar artery (SPA), a branch of the aorta, and the inferior polar artery (IPA), a branch of the aorta that enters the inferior pole of the kidney. The extra-hilar artery is a renal artery from the abdominal aorta that has an extra-hilar branch to the poles. Compared to other arteries of the same size, renal arteries are more prone to show multiplicity (7,8). Comprehending the function of MRA can help avert inadvertent perioperative damage and the subsequent infarction of the impacted area. This has led to easier surgical planning and better outcomes (9).

Knowledge of MRA's existence will aid in preventing unintentional harm during surgery and the ensuing segmental infarction. Better surgical outcomes have resulted from this (6). Accessory renal arteries (ARAs) are present in approximately 22–24% of hypertension patients. Prior research has demonstrated that ARA is connected to renin-dependent hypertension as well as resistant hypertension (9).

For a long time, one of the relative contraindications to kidney transplantation was the presence of multiple renal arteries. Additionally, studies have suggested that anatomical differences in the accessory renal arteries may be linked to post-transplantation hemorrhage, arterial thrombosis, renal artery stenosis, atherosclerosis, and

parenchymal necrosis (6).

There is significant variation in the incidence of MRA, ranging from 8.7 to 75.7% (median 28.2%) (10). MRA are more frequently found unilaterally (30%) than (10%) on both sides (1,11), and there is racial variation in their occurrence (10, 12). While having many arteries is normal in itself, the existence of MRA may make transplant surgery, RA embolization or angioplasty, reconstructive therapy of AA aneurysms, and urological operations more difficult (13, 14, 15). Furthermore, there is a correlation between a greater MRA frequency and the risk of renovascular hypertension (16), hydronephrosis (17), occlusion of the ureteropelvic junction, and chronic pyelonephritis (18).

MATERIAL AND METHODS

From 20 American formalin-embalmed cadavers donated for anatomical practice to the Department of Anatomy, Albert Einstein College of Medicine (AECOM), this study was performed using the AA from 12 cases [12 males, 8 females, age 50-96]. All donors that were approved for the donation and usage for clinical studies were accepted according to New York's Anatomical Gift Law. In this study, ethical approval is not required since the study is based on course cadavers from the Albert Einstein College of Medicine C&DA Department according to the exemption categories in Enstein-IRB-citation104(d). Because of the involvement of metastatic gastric cancer in the para-aortic area, a 52-year-old female case was excluded from the study. The others have no history of previous abdominal injury, pathologic condition, or surgery. The abdominal aorta of the cadavers that were brought to the supine position was approached anteriorly and focused on the branches of the AA. During our studies, we utilized Mitutoyo Digital Caliper (calibration certificated by Mitutoyo America Corp. Calibration Lab.- control number 887014, range 0.000 inch- 0006 inch), goniometer, essential dissection instruments, and a digital camera (Olympus). In our study first, we analyzed abdominal aorta trajectory, branching levels of vertebral column for each branch (Coeliac trunk (CT), superior mesenteric artery (SMA), inferior mesenteric artery (IMA), left renal artery (LtRA), BA) morphological changes, tortuosity, aneurysm, thickness of the AA wall, variations, osteodegenerative changes, and compression fracture vertebral column. We classified vertebral bodies according to their height: upper 1/3, middle 1/3, and lower 1/3. However, some of the AA branches arose from the intervertebral disc level. We used LtRA as a critical landmark regarding literature search in our previous cadaveric study which is called 'Clinical Significance, Variations and Anatomical Relationships of Coeliac Trunk, Superior Mesenteric Artery, Inferior Mesenteric Artery and Left Renal Artery in Colon and Hepatorenal Surgery, Abdominal Aorta Mapping: Cadaveric Study'. CT, SMA, IMA, LtRA, and BA were studied, and transverse, longitudinal, and linear distances

of them, and in addition to this calculation, arteries' origins and their branching angles them were also statistically analyzed. We removed AA from the cadaver and then vertically dissected along the major axis of the AA, starting at the branching point of the right and left common iliac artery, and split into the ventral and dorsal sides. The removed ventral sides of the AA were taken photographs from the intravascular lumen utilizing a digital camera. The horizontal and vertical diameters of the sites of confluence with the IMA, SMA, and CT were evaluated. In addition, the left/right deviation of the sites of confluence from the center line along the vertical axis of the vessels that went through the midpoint among both sides of the branching point of the left renal artery was evaluated. We also evaluated the branching points of the IMA, SMA CT, and left renal artery (LtRA) utilizing the BA as the point of origin, ARAs, and MRAs and measured the distances between the branching points.

RESULTS

In all of 38 kidneys, renal arteries arose from the abdominal aorta. Single renal artery (SRA) was seen in 36 kidneys while MRA(Multiple renal artery) was seen in Double renal arteries (DRA) were noted in 12 (%), and triple renal arteries (TRA) in 0/absent/none (0%). Among the MRA, DRA was seen in two out of 38 (%5.25) right-sided kidneys. There is not left-sided MRA in this study. Only 94.7% of the patients exhibited normal renal arterial anatomy. Both of them found in the male gender. Hilar ARA (100%) was significantly more common than polar ARA.

All 38 renal arteries included in the study branched from the aorta abdominalis. Only 2 double renal arteries were detected. As shown in Figures 1 and 2, in a 62-year-old male cadaver, the right main renal artery was observed to branch just distal to the superior mesenteric artery and enter the right kidney from the renal hilum.

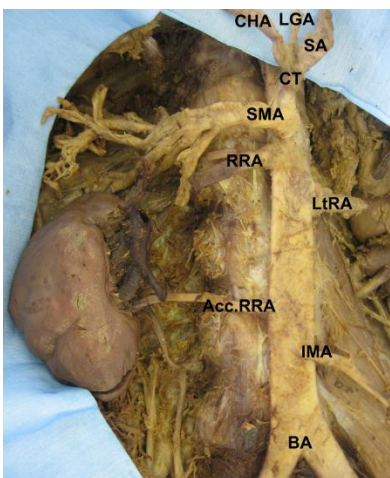


Figure 1. The aspect of the superior side of the supine-positioned cadaver. The accessory renal artery should be paid attention and three branches of coeliac trunk are clearly observed.

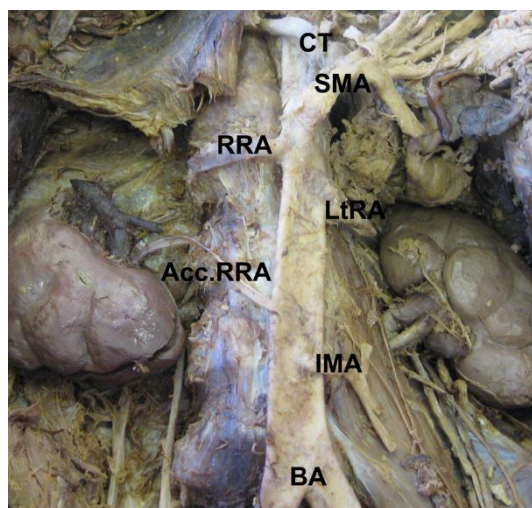


Figure 2. The aspect of the superior side of the supine-positioned cadaver. The diameter of accessory renal artery is thinner than the right renal artery as it is seen in this figure.

As seen in Figure 3, 7 cm distal to the right main renal artery, the right accessory renal artery, which is thinner in diameter than the right main renal artery, was seen to branch from the aorta abdominalis and reach the right renal hilum. The right accessory renal artery was branching from the right edge of the aorta abdominalis, 2 cm proximal to the inferior mesenteric artery.



Figure 3. Abdominal aorta which has accessory renal artery occurred, removed from the cadaver.

In Figure 2, a clearly visible lobulated kidney structure was observed on both sides. Another remarkable formation in this

cadaver was splenomegaly, whose superior-inferior length is shown as 13.5 cm in figure 4.



Figure 4. In addition to this anatomic anomaly, splenomegaly (13.5cm/5.5inch liver) was also observed.

In an 80-year-old male cadaver, two right renal arteries were branching from the aorta abdominalis, as seen in Figure 5 from the outer wall of the aorta abdominalis and as seen from the inner wall of the aorta abdominalis in Figure 6. The diameter of the artery we called right renal artery I (RRA-I) was larger than the diameter of the artery we called right renal artery II (RRA-II). Both renal arteries were branching from the abdominal aorta between the superior mesenteric artery and the left renal artery.

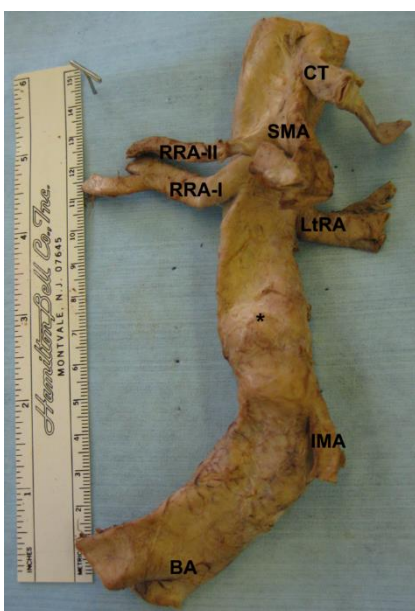


Figure 5. Double renal arteries on the right side arose from abdominal aorta. *Aneurysm of the Abdominal aorta



Figure 6. The lumen of the Abdominal aorta which has accessory renal artery occurred, was dissected ventrally from the line that crosses Aortic bifurcation.



Figure 7. In addition to this anatomic anomaly, abdominal tortuous aorta and L3 vertebrae deviations are observed.

If figure 6 is examined carefully, RRA-II branches from 0.4 mm distal to SMA, RRA-I branches from 0.3 mm distal to RRA II, and separately from the abdominal aorta. Two

aneurysms were detected, the first one with a diameter of 1.5 cm between the left renal artery and the inferior mesenteric artery (Figure 5), the second one with a diameter of approximately 3 cm between the inferior mesenteric artery and the aortic bifurcation (Figure 6). The tortuosity of the abdominal aorta is quite evident in figure 7, and the deviation of the abdominal aorta to the left was observed at the level of the 3rd Lumbal vertebra.

Since the left renal artery was taken as the reference point in previous studies on the abdominal aorta and its branches (19,20,21), in this study, taking into account the variations encountered in the right renal artery, we determined at what level the left renal arteries are located in the abdominal aorta relative to the columna vertebralis. It is shown in Table 1, including the ages and genders of the cadavers. In summary, as seen in graph (Figure 8), 42% of the left renal arteries originate from the upper 1/3 of the 2nd Lumbal vertebra, 32% from the intervertebral disc level of the 1st and 2nd Lumbal vertebra, and 21% from the lower 1/3 of the 1st Lumbal vertebra. It was observed that it branches from the abdominal aorta, 5% from the 2nd lumbar vertebra and the lower 1/3 of the lumbar vertebra. In the case where accessory renal artery was seen, the main renal artery branched from the upper 1/3 part of L2, where the majority of 42% was located, while in the cadaver where RRA I and II were seen, the branching from the abdominal aorta was at the level of the intervertebral disc between L1-L2.

Table 1. Age, gender and branching point of left renal artery from abdominal aorta

Cad. No	Age	Gender	Level of left RA*
1	73	M	L1/2M
2	70	F	L2L
3	79	M	L1L
4	92	M	L1/2-IVD
5	91	M	L2U
6	80	M	L1/2-IVD
7	88	M	L2U
8	84	F	L2U
9	79	F	L2U
10	50	F	L1L
11	82	F	L2U
12	86	F	L1/2-IVD
13	96	M	L1L
14	75	M	L1/2-IVD
15	87	M	L2U
16	65	M	L1L
17	62	M	L2U
18	72	F	L2U
19	83	M	L1/2-IVD

Measured distances between various points are shared in Table 2. Particularly considering the cases in which renal artery variations were observed, the left renal artery was

used as the reference point. The measurements of the case with accessory right renal artery and splenomegaly are shown in the 1st column (Case 1), and the measurements of the cadaver with RRA I and RRA II are shown in the second column (Case 2).

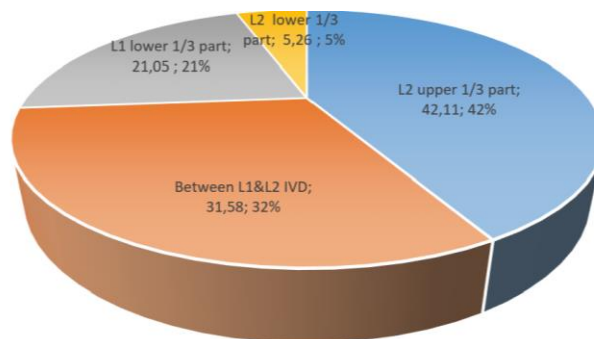


Figure 8. Distribution of Branching points of Left Renal Artery from Vertebral Point

Table 2. Measured distances between various points

Abbreviations*	Distance	Case 1	Case 2
a	Transverse diameter of the AA at level LtRA	19.1 mm	24.08 mm
b1	LtRA-CT linear distance	45.85 mm	40.47 mm
b2	LtRA-CT longitudinal distance	49.92 mm	39.1 mm
b3	LtRA – CT transverse distance	11.48 mm	5.27 mm
c1	LtRA – SMA linear distance	25.16 mm	22.02 mm
c2	LtRA – SMA longitudinal distance	23.52 mm	18.65 mm
c3	LtRA- SMA transverse distance	11.01 mm	9.32 mm
e2	LtRA – BA longitudinal distance	95.77 mm	102.91 mm
e3	LtRA – BA transverse distance	7.01 mm	9.3 mm
LtRA	Arising level of vertebral column	L2U	L1/2-IVD

* a : transverse diameter of the AA at level LtRA, b1 : LtRA-CT linear distance, b2 : LtRA-CT longitudinal distance, b3 : LtRA – CT transverse distance, c1 : LtRA – SMA linear distance, c2 : LtRA – SMA longitudinal distance, c3: LtRA- SMA transverse distance, e2: LtRA – BA longitudinal distance, LtRA: Left Renal Artery, BA: Aortic Bifurcation, IVD: Intervertebral disc, U: Upper 1/3 part of the vertebral body, M: Middle 1/3 part of the vertebral body, L: Lower 1/3 part of the vertebral body

DISCUSSION

In the etiologies of hypertension defined as primary, renovascular or idiopathic, which is one of the most important health problems of recent years, the presence of multiple renal arteries may be in question, as we found in our study. MRA renin-angiotensin-angiotensinogen can play an active role in hypertension and target organ damage by affecting the angiotensinogen system more than normal. Some studies verified that ARA activated the renin-angiotensin system and produced abundant renin, which raised blood pressure in patients with primary hypertension. Stricter blood pressure management was warranted for ARA due to their substantial target organ damage to prevent serious cardiovascular events. Related studies offered compelling proof that hypertensive patients with ARA should get intensive treatment in routine clinical settings (22, 23, 24).

In two cases with numerous and accessory renal arteries, earlier research that was available in the literature was consulted in this investigation (25). Based on this, the landmark, or left renal artery (LtRA), was identified, and measurements were taken of the linear, longitudinal, and transverse distances between them and the aortic bifurcation (BA), superior mesenteric artery (SMA), and coeliac trunk (CT). The left renal artery was used to assess the abdominal aorta's diameter at the same moment. The left renal artery's longitudinal and transverse diameters were measured concurrently, and the outcomes were compared to those of earlier research.

The measurements of AA transverse diameter at the LtRA level in cases 1 and 2 in our investigation were 19.1 mm and 24.08 mm, respectively, matching the findings of Takahashi et al. (25). It was discovered within the 17.5-25.2 mm range that his investigation had established. In Case 1, the linear, longitudinal, and transverse LtRA-CT distances were 45.85 mm, 49.92 mm, and 11.48 mm, respectively. In Case 2, the corresponding values were 40.47 mm, 39.1 mm, and 5.27 mm. These values fall into the ranges that Takahashi et al. found for this distance: 28.9 mm - 51.9 mm, 23.7 mm - 51.0 mm, and 2.1 mm - 18.7 mm, respectively. While LtRA - SMA linear, longitudinal and transverse distances are 25.16 mm, 23.52 mm, 11.01 mm, for Case 1, they are 22.02 mm, 18.65 mm, 9.32 mm for Case 2, and these values are 12.5 mm - 37.7 mm, respectively, found in the study of Takahashi et al. Compatible with 6.6 mm - 35.6 mm, 4.8 mm - 18.6 mm values.

The MRA's nomenclature is still ambiguous and divisive ("multiple"). The labels "main renal," "aortic superior and inferior polar," and "renal inferior polar" arteries were used by Merklin and Michels (1958) (26) for the single RA. The terms "accessory" and "supplementary" refer to RAs that have an aortic ostium that is distinct from the main RA and that enter the hilum directly, respectively, according

to Holden et al. (2005) (26). The renal arteries were divided into hilar and polar (superior and inferior) arteries by Daescu et al. (2010) (26).

Patients were the sample in some angiographic investigations, although dissected cadavers or autopsy specimens were used in many other research. It is suggested that cadaver dissection, as opposed to aortography, likely provides a more accurate estimate of the number of RA (26). Because of their thickness (diameter <2 mm), MRA was less frequently discovered in angiographic studies. They are not visible, and the arteries entering the kidney outside the hilum are sometimes mistaken for the adrenal or capsular arteries, especially when the MRA originated from AA (26). Interestingly, compared to angiography, where the relative incidence was 3%, magnetic resonance angiography was unable to forecast the morphology of the renal arteries in 10% of patients with MRA (26).

Thirty percent was found to be the incidence of MRA in the first investigation (18). Satayapal et al. (2001) (2) examined data from 1883 to 1999 and calculated the MRA incidence to be 28.1%.

The current investigation attempted to compile all pertinent papers published between 2000 and the present and earlier works that were not assessed (26). The incidence of MRA was found in several populations (26), with a mean of 23.3% and a range of 4% to 61.5%. The frequency was calculated based on the specimen: transplant (20.4%), radiographic (21.8%), and cadaveric (28.2%). There is a large variety of MRA incidence within a single community, with Brazilians having an MRA incidence of 18.5-26.5% and Turks having an MRA incidence of 14.5-27%. These differences could be explained by the sample's size, origin, and MRA documentation technique. The estimated incidence of MRA in a Greek population studied in our study was 11.2%. The MRA were found in 11.2% (23/206) of the kidneys. MRA were located on the right side in 52.2% (12/23) and the left side in 47.8% (11/23) of cases. MRA was found in 11.3% (12/106) of the male population, 50% (6/12) on the left side, and 50% (6/12) on the right. Table 1 shows that in females, MRA were found in 11% (11/100), 54.5% (6/11) on the right side, and 45.5% (5/11) on the left. After dissecting 266 kidneys, Sampaio and Passos discovered that 53.3% of the kidneys had a single hilar artery, 7.9% had a double hilar artery, and 5.3% had a hilar with a single inferior polar artery (13).

Thirty percent of kidneys have supernumerary renal vessels. They extend from the 11th thoracic to the 4th lumbar vertebra along the aorta, both in number and with similar periodicity to the sides.

For surgical treatments linked to kidney transplants, abdominal aortic aneurysms, posterior abdominal walls, angiographic interventions, and ureter surgeries, it is

important to understand this anatomical variance and coexisting disorders. Fibromuscular dysplasia in an ARA has the rare potential to cause renovascular hypertension. According to Sampaio et al. (1992) (13), each MRA is a member of the segmental arteries and is susceptible to postoperative hypertension rises, hemorrhage during urological procedures or renal transplants, and segmental ischemia. Since there is currently a huge demand for kidney donations, it is imperative to be aware that donors with numerous renal arteries and accessory renal arteries do exist (26-28). Arteriography is advised before any nephrectomy to design the surgical process and avoid any vascular problems (Sampaio et al., 1992) (13).

According to Feller and Woodburne, The abdominal aorta's lateral displacement, is an important clinical symptom since it could be mistaken for an aneurysm when palpated through the abdominal wall as a pulsatile mass (29). When it comes to invasive vascular treatments and abdominal surgeries, the knowledge of such instances is extremely clinically significant. One of the factors contributing to inferior vena cava inhibition is an Abdominal aorta tortuosity. This defect may result in liver cirrhosis and fibrosis, as well as necrosis and centrilobular congestion, which are ultimately the cause of the condition (30).

The literature is replete with research on supernumerary renal vessels. Urinary and vascular problems are more common after transplantation due to MRA in the graft kidney, according to some of these publications. The MRA rate was reported to be 21% in a study involving 288 live donor nephrectomies. Demir et al. claimed that the presence of MRA had no effect on the clinical outcomes that followed open donor nephrectomies, but that there was more blood loss and a longer recovery time following laparoscopic donor nephrectomies than those without MRA (31). Hypertension, discomfort, and aortic insufficiency can result from aortic lumen blockage, depending on the level and degree of tortuosity of the abdominal aorta.

Further studies on patients who had endovascular aneurysm restoration with ARA covering revealed that 67% to 84% of individuals experienced renal infarction (32,33). Ultimately, the decision of whether to reimplant or immolate ARAs rests on the surgeon's judgment, which is hampered by a number of patient -specific circumstances. As we previously discussed, MRA and ARA are uncommon variants that accompany Abdominal aorta tortuosity. We reported two cases of MRA and ARA independently in our cadaveric study, together with coexisting anatomical anomalies. Considering our background literature review, this is the only cadaveric study that reports splenomegaly in conjunction with ARA.

Patients with a single kidney artery are also said to have lower transplant rejection chances. For a long time, one of the relative contraindications to kidney transplantation was the presence of auxiliary renal arteries (10). Changes in the size of other vessels, such as the testicular arteries, supra renal arteries, or auxiliary phrenic arteries, as a result of accessory renal arteries, are another clinically significant aspect of these arteries (11). Additionally, studies have suggested that atherosclerosis, elevated blood pressure, arterial thrombosis, renal artery stenosis, parenchymal necrosis, and bleeding after transplantation may be linked to structural differences in accessory renal arteries (17) Finding out more about the auxiliary renal arteries and their structural changes is crucial for the diagnosis and treatment of renal disorders. They reported a prevalence rate of 20.2 percent in women and 32.1 percent in males. In order to prevent problems, this issue is especially crucial for artery procedures, kidney damage therapies, and transplant surgeries (17).

The occurrence of the MRA demonstrates racial variability (18, 26), and they are more frequently diagnosed unilaterally (30%) than bilaterally (10%) (1, 29). Multiple artery persons are normal, but the existence of MRAs may complicate procedures such as urological treatments, RA embolization or angioplasty, transplant surgery, and reconstructive therapy of AA aneurysms (20, 30, 31). Furthermore, there is a correlation between a greater MRA frequency and the likelihood of ureteropelvic junction blockage, hydronephrosis, renovascular hypertension, and chronic pyelonephritis (32, 33). According to Gupta and Tello (17), in 24% of the hypertensive individuals, accessory RAs are a vascular anomaly rather than the direct cause of hypertension (18, 22).

Thus, knowledge and a comprehensive preoperative radiological evaluation are crucial for surgical and endovascular procedures to be successful and safe. To establish a safe preoperative and intraoperative management of the renal vascular supply, it is crucial to understand the morphology and topography of the various renal arteries (18).

CONCLUSION

The knowledge of the Topographic and Clinical Anatomy of the Renal Arteries has become significantly important in recent years due to increasing number of kidney transplantations, renovascular surgeries, diagnostic and interventional radiology. Some of the pathologies that coexist with MRA are related to Anatomical structures, such as vertebral column deformities, splenomegaly, abdominal aorta tortuosity, aneurysm. Some studies verified that ARA activated the renin-angiotensin system and produced abundant renin, which raised blood pressure in patients with primary hypertension. More research is required to determine the likely consequences of

additional anomalies and anatomical changes coexisting with ARAs and MRAs. Thus, knowledge and a comprehensive preoperative radiological evaluation are crucial for clinical, surgical and endovascular procedures to be successful and safe.

ACKNOWLEDGMENTS

The authors appreciate the cadaver donations provided by Albert Einstein College of Medicine, Department of Anatomy.

Author Contributions: Working Concept/Design: HC, Data Collection: HC, Data Analysis / Interpretation: HC, Text Draft: HC, Critical Review of Content: HC, Supervision: HC

Conflict of Interest: The authors state that there is no conflict of interest regarding this manuscript.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Ozkan U, Oguzkurt L, Tercan F, Kizilkilic O, Koc Z, Koca N. Renal artery origins and variations: angiographic evaluation of 855 consecutive patients. *Diagnostic and interventional radiology (Ankara, Turkey)* 2006; 12(4): 183-186.
- Satyapal KS, Haffejee AA, Singh B, Ramsaroop L, Robbs JV, Kalideen JM. Additional renal arteries: incidence and morphometry. *Surgical and radiologic anatomy: SRA* 2001; 23(1): 33-38.
- Richard Drake WV. *Gray's Anatomy*. Gunes Medical Bookstore 2017: 324.
- Pestemalci T, Mavi A, Yildiz YZ, Yildirim M, Gumusburun E. Bilateral triple renal arteries. *Saudi journal of kidney diseases and transplantation: an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia* 2009; 20(3): 468-470.
- Pollack HM, McClennan BL, Dyer R, Kenney PJ: *Clinical Urography*. Saunders, Philadelphia; 2000. 10.1148/radiology.219.3.r01jn43822
- Etli M., Avnioglu S., Dikici R. Prevalence of Accessory Renal Artery in Aortic Aneurysms. *Van Medical Journal*. 2020. 27. 520-524. 10.5505/vtd.2020.53386.
- Moore KL DA. *Clinically Oriented Anatomy*. Lippincott Williams & Wilkins Publishers 1999: 286-287.
- Feller I, Woodburne RT. *Surgical anatomy of the abdominal aorta*. *Ann Surg* 1961; 154: 239-52.
- Letti, R., Levoor, P., Vollala, V. R., Potu, B. K., Ravishankar, M., & Virupaxi, R. Multiple variations of the urogenital vascular system in a single cadaver: a case report. *Cases journal*, 2008; 1(1), 344.
- Chung, A. A., Millner, P. R. Accessory Renal Artery Stenosis and Secondary Hypertension. *Case reports in nephrology*, 2020; 8879165.
- Davidovic, L. B., Markovic, M., Kostic, D., Zlatanovic, P., Mutavdzic, P., & Cvetic, V. (2018). Open repair of ruptured abdominal aortic aneurysm with associated horseshoe kidney. *International angiology : a journal of the International Union of Angiology*, 37(6), 471–478.
- Anson BJ. *Morris' Human Anatomy*. 12th Ed., New York, Mc GrawHill Book Company. 1966; 746-47.
- Sampaio FJ, Passos MA. Renal arteries: An anatomic study for the surgical and the radiologic practice. *Surg Radiol Anat*. 1992; 14: 113-17.
- Yufa, A., Mikael, A., Lara, G., Nurick, H., Andacheh, I. Accessory renal arteries involved in atherosclerotic occlusive disease at the aortic bifurcation. *Journal of vascular surgery cases and innovative techniques*, 2008; 6(3), 425–429.
- Zarins, C. K., Xu, C., Glagov, S. Atherosclerotic enlargement of the human abdominal aorta. *Atherosclerosis*, 2001; 155(1), 157–164.
- Aliyu I. Massive splenomegaly, acute kidney injury, and the challenges of diagnosing hyperractive malarial syndrome in a resource-limited setting. *J Med Trop* 2017;19, 140-1
- Gulas, E., Wysiadecki, G., Szymański, J., Majos, A., Stefańczyk, L., Topol, M., et. al. Morphological and clinical aspects of the occurrence of accessory (multiple) renal arteries. *Archives of medical science : AMS*, 2018; 14(2): 442–453.
- Pradhay, G., Gopidas, G. S., Karumathil P.S., Mathew G., Mathew A. J., Sukumaran T. T., et. al. Prevalence and Relevance of Multiple Renal Arteries: A Radioanatomical Perspective. 2021; *Cureus*, 13(10): e18957.
- Kosiński H. Variability of places of origin of the human renal arteries. *Folia Morphol (Warsz)*. 1994;53(2):111-116.
- Ozan H, Alemdaroglu A, Sinav A, Gümüşalan Y. Location of the ostia of the renal arteries in the aorta. *Surg Radiol Anat*. 1997;19(4):245-247.
- Pennington N, Soames RW. The anterior visceral branches of the abdominal aorta and their relationship to the renal arteries. *Surg Radiol Anat*. 2005;27(5):395-403.
- Kang K, Ma Y, Jia C, et al. Relationship between Accessory Renal Artery and Clinical Characteristics of Middle-Aged Patients with Primary Hypertension. *Int J Hypertens*. 2020;2020:7109502. Published 2020 Apr 8.
- Chan PL, Tan FHS. Renin dependent hypertension caused by accessory renal arteries. *Clin Hypertens*. 2018;24:15. Published 2018 Nov 1.
- Davies Er, Sutton D. Hypertension And Multiple Renal Arteries. *Lancet*. 1965;1(7381):341-344.
- Takahashi T, Takeuchi K, Ito T, Hayashi S, Qu N, Itoh M. Positional relationships of abdominal aorta landmarks for angiography: observations from the intravascular space. *Surg Radiol Anat*. 2014;36(7):681-688.
- Kadotani Y, Okamoto M, Akioka K, Ushigome H, Ogino S, Nobori S, et. al. The management and the outcome of living kidney grafts with multiple arteries. *Surg Today*. 2005; 35: 459-66.
- Natsis K, Paraskevas G, Panagouli E, et al. A morphometric study of multiple renal arteries in Greek population and a systematic review. *Rom J Morphol*

- Embryol. 2014;55(3 Suppl):1111-1122.
- 28.Benedetti E, Troppmann C, Gillingham K, Sutherland DE, Payne WD, Dunn DL, et. al. The short- and longterm outcomes of kidney transplants with multiple renal arteries. *Ann Surg.* 1995; 221: 406-14.
- 29.Feller I, Woodburne RT. Surgical anatomy of the abdominal aorta. *Ann Surg* 1961; 154: 239-52.
- 30.Wadhwa, A. & Soni, S.. (2012). An accessory renal artery from a tortuous abdominal aorta: A case report. *Journal of Clinical and Diagnostic Research.* 6. 1292-1293.
- 31.Demir, M., Yesildal, C., Yavuzsan, A. H., Kirecci, S. L., Dokucu, A. I.. First, live donor nephrectomy with abdominal tortuous aorta and two renal arteries: A renal transplantation case report. *Urology case reports*, 2019; 29: 101097.
- 32.Malgor, R. D., Oderich, G. S., Vrtiska, T. J., Kalra, M., Duncan, A. A., Gloviczki, P. et. al. A case-control study of intentional occlusion of accessory renal arteries during endovascular aortic aneurysm repair. *Journal of vascular surgery*, 2013; 58(6): 1467-1475.
- 33.Greenberg JI, Dorsey C, Dalman RL, Lee JT, Harris E, Hernandez-Boussard T, et al. Long-term results after accessory renal artery coverage during endovascular aortic aneurysm repair. *J Vasc Surg* 2012;56:291-7.