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From The Editor In Chief

There are two important news about Turkish Geriatrics Society

1. TURKISH GERIATRICS SOCIETY IS AWARDED

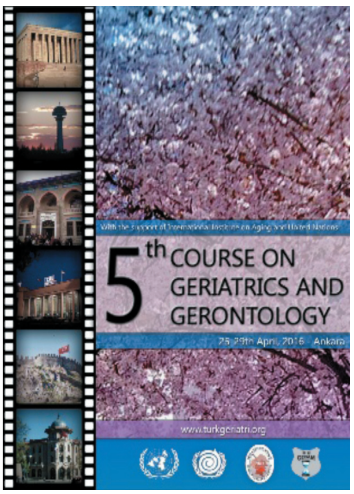
Third Public Health Awards were given with a spectacular ceremonyby Public Health Association of Turkey and Okan University in 15th Dec, 2015 in Okan University Convention Hall in Istanbul. Turkish Geriatrics Society was awarded for its outstanding efforts on prevention of elderly health and public education programmes about healthy aging.





2. FIFTH COURSE ON GERIATRICS AND GERONTOLOGY IS GOING TO BE PERFORMED

Fifth Course on Geriatrics and Gerontology will be held during the 25 th-29 th of April, 2016 in Ankara. All aspects of geriatrics and gerontology will be presented and discussed during this interactive course which will be organized in collaboration with Turkish Geriatrics Society-TGS, the International Institute on Ageing-INIA, United Nations Malta and Hacettepe University Research Center of Geriatric Sciences-GEBAM.



Prof. Yesim GOKCE KUTSAL

Editor in Chief

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INSTRUCTIONS FOR AUTHORS

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Turkish Journal of Geriatrics is on official publication of **Turkish Geriatrics Society** and is published four times a year. Official languages of the journal are Turkish and English. Turkish Journal of Geriatrics invites submission of Original Articles based on clinical and laboratory studies, Review Articles including up to date published material, Original Case Reports, Letters to the Editor and News and Announcements of congress and meetings concerning all aspects of Geriatrics, Aging and Gerontology and related fields.

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2003
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CONTENTS

2016;19(1)

RESEARCHES

- **Continual Assessment of Mortality Risk Factors in Geriatric Patients Hospitalized in Intensive Care Due to Pneumonia** **1-8**
  Nesrin ÖCAL, Deniz DOĞAN, Gürhan TAŞKIN, Birol YILDIZ, Serhat ÖZER, Levent YAMANEL

- **Neuropathic Pain In Elderly: A Multicenter Study** **9-18**
  Yeşim GÖKÇE KUTSAL, Sibel EYİGÖR, Asuman DOĞAN, Sasan ZARDOUST, Bekir DURMUŞ, Deniz EVCİK, Rezzan GÜNAYDIN, Nilay ŞAHİN. Ali AYDENİZ, Pınar ÖZTOP, Kutay O. GÖKKAYA, Sami HİZMETLİ, Pınar BORMAN, Nurdan PAKER, Gülseren DEMİR, Gülseren KAYALAR, Ezgi AYDIN, Özden ÖZYEMİŞCİ

- **Aetiology of Emergency Department Admission of the Elderly: A Retrospective Study in Kars** **19-26**
  Gülşen ÇIĞŞAR, Yeliz AKKUŞ, Günal ELNARE, Esma ERDEMİR ÖZTÜRK, Melek Beyza PALAS

- **Efficacy and Tolerability of Chemotherapy in Elderly Patients with Metastatic Gastric Cancer** **27-34**
  Mehmet TÜRKELİ, Mehmet Naci ALDEMİR, Melih ŞİMSEK, Nilgün YILDIRIM, Mehmet BİLİCİ, Kerim ÇAYIR, Salim Başol TEKİN, HarunYETİMOĞLU

- **Hematologic Parameters in Geriatric Patients with Idiopathic Sudden Sensorineural Hearing Loss** **35-41**
  Hande EZERARSLAN, Mert BAŞARAN

- **Treatment of Intertrochanteric Fractures in Ambulatory Elderly; Bipolar Hemiarthroplasty Or Proximal Femoral Nail ?** **42-49**
  Erbil AYDIN, Burhan KURTULUŞ, Bülent ÇELİK, Mehmet OKAN

www.turkgeriatri.org

CONTENTS

2016;19(1)

CASE REPORT

- **Mycosis Fungoides and Mantle Cell Lymphoma: A Case Report** **50-53**
  Ayşe ÖKTEM, İrem GENÇ, Ferda ARTÜZ, Funda CERAN, Devrim Tuba ÜNAL, Ayşe Yılmaz ÇİFTÇİ
- **Facial Burn Assault of A Geriatric Woman: A Case Report** **54-57**
  Hakan Ahmet ACAR, Yücel YÜCE, Kutlu Hakan ERKAL
- **Spinal Dural Arteriovenous Fistula: A Rare Cause of Progressive Paraparesis** **58-62**
  Ece GÜVENDİ, Ayhan AŞKIN, İdil AYSİN, Neşe SARIKAYA, Hikmet KOÇYİĞİT, Volkan ÇAKIR, Fazıl GELAL

LETTER TO THE EDITOR

- **Radiation Induced Diffuse Cutaneous Basal Cell Carcinoma (BCC) in A Retired Radiology Technician** **63-66**
  Ceyhun CESUR, Fikret EREN, Cenk MELİKOĞLU, İsmail YILMAZ, Ercan KARABACAK

www.turkgeriatri.org

Turkish Journal of Geriatrics
2016;19(1):1-8

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RESEARCH

CONTINUAL ASSESSMENT OF MORTALITY RISK FACTORS IN GERIATRIC PATIENTS HOSPITALIZED IN INTENSIVE CARE DUE TO PNEUMONIA

ABSTRACT

Introduction: The number of geriatric patients is quickly increasing. The present study has been performed to investigate the potential roles of laboratory test results on prognosis and mortality in elderly patients hospitalized in intensive care unit due to pneumonia.

Materials and Method: Prospectively collected data of patients hospitalized in intensive care due to pneumonia were retrospectively analyzed.

Results: Age and length of stay in intensive care were common mortality risk factors for geriatric and non-geriatric patients hospitalized in intensive care due to pneumonia. Moreover, anemia, hypoglycemia, hypoalbuminemia and increased levels of serum lactate dehydogenase were also in association with mortality in all patients ($p<0.001$). 'Average' values, calculated based on prospective data obtained from equal intervals of intensive care stay time, had stronger associations with mortality than the first and last test results. The association of length of stay in intensive care with mortality was more significant in geriatric patients rather than in non-geriatric adults. Additionally, correlations were stronger in geriatric patients with larger correlation ratios.

Conclusion: Age, prolonged length of stay in intensive care, anemia, hypoglycemia, hypoalbuminemia and increased levels of LDH were mortality risk factors in geriatric patients hospitalized in intensive care due to pneumonia. 'Average' value was found to be more accurate for predicting mortality risk in geriatric patients whose mean length of stay in intensive care unit is longer than non-geriatrics.

Key Words: Geriatric; Aged; Pneumonia; Critical Care; Mortality.

ARAŞTIRMA

PNÖMONİ TANISI İLE YOĞUN BAKIMDA YATAN GERİATRİK HASTALARDA MORTALİTE RİSK FAKTÖRLERİNİN SÜREĞEN DEĞERLENDİRİLMESİ

ÖZ

Giriş: Geriatrik hastaların sayısı hızla artmaktadır. Bu araştırma pnömoni tanısıyla yoğun bakım ünitesine yatırılan yaşlı hastalarda laboratuvar test sonuçlarının prognoz ve mortalite üzerine olası rollerini araştırmak için yapılmıştır.

Gereç ve Yöntem: Pnömoni nedeniyle yoğun bakımda yatan hastaların prospektif olarak toplanan verileri retrospektif olarak analiz edildi.

Bulgular: Yaş ve yoğun bakımda kalış süresi pnömoni nedeniyle yoğun bakımda yatan geriatrik ve geriatrik olmayan hastalar için ortak mortalite risk faktörü olarak saptandı. Anemi, hipoglisemi, hipoalbuminemi ve LDH artışı mortaliteyle ilişki laboratuar değerleri olarak izlendi ($p<0,001$) Yoğun bakım kalış süresi boyunca eşit aralıklarla alınan prospektif verilere dayalı hesaplanan 'ortalama' değerler, ilk ve son test sonuçlarına göre mortaliteyle daha güçlü bir ilişki göstermekteydi. Yoğun bakımda yatış süresi ile mortalite ile arasındaki ilişki geriatrik hastalarda geriatrik olmayan erişkinlere göre daha belirgindi. Ayrıca, korelasyonlar büyük korelasyon oranları ile birlikte geriatrik hastalarda daha güçlüydü.

Sonuç: Yaş, uzamış yoğun bakım yatışı, anemi, hipoglisemi, hipoalbüminemi ve LDH düzeylerinde artış pnömoni nedeniyle yoğun bakımda yatan geriatrik hastalarda mortalite risk faktörleri olarak izlenmiştir. 'Ortalama' değer, yoğun bakım kalış süreleri geriatrik olmayan hastalara göre daha uzun olan geriatrik hastalarda mortalite değerlendirilmesi için daha güvenilir bir değerlendirme olarak izlendi.

Anahtar Sözcükler: Geriatrik; Yaşlı; Pnömoni; Yoğun bakım; Mortalite.

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Introduction

Average life expectancy is steadily increasing, leading to an increase in the geriatric patient population. As in many clinical areas, elderly patients constitute an important proportion of respiratory intensive care patients, attracting attention as a population of particular risk, prone to developing multiple serious comorbidities (1). Treatment, clinical follow-up and prognosis of elderly patients differ from the general population in many ways. In this regard they may require a specialized clinical approach.

Geriatric patients represent a significant segment of patients admitted to intensive care unit (ICU) in terms of prolonged hospital stay and increased mortality rates. Among dependent geriatric patients with morbidities such as Alzheimer, dementia, or neurological disorders, pneumonia, especially aspiration pneumonia, is one of the most common disorders resulting in admission to respiratory ICU (2). Swallowing disorders, weakened cough reflex, and confusion may commonly cause aspiration of food into the airways in the elderly (3). Considering the fact that aging patients are prone to developing multiple systemic comorbidities, their response to treatment and intervention is also more sophisticated than in other patients. For instance, thoracic radiological findings may emerge later and the recovery may be delayed, fluid replacement should be planned in accordance with cardiac and renal reserves and biochemical imbalances may be observed due to poor nutrition, which is a common condition in geriatric patients (2, 3). On the other hand, scoring systems developed to assess the severity of pneumonia such as pneumonia severity index (PSI) and CURB-65, only give an idea in terms of hospitalization or admission to ICU, but are not useful for clinical follow up of these patients in ICU. Nevertheless, the Acute Physiology and Chronic Health Evaluation (APACHE) II scoring system developed for intensive care is based on the first day clinical status of the patient; therefore, it can be said that its predictive value decreases in patients with prolonged ICU stay (4, 5).

The difficulty of serial clinical monitoring in elderly patients and their fragility due to clinical variables reflect the main reasons for the frequent sudden worsening and deaths. In this regard, routine laboratory assays may have an important role in the serial clinical follow-up of internal balance of the geriatric patients in ICU (6). Meanwhile, there are limited data on the predictive role of laboratory assays on the length of stay in ICU and mortality rates in geriatric patients with pneumonia in comparison with non-geriatric adult patients. We performed the present study to investigate the potential role of laboratory test results in terms of predicting prognosis and mortality in elderly patients hospitalized in ICU with pneumonia and to compare the results with non-geriatric adults.

Materials and Method

The present study is a retrospective analysis of prospectively collected data of patients with pneumonia hospitalized in ICU between September 1, 2014 and September 1, 2015. Data on age, gender, diagnosis, radiological findings, comorbidities, length of ICU stay, survival times, status of the patient at hospital discharge and laboratory assays were retrieved. Variables were assessed in the groups of patients stratified by age (non-geriatric adult patients,<65 years; geriatric patients,≥65 years [young–elderly,65–74 years;middle–elderly,75–84 years; oldest–elderly,≥85 years]). Patients who died in ICU were defined as "death group" and the patients who were discharged from ICU were defined as "survival group". Laboratory assays included complete blood count and routine biochemistry results. White blood cell (WBC), hemoglobin (Hgb), platelet (Plt) and absolute eosinophil (#eosinophil) counts were evaluated along with serum lactate dehydrogenase (LDH), serum albumin, and serum glucose levels. Laboratory test results were analyzed in serial intervals divided into certain periods according to length of ICU stay. For patients who were inpatients for less than 5 days, laboratory results were recorded for each day, and the 'average' value was calculated. For patients who were inpatients for at least 5 days, ICU stay time was divided into four equal intervals from the first day to the last day. Laboratory results for each interval were recorded, and the 'average' value was determined. For example, for a patient hospitalized for 20 days, the test results of the 0^{th}, 5^{th}, 10^{th}, 15^{th}, and 20^{th} days were determined, and eventually the 'average' value was calculated. Thus, the 'average' value, representing the changes in laboratory test results of the patients for the entire ICU stay, was obtained for each parameter.

Relationships between investigated parameters were evaluated statistically. SPSS software (SPSS Inc, Chicago, IL) was used for statistical evaluation. Frequencies and percentages for discrete data, and means ± standard deviations for continuous variables were used for descriptive statistics. The Mann–Whitney U test was used for comparing differences between groups. Probability (p) values less than 0.05 were considered statistically significant.



RESULTS

Data of 186 patients (82 females, 104 males) were recorded and assessed. The mean age of the patients was 63.7±20.5 (20-89) years. While 72 (39%) of the patients were non-geriatric adult patients (ages between 18 and 65 years), 114 patients (61%) were geriatric cases (age ≥ 65). A total of 37 of the geriatric patients (32.45%) were young-elderly, 55 (48.24%) were middle-elderly, and 22 (19.29%) were oldest-elderly cases. The overall mortality rate was 41.9%, being 38.8% in non-geriatric adults and 43.8% in geriatric cases (43.2% in early-elderly cases, 38.1% in middle-elderly cases, and 59.1% in oldest-elderly cases). The mortality rate was higher in geriatric patients and significantly higher in oldest-elderly patients. While overall mean ICU stay time was 23.15±22.20 (2-93) days, 19.61±19.47 days in non-geriatric adults, and 25.38±23.58 days in geriatric patients (21.32±18.32 days in early-elderly cases, 26.43±25.62 days in middle-elderly cases, and 30.88±26.83 days in oldest-elderly cases). The mean values of all detected parameters for all groups are summarized in Table 1. There was no significant difference between groups except for the mean 'average' Plt value, which was significantly higher in middle-elderly and oldest-elderly cases (Table 1).

When we compared the data of survival group with death group in all patient groups and sub-groups, we observed significant differences that are accounted for in the following.

All Cases

While the mean age of the survival groups was 59.42±20.98, the mean age was 68.07±17.04 in the death group. The mean length of stay in ICU was 16.23±14.75 days in survival group and 32.29±26.86 days in death group (p<0.001). The mean age and the mean length of stay in ICU were significantly higher in death group (p=0.01). Among the mean laboratory test results for the first day; values for WBC, Hgb, #eosinophil, serum glucose and albumin were significantly low, and the mean serum LDH level was significantly higher in death group (p=0.028, p<0.001, p=0.002, p<0.001, p<0.001, and p=0.009 respectively). Among the mean labo-

Table 1— Mean 'Average' Values ± Standard Deviations of All Parameters for All Patient Groups.

	All Patients			Geriatric Patients			
	Geriatric Patients	Non-geriatric Patients	p	Early-elderly	Middle-elderly	Oldest-elderly	p
Mortality rate	43.8%	38.8%	NS	43.2%	38.1%	59.1%	NS
Days	25.38 ± 23.58	19.61 ± 19.47	NS	21.32 ± 18.32	26.43 ± 25.62	30.88 ± 26.83	NS
WBC (x 103/μL)	10072.31 ± 2933.41	9940.83 ± 2623.15	NS	10399.46 ± 3143.23	9799.81 ± 2651.00	10208.51 ± 3633.27	NS
Hgb (g/dL)	11.34 ± 1.72	11.64 ± 1.66	NS	11.43 ± 1.61	11.35 ± 1.89	11.12 ± 1.62	NS
Plt (x 103/μL)	309826.61 ± 79883.89	287668.05 ± 63623.54	NS	290813.51 ± 93604.91	319638.18 ± 74620.13	321574.07 ± 64243.77	0.01
#eos. (x 103/μL)	142.07 ± 77.79	150.11 ± 57.84	NS	151.83 ± 72.58	136.79 ± 82.210	133.66 ± 69.55	NS
Glucose (mg/dL)	145.39 ± 36.24	144.69 ± 39.09	NS	143.51 ± 43.93	149.55 ± 34.73	143.90 ± 29.84	NS
Albumin (g/L)	2.57 ± 0.43	2.57 ± 0.39	NS	2.62 ± 0.52	2.62 ± 0.41	2.57 ± 0.39	NS
LDH (U/L)	339.12 ± 176.03	346.84 ± 171.53	NS	325.85 ± 155.48	321.06 ± 176.26	141.84 ± 319.56	NS

Days: number of days of ICU stay, WBC: white blood cell, Hgb: hemoglobin, Plt: platelet, #eos. : #eosinophil count, LDH: lactate dehydrogenase, NS: non-significant.

Table 2— Comparison of the Mean Values ± Standard Deviations of Ages, Length of Stay in ICU and Mean Values ± Standard Deviations of First, Last and 'Average' Results of Detected Parameters Between Survival and Death Groups in All Patients.

		Survival Group	Death Group	p
Age		59.42 ± 20.98	68.07 ± 17.04	0.008
Days		16.23 ±14.75	32.29 ± 26.86	<0.001
First day results	WBC (x 10^3/μL)	12178.70 ± 4799.35	10132.05 ± 4318.50	0.028
	Hgb (g/dL)	12.39 ± 1.84	10.94 ± 1.45	<0.001
	Plt (x 10^3/μL)	242287.03 ± 55552.62	233076 ± 72300.55	NS
	#eos. (x 10^3/μL)	132.22 ± 59.42	109.87 ± 66	0.002
	Glucose (mg/dL)	243.07 ± 66.75	109.55 ± 22.74	<0.001
	Albumin (g/L)	2.83 ± 0.57	2.44 ± 0.3	<0.001
	LDH (U/L)	304.50 ± 139.1	417.51 ± 231.76	0.009
Last day results	WBC (x 10^3/μL)	7718.51 ± 2730.38	9725.64 ± 7902.74	NS
	Hgb (g/dL)	12.59 ± 2.03	9.87 ± 1.31	<0.001
	Plt (x 10^3/μL)	305879.62 ±80804.21	309269.23 ± 91074.77	NS
	#eos. (x 10^3/μL)	163.61 ± 112.56	182.05 ± 161.11	NS
	Glucose (mg/dL)	131.53 ± 57.58	117.69 ± 37.14	NS
	Albumin (g/L)	2.73 ± 0.44	2.52 ± 0.29	<0.001
	LDH (U/L)	359.77 ± 155.02	502.18 ± 375.91	NS
'Average' results	WBC (x 10^3/μL)	10236.32 ± 3016.23	9723.84 ± 2487.14	NS
	Hgb (g/dL)	12.43 ± 1.44	10.11 ± 0.94	<0.001
	Plt (x 10^3/μL)	301195.67 ± 65131.59	301323.07 ± 86510.00	NS
	#eos. (x 10^3/μL)	149.87 ± 67.38	143.17 ± 72.45	NS
	Glucose (mg/dL)	165.21 ± 40.36	123.00 ± 18.23	<0.001
	Albumin (g/L)	2.80 ± 0.42	2.32 ± 0.19	<0.001
	LDH (U/L)	272.08 ± 86.10	411.33 ± 210.19	0.001

Days: number of days of ICU stay, WBC: white blood cell, Hgb: hemoglobin, Plt: platelet, #eos. : #eosinophil count, LDH: lactate dehydrogenase, NS: non-significant.

ratory test results pertaining to the last day of the ICU stay; the mean Hgb and serum albumin levels were significantly lower in death group (p<0.001 for both). Among the means of 'average' values of detected parameters; the mean 'average' Hgb, serum glucose and albumin levels were significantly lower and the mean 'average' LDH level was significantly higher in the death group (p<0.001, p<0.001, p<0.001 and p=0.001 respectively) (Table 2).

Non-geriatric Adults

The mean length of stay in ICU was significantly higher in the death group (p=0.002). The mean 'average' values of Hgb, serum glucose and albumin were significantly lower in the death group (p<0.001 for all of the three parameters) (Table 3).

Geriatric Patients

The mean length of stay in ICU was significantly higher in death group (p<0.001). The mean 'average' values of Hgb, serum glucose and albumin were significantly lower in the death group (p<0.001 for all of these three parameters) (Table 3). Length of stay in ICU was found to be a more significant risk factor of mortality in geriatric patients than in non-geriatric adults.

Young-elderly Patients

The mean length of stay in ICU was significantly higher in the death group (p=0.006). The mean 'average' values of Hgb, serum glucose and albumin were significantly lower in the death group (p<0.001, p<0.001 and p=0.001) (Table 4).

Middle-elderly Patients

The mean length of stay in ICU was significantly higher in the death group (p=0.003). The mean 'average' values of Hgb, serum glucose and albumin were significantly lower in the death group (p<0.001, p=0.001, p<0.001) (Table 4).

Oldest-elderly Patients

The mean 'average' values of Hgb, serum glucose and albumin were significantly lower in the death group (p=0.002,



Table 3— Comparison of the Mean 'Average' Values ± Standard Deviations Between Survival and Death Groups in Geriatric and Non-geriatric Groups.

	Geriatric Patients			Non-Geriatric Patients		
	Survival Group	Death Group	p	Survival Group	Death Group	p
Days	17.42 ± 15.35	35.58 ± 28.11	<0.001	14.50 ± 13.83	27.64 ± 24.23	0.002
WBC (x 10^3/µL)	10423.30 ± 3012.95	9622.40 ± 2793.64	NS	9963.63 ± 3034.78	9905.00 ± 1850.55	NS
Hgb (g/dL)	12.37 ± 1.43	10.01 ± 0.98	<0.001	12.51 ± 1.46	10.28 ± 0.83	<0.001
Plt (x 10^3/µL)	307791.14 ± 75505.56	312432.00 ± 85872.35	NS	291602.27 ±45213.98	281485.71 ± 85580.48	NS
#eos.(x 10^3/µL)	148.49 ± 78.08	133.87 ± 77.41	NS	143.95 ± 55.98	159.78 ± 60.40	NS
Glucose (mg/dL)	161.85 ± 38.22	124.32 ± 18.54	<0.001	159.99 ± 41.34	120.64 ± 17.74	<0.001
Albumin (g/L)	2.76 ± 0.47	2.34 ± 0.21	<0.001	2.74 ± 0.40	2.29 ± 0.16	<0.001
LDH (U/L)	302.00 ± 138.42	386.64 ± 206.69	NS	310.27 ± 129.72	404.30 ± 212.06	NS

Days: number of days of ICU stay, WBC: white blood cell, Hgb: hemoglobin, Plt: platelet, #eos. : #eosinophil count, LDH: lactate dehydrogenase, NS: non-significant.

Table 4— Comparison of the Mean 'Average' Values ± Standard Deviations Between Survival and Death Groups in Sub-groups of Geriatric Patients.

	Early-Elderly			Middle-Elderly			Oldest-Elderly		
	Survival Group	Death Group	p	Survival Group	Death Group	p	Survival Group	Death Group	p
Days	14.00 ± 7.63	30.93 ± 23.54	0.006	18.23 ± 16.79	39.71 ± 31.74	0.003	18.57 ± 19.32	38.72 ± 28.74	NS
WBC (x 10^3/µL)	10534.28 ± 3172.77	10222.50 ±3198.58	NS	9978.52 ± 2601.71	9510.47 ±2768.42	NS	12116.19 ±4429.47	8994.54 ±2549.58	NS
Hgb (g/dL)	12.42 ± 1.23	10.12 ± 1.01	<0.001	12.33 ± 1.60	9.75 ± 1.04	<0.001	12.52 ± 1.54	10.22 ± 0.88	0.002
Plt (x 10^3/µL)	295900 ±80113.64	284137.50 ±111297.60	NS	315008.82 ±75232.59	327133.3 ±74831.2	NS	311904.76 ±70878.6	327727.2 ±62409.7	NS
#eos. (x 10^3/µL)	162.09 ± 77.82	138.37 ± 65.02	NS	133.82 ± 75.56	141.59 ± 93.73	NS	165.42 ± 69.96	113.45 ± 64.27	NS
Glucose (mg/dL)	166.28 ± 44.43	113.62 ± 17.92	<0.001	162.06 ± 36.96	129.3 ± 17.5	0.001	166.28 ± 33.85	129.65 ± 15.89	0.46
Albumin (g/L)	2.87 ± 0.54	2.30 ± 0.22	0.001	2.78 ± 0.44	2.35 ± 0.17	<0.001	2.85 ± 0.40	2.39 ± 0.27	0.008
LDH (U/L)	292.77 ± 114.48	369.26 ± 192.35	NS	272.58 ± 101.23	399.56 ±237.72	NS	330.46 ± 92.29	312.63 ± 170.16	NS

Days: number of days of ICU stay, WBC: white blood cell, Hgb: hemoglobin, Plt: platelet, #eos. : #eosinophil count, LDH: lactate dehydrogenase, NS: non-significant.

p=0.046 and p=0.008). On the other hand, the mean length of stay in ICU was higher in the death group, but this difference was not statistically significant (p=0.07) (Table 4).

The p values and correlation ratios for correlations between age, length of stay in ICU and 'average' values of detected parameters are given in Table 5. Statistically significant positive correlations were observed between age and Plt, Hgb and serum glucose, Hgb and serum albumin, serum glucose and serum albumin, serum glucose and serum LDH, whereas statistically significant negative correlations were observed between Hgb and length of stay in ICU in both geriatric and non-geriatric patients. Additional correlations were observed in geriatric patients; as follows: Statistically significant positive correlations were observed between WBC and #eosinophil count, WBC and serum LDH, #eosinophil count and serum albumin, whereas a statistically significant negative correlation was observed between serum albumin and length of stay in ICU (Table 5).

Hence, we identified that age and length of stay in ICU were common mortality risk factors for all cases hospitalized in ICU due to pneumonia. Anemia, hypoglycemia, hypoalbuminemia and increased levels of LDH were laboratory risk factors of mortality in all groups. The association between the length of stay in ICU with mortality was more significant in geriatric patients than in non-geriatric adults. Additionally, the correlations were stronger in geriatric patients with larger correlation ratios.

Table 5— The p Values and Correlation Ratios for Correlations Between Age, Length of Stay in ICU and 'Average' Values of Detected Parameters in All Groups and Sub-groups

		Correlation	r	p	Correlation	r	p
All patients		age ~ days	0.157	<0.05	Hgb ~ days	-0.428	<0.01
		age ~ Plt	0.198	<0.01	#eos. ~ albumin	0.207	<0.01
		WBC ~ #eos.	0.363	<0.01	glucose ~ albumin	0.503	<0.01
		WBC ~ LDH	0.168	<0.05	glucose ~ LDH	0.271	<0.01
		WBC ~ days	0.143	<0.05	albumin ~ LDH	-0.143	<0.05
		Hgb ~ glucose	0.461	<0.01	albumin ~ days	-0.219	<0.01
		Hgb ~ albumin	0.500	<0.01			
Non-geriatrics		age ~ Plt	0.936	<0.01	Hgb ~ days	-0.429	<0.01
		WBC ~ days	0.266	<0.01	glucose ~ albumin	0.485	<0.01
		Hgb ~ glucose	0.487	<0.01	glucose ~ LDH	0.228	<0.05
		Hgb ~ albumin	0.543	<0.01			
Geriatrics		age ~ Plt	0.252	<0.01	Hgb ~ days	-0.424	<0.01
		WBC ~ #eos.	0.391	<0.01	#eos. ~ albumin	0.206	<0.05
		WBC ~ LDH	0.37	<0.05	glucose ~ albumin	0.509	<0.01
		Hgb ~ glucose	0.458	<0.01	glucose ~ LDH	0.321	<0.01
		Hgb ~ albumin	0.535	<0.01	albumin ~ days	-0.276	<0.01
Geriatric patients	early-elderly	age ~ Plt	-0.563	<0.01	Hgb ~ days	-0.538	<0.01
		WBC ~ #eos.	0.352	<0.05	glucose ~ albumin	0.379	<0.05
		Hgb ~ glucose	0.466	<0.01	glucose ~ LDH	0.338	<0.05
		Hgb ~ albumin	0.551	<0.01	albumin ~ days	-0.610	<0.01
	middle-elderly	age ~ Plt	0.598	<0.01	Hgb ~ days	-0.376	<0.01
		WBC ~ #eos.	0.454	<0.01	#eos. ~ LDH	-0.316	<0.01
		Hgb ~ glucose	0.501	<0.01	glucose ~ albumin	0.615	<0.01
		Hgb ~ albumin	0.534	<0.01	glucose ~ LDH	0.289	<0.05
	oldest-elderly	age ~ Plt	-0.555	<0.01	glucose ~ LDH	0.454	<0.01
		Hgb ~ #eos.	0.456	<0.01	albumin ~ LDH	0.538	<0.01
		Hgb ~ albumin	0.481	<0.01			

Days: number of days of ICU stay, WBC: white blood cell, Hgb: hemoglobin, Plt: platelet, #eos. : #eosinophil count, LDH: lactate dehydrogenase, r: correlation ratio.



Discussion

Average life expectancy is gradually increasing. According to estimates, by 2050 the number of the world population aged over 80 years will be doubled (7). While senility is a life period accompanied by a reduction in cardiopulmonary and renal reserves and severe comorbidities, the mean age of the patients hospitalized in ICU are increasing day by day as expected. Due to the frequency of progressive multiple organ failure, elderly patients constitute a particular group at risk in respiratory ICUs (5, 6). During the aging process, several respiratory deteriorations occur in the structure of the lung parenchyma, respiratory muscle functions, central regulation of breathing and natural defense mechanisms of the respiratory tract. All these deteriorations in the respiratory system of the geriatric population, result in pneumonia, especially aspiration pneumonia, being a frequent and severe clinical entity (6, 8). This is why pneumonia in the geriatric population represents a large proportion of the ICU patient population.

While PSI and CURB-65 represent the most common scoring systems in the assessment of the severity of pneumonia, they have not been considered ideal for predicting ICU admission and mortality rates. PSI and CURB-65 are useful for decisions to whether the patient must be treated in home or at hospital and to determine the need for ICU admission (9). PSI can estimate the severity of the diseases lower especially in the young cases without comorbidities other than respiratory failure. CURB-65, although easier, scores the severity lower in elderly patients with multiple comorbidities. The predictive values of both pneumonia severity scoring systems are low in terms of mortality in intensive care (10). On the other hand, the APACHE II scoring system is based on the clinical state of the patient on the first day of ICU admission; therefore, it can be said that its predictive value decreases in elderly patients with prolonged ICU stay, in whom clinical status and laboratory findings may rapidly alter. APACHE II scoring does also not include commonly used biomarkers such as serum albumin and serum LDH (11). While these known scoring systems only rely on daily evaluation of the clinical status, their predictive value may not be accurate for patients with prolonged ICU stay (10, 11). From this point, easier, quicker and continual assessment methods are still needed in risk assessment of geriatric patients with regard to prognosis and mortality. Serial laboratory findings may be suggested in this regard. In the present study, 'average' values which were determined based on serial laboratory test results, were found to be more reliable and useful especially in terms of serum LDH.

In the previous literature, some studies on risk factors affecting mortality in elderly patients are available. Low albumin levels and elevated creatinine levels were reported to be associated with mortality in geriatric in-patients (12-14). Ponzetto et al (13) studied risk factors affecting mortality in hospitalized patients aged ≥70 years. They observed that serum albumin levels of 3.0–3.4 g/dL, fibrinogen levels ≥452mg/dL and creatinine levels of 1.5–3mg/dL and >3mg/dL are independent risk factors of mortality in elderly patients. Sousa et al (14) investigated data from geriatric in-patients immediately upon hospital admission and reported that low serum albumin and WBC counts are correlated with mortality. In another study, WBC and lymphocyte counts, ESR, CRP, insulin-like growth factor, triiodothyronine, serum albumin, iron, total cholesterol and LDL cholesterol were found to be associated with mortality in elderly patients (15). Red blood cell distribution width (RDW) and serum vitamin B12 levels were also demonstrated to be associated with mortality in hospitalized elderly patients (16-18). Hypoglycemia is known to be a serious clinical state in intensive care, particularly so in geriatric patients. In the study by Kagansky et al (19) study, performed on geriatric patients, mortality rates were reported to be two times higher for hypoglycemic cases than for non-hypoglycemic cases. In the present study, anemia, hypoglycemia, hypoalbuminemia and altitude levels of serum LDH were laboratory risk factors of mortality in all patient groups hospitalized in ICU due to pneumonia. We also identified significantly positive correlations between age and Plt, Hgb and serum glucose, Hgb and serum albumin, serum glucose and serum albumin, serum glucose and serum LDH, and a significant negative correlation between Hgb and length of stay in ICU in both geriatric and non-geriatric patients.

In several previous studies, age and length of stay in ICU were also reported as mortality risk factors for ICU patients (20-22). We confirmed that age and length of stay in ICU were common mortality risk factors for all cases hospitalized in ICU due to pneumonia. The association between length of stay in ICU with mortality was more significant in geriatric patients than in non-geriatric adults according to our results. Mortality rate was higher in geriatric patients and significantly higher in the oldest-elderly patients. The mean ICU stay time was also longer in geriatric patients.

In this study, we performed a distinct evaluation of laboratory findings which gives us the opportunity of performing prolonged assessment of the results. We think that the 'average' values of the laboratory data, calculated based on the data obtained from equal intervals, may represent the overall alterations in test results obtained during the ICU stay time of

patients. Our results indicate that 'average' values had stronger associations with mortality than the first and last test results. Therefore, this assessment should be accepted more accurate for mortality assessment of geriatric patients whose ICU stay times are longer than for non-geriatrics.

As a conclusion; we report that age, prolonged length of stay in ICU, anemia, hypoglycemia, hypoalbuminemia and increased levels of LDH were risk factors for mortality in geriatric patients hospitalized in ICU due to pneumonia. Considering the fact that the number of the geriatric patients is steadily increasing, it is necessary to well define the prognostic markers and mortality risk factors for elderly patients. The retrospective design is a limitation of our study and prospective studies are required to improve these findings.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this article.

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RESEARCH

NEUROPATHIC PAIN IN ELDERLY: A MULTICENTER STUDY

ABSTRACT

Introduction: Aging brings with it an increase in the prevalence of pain. For effective pain treatment, it is important to determine pain prevalence, its nature, and the factors affecting it. However, epidemiologic information on neuropathic pain in the elderly is inadequate. In our cross-sectional multicenter study, we aimed to determining the prevalence of neuropathic pain in elderly patients and the relationship of neuropathic pain with socio-demographic and clinical factors.

Materials and Method: Thirteen centers in different regions of Turkey. The study included 1163 individuals over age 65. Physicians conducted face-to-face interviews to obtain clinical and socio-demographic data and The Douleur Neuropathic 4 (DN4) and The Self-completed Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scales were used to assess neuropathic pain. Patients who scored ≥4 or ≥12 on the DN4 and S-LANSS scales, respectively, were determined to be experiencing neuropathic pain.

Results: Neuropathic pain was found in 52.5% of the patients (n=610) in this study. Approximately 67.5% of the patients with neuropathic pain were in the 65-74 age group, and 72.1% (n=440) were females. Of the patients who were experiencing neuropathic pain, 48.4% were graduates of primary school, 91.6% engaged in very little or no physical activity, and 56.7% were taking four or more medications.

Conclusions: Neuropathic pain prevalence was 52.5% in the elderly over age 65 who had presented with pain complaints. Neuropathic pain was more frequently seen in women, patients with comorbidities, those with poor levels of ambulation, those using walking aids, and those using multiple drugs. Interrogating the elderly for neuropathic pain seems important for effective treatment.

Key Words: Aged; Chronic Pain; Neuralgia.

ARAŞTIRMA

YAŞLILARDA NÖROPATİK AĞRI: ÇOK MERKEZLİ ÇALIŞMA

ÖZ

Giriş: Yaşlanma ile birlikte ağrı sıklığında artış olmaktadır. Etkin ağrı tedavisi için ağrı sıklığı ve etkileyen faktörleri belirlemek önemlidir. Ancak yaşlılarda nöropatik ağrının epidemiyolojik verisi ile ilgili bilgiler yetersizdir. Çalışmamızda amaç; yaşlı hastalarda nöropatik ağrı sıklığı, nöropatik ağrının sosyodemografik ve klinik özellikler ile ilişkisini belirlemektir.

Gereç ve Yöntem: Çalışmaya Türkiye'nin farklı bölgelerinden, 13 merkez fizik tedavi ve rehabilitasyon polikliniklerine ağrı şikayeti ile başvuran 65 yaş üstü 1163 hasta alındı. Klinik ve sosyodemografik veriler yüzyüze sorgulama yöntemi ile elde edildi. Hastalarda nöropatik ağrıyı değerlendirmek için DN 4 ve S-LANSS ağrı ölçeği kullanıldı. DN4 ≥4 veya S-LANSS ağrı ölçeği ≥12 üzerinde olanlarda nöropatik ağrı olduğu kabul edildi.

Bulgular: Çalışmaya dahil edilenlerin %52,5'inde (n=610) nöropatik ağrı saptandı. Hastaların %67,5'si 65-74 yaş aralığında ve %72,1'i (n=440) kadındı. Nöropatik ağrısı olanların; %48,4'ü ilköğretim mezunu, %91,6'sının fiziksel aktivitesi hiç yok ya da çok düşüktü, %56,7'si 4 ve üzeri ilaç kullanıyor olarak bulundu.

Sonuç: Ağrı şikayeti olan 65 yaş üzeri yaşlılarda nöropatik ağrı sıklığı %52,5 olarak saptandı. Kadınlarda, komorbiditesi olanlarda ,ambulasyon düzeyi kötü olanlarda, yürümede yardımcı cihaz kullananlarda ve çoklu ilaç kullananlarda nöropatik ağrı daha sık görülmekte olup yaşlıların nöropatik ağrı açısından sorgulanması etkin tedavi açısından önem taşımaktadır.

Anahtar Sözcükler: Yaşlı; Kronik ağrı; Nöropatik ağrı

INTRODUCTION

The prevalence of pain increases with aging (1,2). Chronic pain can be nociceptive, neuropathic, or mixed (3). The increased prevalence of pain in the elderly may be associated with age related factors, physiological changes and disorders in bones and muscles or comorbid diseases and conditions, such as diabetes, cancer, stroke, and surgery (4,5). These conditions, which cause neuropathic pain (NP), are more common in older people (6). NP in the older population is important because it restricts functional activities, decreases activities of daily living, and can eventually lead to disability (7-9). Ability to cope with pain in elderly patients requires identifying the types and causes of pain and its prevalence. NP prevalence is 0.9%–17.9% in the general population and 8%–9% in the elderly (3,4,10). Large studies of people with chronic pain from any cause found the prevalence of NP to be 8.2% among UK family practice patients and 6.9% in a national population-based cohort in France (4,5). Bouhassira et al. reported NP characteristics in 21.7% of their large sample who had chronic pain (5). However, data on actual NP prevalence remain inadequate and variable, respectively, owing to lack of agreement on standard, valid criteria for assessing NP (6). Additionally, data on the prevalence of NP in older populations, which tend to have cognitive and communication problems, are also limited and show variations. It is for this reason, we believe that NP prevalence is underestimated and that higher rates of prevalence exist among the elderly.

Here we aimed to determine NP prevalence in elderly patients and its relationship with socio-demographic and clinical factors.

MATERIALS AND METHOD

Study Population

The present study was designed as a cross-sectional, multicenter study. Included were patients who had presented with pain complaints to Physical Medicine and Rehabilitation outpatient clinics at 13 centers in 8 cities located in various regions of Turkey. Subjects were patients ≥65 years of age who had applied to the outpatient clinics of the study centers and provided participation consent. Inclusion criteria included having had pain for at least 3 months and severity of pain denoted as ≥4 on the visual analogue scale (VAS). Exclusion criteria included having had no pain in the last week and severe depression, delirium, dementia, or cognitive dysfunction. The study was organized by the Turkish Society of Physical Medicine and Rehabilitation, Geriatric Rehabilitation Research Group. Local ethics committees were informed that ethics committee approval had been obtained from a single site in the name of all 13 centers in this multicenter study. All patients who voluntarily chose to participate in the study signed informed consent forms. All procedures were conducted in compliance with good clinical practices.

Outcomes

Physicians conducted face-to-face interviews to obtain clinical and socio-demographic data. Demographic data and socioeconomic information based on occupation, education level, annual income, geographical and domestic living space, and marital status were recorded. Medical histories, including comorbid diseases, polypharmacy, and smoking habits were reviewed. Fatigue, sleep disorder, and falling history during the last year were specifically noted and recorded. Questions were asked to obtain patient activity levels and ambulation needs. Activity levels were grouped as sedentary, walking for fun, regular exercise (3 h/week), and athletic (>4 h/week). The Holden Functional Ambulation Scale was used to evaluate independency of patients for ambulation. Patients were categorized on the basis of basic motor skills necessary for functional ambulation without assessing the factor of endurance. Categorization begins with "category 1" where a "nonfunctional ambulatory patient" requires more than one person for supervision or for physical assistance and goes up to "category 6"where an "ambulatory patient" is able to ambulate independently on non-level and level surfaces, stairs, and inclines (11). The health perceptions of the elderly was assessed as very poor, poor, moderate, well, and very well.

Neuropathic Pain

Intensity of pain was assessed with the visual analog scale. The severity of initial pain was estimated using a 10-point VAS, which rates severity of pain from 0 (no pain) to 10 (worst pain you can imagine). For VAS assessment, a 10-cm long horizontal scale was used. Patients were asked to mark their severity of pain at a point along this line where they considered appropriate and these values were recorded in the questionnaire.

The Douleur Neuropathic 4 (DN4) Test and S-LANSS pain scales were used to assess NP. Patients who scored ≥4 on the DN4 scale or ≥12 on the S-LANSS scale were determined to be experiencing NP.

The DN4 Test, which was developed to assess NP, consists of a total of 10 binary response items grouped into four sections. Section one consists of three items related to the type



of pain (burning, painful cold, and electric shock); Section 2 consists of four items related to the association of pain with abnormal sensations (*i.e.,* tingling, pins-and-needles sensation, numbness, and itching). Sections 3 and 4 (three items each) are related to clinical signs in the painful area (*i.e.,* touch hypoesthesia, pinprick hypoesthesia, tactile allodynia, or brushing). For each positive (yes) item, the score is 1. The total score is calculated as the sum of the 10 items, and the cut-off value for the diagnosis of NP is a total score of ≥4 out of 10 (12,13).

The Self-completed Leeds Assessment of Neuropathic Symptoms and Signs pain scale (S-LANSS) has been validated to identify pain of predominantly neuropathic origin in patients with chronic pain of any cause (14,15). The S-LANSS was selected over other NP questionnaires because it has been validated in people with mixed neuropathic and nociceptive pain, it does not have a physical exam component, and it is the most widely used measure (14). The S-LANSS consists of 7 items, termed dysesthesia, autonomic, evoked, paroxysmal, thermal, allodynia, and tender/numb (15). Participants fillled out questionnaires regarding whether they had felt the symptoms of any of the 7 items over the last week. Each item was assigned a score of 1–5, and the total score could be 0–24. The higher scores suggest that the pain is predominantly neuropathic not nociceptive. Turkish versions of the forms, which were tested for validity in Turkish, were used to assess NP (16,17). Doctors helped illiterate patients to fill in the questionnaires.

Statistical Analyses

Statistical analyses were conducted using the SPSS 11.5 software package program. P <0.05 was considered statistically significant. Data were described with percentage values, standard deviation, means, and medians (minimum–maximum). Differences between groups with and without NP were evaluated using the Mann–Whitney U test (annual income, number of drugs used, number of comorbidities, perceived health, and VAS), student's t-test (height, weight, and body mass index), and Chi-Square test (NP risk factors). After comparing risk factors, we sent the factors with P values < 0.10 to the logistic model, which was created by using the Backward LR method. Factors used to create the model included sex, education, marital status (married, widowed, or single), smoking, ambulation status, presence of comorbidity, history of falling, four or more drugs use, depression, attention deficit, insomnia, lack of energy, anxiety, and loss of appetite. Odds ratio (OR) and confidence interval (CI) were calculated.

RESULTS

Study Sample

We received a total of 1173 patient questionnaires from the 13 centers. Of the 1173 questionnaires, 10 were excluded, some for missing parts and others for failure to meet inclusion criteria, leaving a total of 1163 patients. We observed that 52.5% of the 1163 patients (n=610) had NP. The ages of 67.5% of patients with NP (n=412) were between 65 and 74 years; the ages of 28.9% of patients (n=176) were between 75 and 84 years, and the ages of 3.6% of patients (n=22) were over 85years. Of the 610 patients with NP, 72.1% (n=440) were women. Socio-demographic and clinical characteristics of the patients are shown in Tables 1-2. There are comparison of risk factors and complaints accompanying with and without neuropathic pain in Table 1. Complaints accompanying NP included fatigue for 75.1% (n=459) of patients, insomnia for 63.6% (n=388) of patients, anxiety for 44.8% (n=273) of patients, and loss of appetite for 27.2% (n=166) of patients. A history of falling in the last year was reported by 31.1% (n=190) of patients (Table 1). Holden Ambulation Scale, activity level and severe pain region of the patients with and without neuropathic pain are shown in Table 3. Regions where the pain was most intense were the low back (23.8%), foot–ankle (19.5%), and knee (19%). Although hand pain came 4th in line (n:63), 91.3 % of pain was found to be neuropatic character.

Comorbidities and distribution of neuropathic pain by disease type are shown in Table 4. The top comorbidities were osteoarthritis for 41.6% (n=254) of patients, low back pain for 35.2% (n=215) of patients, osteoporosis for 29.0% (n=177) of patients, diabetes for 29.8% (n=182) of patients, and entrapment neuropathy for 10.7% (n=65) of patients. When they were compared with respect to comorbidities, a statistically significant difference was found between in cerebrovascular event, entrapment neuropathy, plexus neuropathy, low back pain, depression, diabetes and osteoporosis (Table 4).

Neuropathic Pain

When patients with and without NP were compared with respect to all variables, a statistically significant difference was found between the groups in terms of sex, marital status, four or more drugs use, presence of comorbidity, use of walking aid, fatigue, lack of energy, loss of appetite, insomnia, Holden ambulation score, perceived health, region of most severe pain, and VAS (p <0.05). No statistically significant dif-

Table 1— Comparison of Risk Factors and Complaints Accompanying With and Without Neuropathic Pain

	NP (+)		NP (–)		*p*
	n	%	n	%	
Sex					
Female	440	67.7	210	32.3	0.004
Male	170	58	123	42	
Education					
Literate	179	68.1	84	31.9	0.061
Primary–Secondary	295	63.7	168	36.3	
High School	104	67.5	50	32.5	
University	32	50.8	31	49.2	
Marital Status					
Married	386	62.2	235	37.8	0.024
Widowed/Single	224	69.6	98	30.4	
Smoking					
Yes	43	54.4	36	45.6	0.071
No	458	66.6	230	33.4	
Gave up	109	61.9	67	38.1	
More than four drugs					
Yes	346	72.5	131	27.5	0.000
No	264	56.7	202	43.3	
Comorbidity					
Yes	584	66.6	293	33.4	0.000
No	26	39.4	40	60.6	
Falling					
Yes	190	69.1	85	30.9	0.069
No	420	62.9	248	37.1	
Insomnia					
Yes	388	68.1	182	31.9	0.008
No	222	59.7	150	40.3	
Loss of appetite					
Yes	166	70.3	70	29.7	0.036
No	444	62.8	263	37.2	
Anxiety					
Yes	273	73	101	27.0	0.000
No	337	59.2	232	40.8	
Attention deficit					
Yes	270	70.9	111	29.1	0.001
No	340	60.5	222	39.5	
Fatigue					
Yes	459	66.7	229	33.3	0.032
No	151	59.2	104	40.8	
Lack of energy					
Yes	425	68.8	193	31.2	0.000
No	185	56.9	140	43.1	

NP: Neuropathic Pain



Table 2— Patient Characteristics

	NP (+)		NP (–)		
	Mean ± sd	**Median (Min–Max)**	**Mean ± sd**	**Median (Min–Max)**	**p***
Annual income TL / year	7.789 ± 5.933	6.000 (600–33.120)	7.410 ± 4.581	6.000 (720–39.580)	0.758
Drug number	4.44 ± 2.18	4 (1–12)	3.87 ± 2.36	4 (1–15)	**0.000**
Number of comorbidities	3.92 ± 2.11	4 (1–16)	2.88 ± 1.46	3 (1–8)	**0.000**
Height	162.13 ± 7.90	160 (130–193)	162.53 ± 8.47	160 (138–190)	0.475
Weight	73.86 ± 11.17	75 (27–110)	73.54 ± 12.34	73 (7–115)	0.698
BMI	28.49 ± 4.78	28 (18–42)	27.76 ± 4.40	28 (18–46)	1.000
Health Perception	3 ± 0.86	3 (1–5)	3.39 ± 0.73	3 (1–5)	**0.000**
VAS	6.82 ± 1.60	7 (1–10)	6.20 ± 1.89	6 (1–10)	**0.000**

SD: Standard deviation, NP: Neuropathic Pain, BMI: Body mass index, VAS: Visual analog scale

Table 3— Comparison of Patients with and without Neuropathic Pain in terms of Ambulation, Using Walking Aid and Pain Site

	NP (+)		NP (–)		*p*
	n	**%**	**n**	**%**	
Holden Ambulation Scale					
Nonfunctional	14	63.9	8	36.4	**0.002**
More than one support	19	79.2	5	20.8	
One manual contact	18	75.0	6	25.0	
Smooth surface support	123	75.9	39	24.1	
Support at staircase	91	68.4	42	31.6	
Fully independent	345	59.7	233	40.3	
Activity					
Sedentary	328	65.2	175	34.8	0.553
Leisurely walk	230	65.2	123	34.8	
Regular sports	51	59.3	35	40.7	
Athletic	-	-	-	-	
Walking aid					
Walker	23	76.7	7	23.3	**0.000**
Walking stick	187	74.8	63	25.2	
Wheelchair	22	62.9	13	37.1	
None	378	60.2	250	39.8	
Severe pain region					
Neck	36	54.5	30	45.5	**0.000**
Shoulder	43	51.8	40	48.2	
Elbow	12	54.5	10	45.5	
Hand	63	91.3	6	8.7	
Back	13	56.5	10	43.5	
Low back	145	66.2	74	33.8	
Hip	23	53.5	20	46.5	
Knee	116	53.5	101	46.5	
Foot-ankle	119	84.4	22	15.6	
Chest	-	-	1	100.0	
Other	40	67.8	19	32.2	

NP: Neuropathic Pain

Table 4— Comorbidities and Distribution of Neuropathic Pain by Disease Type

	NP (+)		NP (–)		*p*
	n	%	n	%	
Parkinsonism					
Yes	14	73.7	5	26.3	0.407
No	596	64.5	328	35.5	
Cerebrovascular event					
Yes	49	79.0	13	21.0	**0.014**
No	561	63.7	320	36.3	
Multiple sclerosis					
Yes	3	100.0	-	-	0.200
No	607	64.6	333	35.4	
Alzheimer's disease					
Yes	15	83.3	3	16.7	0.095
No	595	64.3	330	35.7	
Neurogenic claudication					
Yes	27	79.4	7	20.6	0.067
No	583	64.1	326	35.9	
Phantom pain					
Yes	1	50.0	1	50.0	1.000
No	609	64.7	332	35.3	
Trigeminal neuralgia					
Yes	1	100.0	-	-	1.00
No	608	64.6	333	35.4	
Entrapment neuropathy					
Yes	65	90.3	7	9.7	**0.000**
No	545	62.6	326	37.4	
Plexus neuropathy					
Yes	12	92.3	1	7.7	**0.036**
No	598	64.3	332	35.7	
Post herpetic neuralgia					
Yes	3	75.0	1	25.0	1.00
No	607	64.6	332	35.4	
Spinal cord injury					
Yes	5	71.4	2	28.6	1.00
No	605	64.6	331	35.4	
Osteoarthritis					
Yes	254	64.5	140	35.5	0.945
No	356	64.8	193	35.2	
Low back pain					
Yes	215	73.6	77	26.4	**0.000**
No	395	60.7	256	39.3	
Depression					
Yes	57	77.0	17	23.0	**0.021**
No	553	63.6	316	36.4	
Fibromyalgia					
Yes	19	67.9	9	32.1	0,722
No	591	64.6	324	35.4	
Diabetes					
Yes	182	85.8	30	14.2	**0.000**
No	428	58.5	303	41.5	
Osteoporosis					
Yes	177	72.7	68	27.8	**0.004**
No	433	62.0	265	38.0	

NP: Neuropathic Pain



ference was observed between the groups in terms of education, smoking, annual income, activity level and history of falling ($p>0.05$). When they were compared with respect to comorbidities, a statistically significant difference was found between the groups ($p<0.05$) (Tables 1-4).

Multivariable Modeling

When a logistic regression model was formed using the backward LR method for the variables of sex, education, marital status (married, widowed, or single), smoking, ambulation status, presence of comorbidity, history of falling, use of 4or more drugs, depression, attention deficit, insomnia, lack of energy, anxiety, and loss of appetite, NP was found to be 2.05 times higher in patients with comorbidities (95% CI 1.2–3.5), 1.6 times higher in patients with anxiety (95% CI 1.2–2.2), and 1.7 times higher in patients who took four and more drugs (95% CI 1.3–2.3) ($p<0.05$).

Discussion

Here the prevalence of NP in patients who presented to the hospital with pain was 52.5%. When the groups were compared on the basis of the presence of NP, a statistically significant difference was found between the groups in terms of sex, marital status, four or more drugs use, presence of comorbidity, use of walking aid, fatigue, lack of energy, loss of appetite, insomnia, Holden ambulation score, perceived health, region of most severe pain, and VAS. NP was 2.05 times higher in patients with comorbidities, 1.6 times more in patients with anxiety, and 1.7 times higher in patients who took 4 and more drugs.

NP prevalence in the community according to self-administered questionnaires varies between 3% and 8% (4,5,10), The NP prevalence was reported to be 17.9% in the general Canadian population (18). Large studies of people with chronic pain from any cause found the prevalence of NP to be 8.2% among UK family practice patients and 6.9% in a national population-based cohort in France (4,5,10). But the prevalence appears to be considerably higher in populations with chronic pain. Bouhassira et al. reported that 21.7% of the large number of patients in his study who had chronic pain had neuropathic characteristics (5). Freynhagen et al. found that among patients with chronic low back pain, 37% had symptoms indicating NP (19). Amris et al. found that 75% of patients with chronic widespread musculoskeletal pain had somatosensory symptoms indicating NP (20). The reason for the high prevalence of neuropathic pain in our study may be because only those patients who presented with pain to the physical therapy and rehabilitation department outpatient clinics were assessed. Face-to-face interviews were also important for objectivity reasons. Furthermore, patients with mixed-type NP may have influenced this rate. However, commenting on mixed-type NP based on data in the literature and the results of the present study can be quite difficult. Moreover, potential explanation for the variability in NP prevalence estimates across studies include (1) differential recruitment practices (estimates based on patients recruited from specialists' offices have been consistently higher than those from community-based studies), (2) variable exclusion criteria or statistical control for other potential sources of NP, and (3) use of different NP measures (14,21). We should also reiterate that the questionnaires used in the present study have not been tested for validity and reliability in the elderly population. The diagnosis of NP remains a challenge, and one way to detect it is to use a series of specific descriptors that have been used to prepare different scales and questionnaires. According to one expert panel, the main clinical strength of questionnaires as screening tool lies in their ability to identify patients with possible neuropathic pain, but they cannot replace clinical judgment (3). Clinical judgment has been considered a valid standard in testing the diagnostic accuracy of questionnaires for NP (13,22).

In the literature, older age, being female, low education level, and poor economic status seem to be associated with pain and neuropathic pain (4,6,23). We also found an association between female sex and neuropathic pain. Although the percentage of NP appears higher in the 65–74 age group than in the other two age groups, no statistical significance could be established. There was also a higher prevalence of chronic pain with neuropathic characteristics in patients from the 50–64 age group in a study (5). The relationship between older age and NP as described in the literature was not observed in our study. The fact that we included patients >65 years and that we assessed them by grouping according to age may have produced this result. We feel certain that the results of the present study will become clearer after further similar studies are conducted with larger numbers of patients. No differences were noted between the two groups in height, weight, and body mass index, which agrees with other studies (17, 24). The existence of an NP component is associated with a higher level of education (24). This could be interpreted as a sign that patients with low literacy levels have difficulty understanding some of the language or terms used in NP questionnaires (13). Although we also found in our study that NP

was less observed in persons with higher levels of education, this finding was not statistically significant. Finally, this finding may be associated with health care, health behaviors, self-efficacy, and income.

NP was observed more in lower back, foot–ankle, knee and hand regions in our study, but none of the pain areas were indicative of NP. It is stated in the literature that back and lower extremities are affected frequently and pain in the back, hand, thigh and foot regions is said to be indicative of NP (9). The association between neuropathic pain and hand region could be due to trapped nerve, but comments on this are not possible in the present study. Extremity involvement is more frequent in the literature (4,5,14), and it is associated with the possibility that multiple painful joints may be at greater risk for central sensitization, owing to cumulative nociceptive input. Alternatively, central sensitization may contribute to the sensation of pain at multiple body sites (14). Identifying pain areas may guide us in clinical practice.

When the groups of older people with and without NP were compared, statistically significant difference was observed between the groups in terms of insomnia, loss of appetite, anxiety, attention deficit, fatigue, and lack of energy. In our study, NP was 1.6 times higher in patients with anxiety. Although the association between psychological symptoms and NP has been discussed in the literature, the effects of how these symptoms may relate to NP have not been discussed (14). This might partially explain the high comorbidity rates for chronic pain, sleep disorders, and psychological conditions such as depression and why drugs that are effective for one condition may not be effective in others (1,25). Inclusion of the aforementioned symptoms in future studies would help to assess patients from a different viewpoint.

Patient-administered screening tools for NP have also been applied in studies of specific sensory profiles in established NP conditions and in patients suffering from highly different chronic pain conditions such as cancer pain, low back pain, knee osteoarthritis, fibromyalgia, spinal cord injury, and persistent postoperative pain [4–6,8,10,14,15,19]. The prevalence of polyneuropathy in diabetic patients is 26%-50% (23,26). In diabetic polyneuropathy, pain prevalence is said to alter with age, duration of diabetes, and pathologic progression of the disease (6). We also showed in our study the percentages of patients with various diseases who had been diagnosed with NP. NP was 2.05 times higher in patients with comorbidities and 1.7 times higher in patients who took four or more drugs. These data are found particularly in studies where the cause of NP is investigated (27). However, the literature has not mentioned that these variables have been included as indicative factors for NP. This issue needs to be considered in persons with comorbidities, especially in the elderly, and patients should be assessed with respect to neuropathic pain. A definite need exists for society-based studies with broader series to demonstrate related diseases.

The strong aspects of our study include recruiting large number of patients, assessing patients through face-to-face interviews (rather than over the phone), using two different instruments to screen NP, and having obtained specific data by including only patients ≥65 years of age.

The biggest limitation of the present study was that the use of drugs for NP was not dealt with (which could mean higher rates of neuropathic pain and a greater health problem than suspected). We recommend further studies where patients with cognitive dysfunction are included.

In conclusion, NP was found in nearly half of patients aged ≥65 years who presented with pain. On the basis of the literature and the present study, it seems apparent that diagnosis of neuropathic pain has been ignored and/or underestimated in the elderly. To succeed in NP management, it must first be identified and diagnosed. We believe the present study will increase awareness in this matter.

Conflict of Interest

We had no financial support for this research and no conflicts of interest.

Author's Contributions

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RESEARCH

AETIOLOGY OF EMERGENCY DEPARTMENT ADMISSION OF THE ELDERLY: A RETROSPECTIVE STUDY IN KARS

ABSTRACT

Introduction: The demand for emergency services has been growing with increasing elderly population. This study aims to determine the underlying aetiologies of the emergency department visits by the elderly for proper planning of future services.

Materials and Method: The medical records of patients above the age of 65 years who visited the Emergency Department of the Health, Research and Training Hospital of Kafkas University between 1 January 2013 and 1 January 2015 were retrospectively analysed using the ICD-10 diagnostic codes for data classification.

Results: Geriatric patients rate amongst total number of emergency cases were 19.6%. The average age of patients included in this study was 74.29±7.04 and 53.6% of them were males. The majority of emergency department visits by the elderly were during summers, and 46.3% of them were included in the category red. Circulatory system diseases (46.3%); respiratory system diseases (15.6%); musculoskeletal diseases (9%); endocrine, nutritional and metabolic diseases (6.5%) and non-specific symptoms and abnormal clinical and laboratory findings (4.5%) were the top five causes for the emergency department visits by the elderly. In addition, our results indicated that 5.2% of the elderly patients were admitted mostly to the coronary intensive care.

Conclusion: Circulatory disorders were the most common cause of the emergency visits and hospitalization of elderly patients. These results highlight the need for new studies for prevention of circulatory system diseases, strategic planning for emergency care services and development of relevant protocols and policies.

Key Words: Emergency; Aged; Chronic Disease, Emergency Treatment.

ARAŞTIRMA

YAŞLILARIN ACİL SERVİSE BAŞVURMA NEDENLERİ: KARS'TA RETROSPEKTİF BİR ÇALIŞMA

ÖZ

Giriş: Yaşlı nüfusun artmasıyla birlikte acil hizmetlere de gereksinim artmaktadır. Bu çalışma hizmetlerin uygun şekilde planlanması amacıyla acil servise başvuran yaşlıların başvurma nedenlerinin belirlenmesidir.

Gereç ve Yöntem: Kafkas Üniversitesi Sağlık, Araştırma ve Eğitim Hastanesi Acil servisine 1 Ocak 2013 ve 1 Ocak 2015 tarihleri arasında başvuran 65 yaş üstü yaşlıların tıbbi kayıtları ICD-10 tanı kodları sınıflama sistemine göre retrospektif olarak analiz edilmiştir.

Bulgular: Toplam hastalar içinde acil servise başvuran yaşlı hasta yüzdesi 19,6'dır. Çalışmaya katılan yaşlıların yaş ortalaması 74,29±7,04, %53,6'sı erkek hastadır. Yaşlı hastalar en fazla yaz mevsiminde acil servise başvurmuştur ve %46,3'ü kırmızı odaya alınmıştır. Yaşlıların acil servise başvuru nedenleri arasında ilk beş sırada dolaşım sistemi hastalıkları (%46,3), solunum sistemi hastalıkları (%15,6), kas iskelet sistemi hastalıkları (%9), endokrin beslenme ve metabolik hastalıklar (%6,5), semptomlar ve anormal klinik ve laboratuar bulguları (%4,5) yer almaktadır. Ayrıca yaşlıların %5,2 sıklıkla en fazla koroner yoğun bakım ünitesine yatırıldığı belirlenmiştir.

Sonuç: Yaşlı hastaların acile başvuru ve yatış nedenleri arasında dolaşım problemleri birinci sırada yer almaktadır. Bu nedenle dolaşım sistemi hastalıklarına yönelik korunma amacıyla yeni çalışmaların yapılması, acil bakım hizmetlerinin planlanması ve protokol ve sistemlerin geliştirilmesi önerilmiştir.

Anahtar Sözcükler: Acil; Yaşlı; Kronik Hastalık; Acil Servis Tedavi.

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INTRODUCTION

There has been a rapid increase in the elderly population globally, including Turkey. According to data from Turkey Statistical Institute (TSI), the percentage of population aged 65 years or above has been predicted to increase from 8% in 2014 to 10.2%, 20.8% and 27.7% in 2023, 2050 and 2075, respectively, and the elderly dependency rate has been indicated to be 11.8% (1).Such a rapid increase in the elderly population in all age groups is associated with numerous problems, including health, economic and social issues, consequently increasing the need for emergency services as the elderly seek substantially more medical care. Karadag *et al.* reported that 20% of the patients visiting emergency departments were elderly (2). In addition, a report published in USA stated that emergency department visits increased with increasing age. The rate of these visits made by patients over the age of 65 years was 15% and rose to 54.3% for those aged 85 years and above (3).

Acute and chronic conditions ailing elderly patients are important during visits to the emergency department. The prevalence of chronic diseases among elderly, which depends on their environment, ranges from 51% to 92.2% (4-6). Cardiovascular diseases leading to sudden death are the most common of all the chronic diseases in the elderly (7-9). Moreover, the utilization of drugs for chronic diseases is also high and varies between 84.9% and 86% according to different studies (6-7). Other important causes of the emergency department visits are falls; fractures and severe soft tissue injuries (which are serious) in 10%–25% of the elderly individuals (10). Sütoluk *et al.* reported that elderly were more prone to home accidents and falls comparison with other age groups (11). Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality among the elderly, and acute respiratory tract infections commonly precipitate COPD exacerbation. Furthermore, infectious diseases are a significant cause of the emergency department visits by the elderly. They are more severe and associated with higher mortality rates in the elderly than in the younger age groups (12). One study reported upper respiratory tract infections (34.3%) as the main cause of the emergency department visits by the elderly (9).

Compared with younger patients, evaluation of the elderly at emergency department presents more challenges as their health issues are more complex and atypical. In addition, they may not easily express their feelings or convey the problems they might be experiencing, and tend to be more satisfied with the service they have received (13). They are also more likely to be confused due to dementia, Alzheimer's disease, delirium or circulatory disorders and are more likely to suffer from sensory or perception disorders. Furthermore, they require more extensive laboratory and radiological processing and have to stay longer at the emergency department (4). Therefore, ensuring that a sufficient time is available for a more comprehensive and age group-specific evaluation is critical in addition to the development of an age specific training for evaluating the elderly in emergency department settings (14). Nonetheless, in the current health system, the services for elder care, the number of trained personnel in this field and the protocols and policies are insufficient. Therefore, this study aimed to provide necessary information regarding staff training, strategic planning and development of protocols and policies for elderly care in the emergency department settings.

MATERIALS AND METHOD

Kars is located in the Eastern Anatolian region of Turkey at an altitude of 1768 metres above the sea level. The average coldest and hottest temperatures in Kars are -12.1 °C and 17.5 °C, respectively, with an average annual temperature of 4.1 °C and ample rain throughout the year. The health care system in Kars can be classified as primary, secondary and tertiary level health care, reflecting health services administered across Turkey. Emergency health services are provided at secondary and tertiary health care facilities. Patients who cannot be treated at the secondary care facilities are directed to a tertiary hospital or to a more advanced one. According to data obtained from Kars Public Health Unit, the elderly comprised 7.6% of the population in Kars. They are given priority in provision of health services across the country, and these services are legally guaranteed.

Additionally, in 2009, Turkish Ministry of Health mandated a three level emergency triage scale intending to designate the severity of the case which were categorized with the colours of red, yellow and green (Table 1).

In Kars, two emergency units, a second stage and a third stage, are affiliated with two separate hospitals. The Emergency Department of the Health, Research and Training Hospital of Kafkas University started accepting patients in November 2012. The nearest university hospital is located in Erzurum, about 3 hours away. Therefore, information gained from this study will provide a critical database for future planning.

Table 1— Emergency Triage Scale

TRIAGE COLOR	DESCRIPTION OF CATEGORY	CLINICAL DESCRIPTORS (MODEL CASES)
RED	Conditions that are threats to life (or imminent risk of deterioration) and require immediate aggressive intervention.	Cardiac arrest Respiratory arrest Immediate risk to airway Major multi trauma Respiratory rate < 10/min BP < 80 mmHg (adult) or severely shocked child/infant Unresponsive or responds to pain only Ongoing / Prolonged seizure IV overdose and unresponsive or hypoventilation Chest pain of likely cardiac nature
	The patient's condition is serious enough or deteriorating so rapidly that there is the potential of threat to life, or organ system failure, if not treated within ten minutes of arrival	Extreme respiratory distress or pulse oxymetry <90 Airway risk-severe stridor or drooling with distress Circulation compromise - Clammy or mottled skin, poor perfusion - HR <50 or >150 - Hypotension with hemodynamic effects Acute hemiparesis/dysphasia Fever with sign of lethargy (any age) Acid or alkali splash to eye – requiring irrigation Severe localised trauma – major fracture, amputation Very severe pain – any cause Significant sedative or other toxic ingestion Behavioral/Psychiatric: - Violent or aggressive - Immediate threat to self or others

This study was conducted by retrospective medical record analysis of patients visiting the Emergency Department of the Health, Research and Training Hospital of Kafkas University over a 2-year period between 1 January 2013 and 1 January 2015. Demographic data, including age and gender, seasons of visits, triage categories, diagnoses and prognoses of elderly patients were investigated utilizing the ICD-10 coding system. The study was approved by the Ethics Committee Presidency of Clinical Research of the School of Medicine at Kafkas University. Data were represented as numbers with percentages and/or means±standard deviation, and $^{-2}$ test was used for further analysis with SPSS 20.0 software (IBM, USA).

RESULTS

46.559 patients applied to emergency care unit during the study period. A total of 9140 patients visited the emergency department during the study period. Geriatric patients rate amongst total number of emergency cases were 19.6%. The average age of the elderly was 74.29±7.04, and 53.6% of them were male. The average hospital stay of elderly patients was 8.30±7.50 hours. No relationship was detected between the age and the length of stay at the emergency department (r=0.00, p=0.57).

Table 2 shows the gender and season distribution among elderly patients visiting the emergency department. Statistical analysis determined that the emergency department visits by the elderly were more frequent during summers (28.1%) compared with other seasons (28.1% versus 23.5% winter and spring). However, there was no relationship between seasons, gender and diagnosis (p=0.17).

Further analysis revealed that 46.3% of the elderly patients were taken to the category red, and 52.7% of them were

Table 2— Season That the Elderly Patients Applied to the Emergency Department, by Sex

Seasons	Sex						
	Male		Female		Total		
	Number	Percent	Number	Percent	Number	Percent	$\chi 2=5.022$ p=0.17*
Spring	1193	55.6	953	44.4	2146	23.5	
Summer	1363	53.0	1208	47.0	2571	28.1	
Autumn	1221	53.6	1055	46.4	2276	24.9	
Winter	1125	52.4	1022	47.6	2147	23.5	
Total	4902	53.6	4238	46.4	9140	100.0	

* Chi-square test was used.

Table 3— Distribution of Triage Category Cases of the Elderly Applying to the Emergency Department, by Sex

Triage Category	Sex						
	Male		Female		Total		
	Number	Percent	Number	Percent	Number	Percent	$\chi 2=16.090$ p=0.00*
Red	2230	52.7	2000	47.3	4230	46.3	
Yellow	1945	55.8	1539	44.2	3484	38.1	
Green	712	50.8	689	49.2	1401	15.3	
Unknown	15	52.4	10	47.6	21	0.3	
Total	4902	53.6	4238	46.4	9140	100	

* Chi-square test was used.

male. The number of male elderly patients admitted to the triage area was significantly high (p=0.00, Table 3).

As seen in Table 4, there was no relationship between diagnosis and gender. Circulatory system diseases (46.3%); respiratory system diseases (RSDs, 15.6%); musculoskeletal diseases (9%); endocrine, nutritional and metabolic diseases (ENMDs, 6.5%) and non-specific symptoms and abnormal clinical and laboratory findings (4.5%) comprised the five most common causes of the emergency department visits by the elderly (Table 4). Also urogenital diseases were the sixth most common cause of the emergency department visits by the elderly (Table 5). Among circulatory system disorders, the rates of ischemic heart disease, hypertensive disease, cerebrovascular disease, pulmonary heart and circulation disorders and other forms of heart disease were 61.9%, 26.4%, 4.4%, 3.7% and 3.6%, respectively.

The analysis of distribution of the diagnostic groups according to age group, as shown in Table 5, revealed that the number of visits were higher for those between the ages of 65 and 74 years.

Finally, as shown in Table 6, 78.5% of the elderly patients were discharged or transferred; in addition, 5.2% of the elderly patients were admitted to the coronary intensive care.

Discussion

To our knowledge, this is a novel study that examined the emergency department visits by the elderly in the Eastern Anatolian region of Turkey. However, our study has several limitations. The study encompassed data from only one health care facility. In addition, data regarding medications used by patients, means of their arrival to the emergency department (i.e. ambulance) and number of emergency department visits were not included in the final analysis.

The seasonal differences in the visits shown by this study have been shown by other groups as well (15-18), and the dif-

Table 4— Diagnosis, Groups of Elderly Patients, by Sex

Diagnosis Groups	ICD-10 Codes	Sex					
		Male*		Female*		Total**	
		Number	Percent	Number	Percent	Number	Percent
Diseases of the circulatory system	I00-I99	2232	52.7	2000	47.3	4232	46.3
Diseases of the respiratory system	J00-J99	802	56.4	620	43.6	1422	15.6
Diseases of the musculoskeletal system and connective tissue	M00-M99	427	52.1	392	47.9	819	9.0
Endocrine, nutritional and metabolic diseases.	E00-E90	283	48.0	307	52.0	590	6.5
Symptoms, signs and abnormal clinical and laboratory findings	R00-R99	218	52.5	197	47.5	415	4.5
Diseases of the genitourinary system	N00-N99	264	65.0	142	35.0	406	4.4
Other reasons		665	54.0	570	46.0	1230	13.4
Unknown		11	52.4	10	47.6	21	0.2
Total		4902	53.6	4238	46.4	9140	100.0

*Line percentage was used.

** Column percentage was used.

Table 5— Distribution of Diagnosis Groups Was Examined by Age Group*

Diagnosis Groups		Age Groups					
		65-74		75-89		90 ↑	
		Number	Percent	Number	Percent	Number	Percent
Diseases of the circulatory system	I00-I99	2349	55.5	1757	41.5	126	3.0
Diseases of the respiratory system	J00-J99	808	56.8	584	41.1	30	2.1
Diseases of the musculoskeletal system and connective tissue	M00-M99	536	65.4	266	32.5	17	2.1
Endocrine, nutritional and metabolic diseases.	E00-E90	330	55.9	244	41.4	16	2.7
Symptoms, signs and abnormal clinical and laboratory findings	R00-R99	251	60.5	152	36.6	12	2.9
Diseases of the genitourinary system	N00-N99	204	50.2	193	47.5	9	2.2
Other reasons		692	55.5	510	40.9	43	3.45
Unknown		12	57.1	9	42.9	-	-
Total		5182	56.7	3715	40.6	243	2.7

*Line percentage was used.

ferences in outcomes among the studies are suggested to be due to seasonal, environmental and socio-economic conditions. The emergency department visits by the elderly in Kars were predicted to increase during winters. One possible explanation for this contrary outcome would be temporary translocation of the elderly to warmer provinces due to difficult living conditions and transportation problems in the villages and towns around Kars in winters.

In our study, nearly half of the elderly patients visiting the emergency department were taken to the category red according to triage coding. Previous studies did not include information on triage cases involving the elderly; however, the

Table 6— Prognoses of Elderly Patients Applying to the Emergency Department

Prognoses of Elderly Patients Applying to The Emergency Department	Number	Percent
Discharge/Dispatch	7184	78.5
Coronary Intensive Care Unit	474	5.2
Internal Medicine and Internal Medicine Intensive Care Unit	453	5.0
Cardiology and Angiography Unit	289	3.2
General Surgery and General Surgery Intensive Care Unit	192	2.1
Neurology and Neurology Intensive Care Unit	116	1.3
Orthopedy	111	1.2
Chest Diseases	90	1.0
Cardiyovascular Surgery and Cardiovascular Intensive Care Unit	81	0.9
Urology	44	0.5
Nephrology	32	0.4
Brain Surgery	28	0.3
Infection Diseases	19	0.2
Other	23	0.2
Death	4	0.1
Total	9140	100.0

high rate of category red triage cases in this study could be due to more complex cases transferred to our centre, which is located within the highest-level hospital in the province.

Cardiovascular disease is the most common cause not only of the use of health care services but also of morbidity and mortality among the elderly (19). According to a report published in 2013 by the American Heart Association, 66% of the cardiovascular deaths occurred at or after the age of 65 years (20). According to a study data in 2009, in Turkey, cardiac diseases were the most common cause of overall death at 39.8% (21), and circulatory system diseases and cardiac issues were the most common cause of the emergency department visits by the elderly (8,15,17,18). Similarly, in our study, circulatory system problems were the most common cause of the emergency department visits by the elderly. These findings are in agreement with the results of our literature review which indicated circulatory system diseases as the most common cause of emergency department visits (8,22). The rates of cardiovascular diseases observed in our study are higher than those observed in other studies. As Kars is a high-altitude city in Eastern Anatolian region of Turkey with a cold climate, both the young and old individuals tend to stay indoors with subsequent decreased activity.

Respiratory system diseases (9.8%) constitute the third most common cause of death in Turkey (21). While there are no studies on RSDs or COPD prevalence in the elderly in Turkey, COPD prevalence reaches 15-20% above 40 ages (23). Our results showed RSD as the second most common cause of the emergency department visits by the elderly, which ranged between 9.5% and 17% in other studies (8,15). The high rate of RSD-related emergency visits to our facility was noticeable given the lack of industry in Kars. One reason might be the utilization of biomass, which is a significant indoor air pollutant, during the long winter season in Kars due to the low socio-economic level.

Musculoskeletal diseases increase with age and are a source of debilitating pain that adversely affects quality of life of the elderly. Thus, musculoskeletal diseases are predicted to constitute a significant portion of the emergency department visits by the elderly. In our study, musculoskeletal diseases were the third most common cause, which was in agreement with previously reported range of 6.6%–16.7% (8,9,15). One underlying reason may be the distinct and variable environmental conditions. Further, as mentioned above, vitamin D deficiency as well as lack of exercise and social opportunities in the elderly may be a significant risk factor for this outcome.

The most important ENMD of the emergency department visits by the elderly was diabetes mellitus (DM). While comprehensive data on the prevalence of DM in the elderly in

Turkey is lacking, our results indicated ENMDs as the fourth most common cause for the emergency department visit by the elderly, and this finding is not in agreement with previous studies. For example, endocrine disorders were reported as the tenth most common cause (4.7%) and fifth most common cause (4.2%) in the studies by Baz *et al.* and Kılınç *et al.,* respectively. Furthermore, they were the fifth most common cause (5.1%) in a study conducted by Nur *et al.* that included 112 emergency medical services (8,15,17). There are several potential reasons for the higher rate of ENMDs in our study than in the earlier studies, which include increased incidence of DM, insufficient patient education on DM, increased acute or chronic complications due to failure in treatment compliance and socio-economic or socio-cultural differences.

Elderly healthcare is a major health issue in Turkey. The city of Kars does not have any nursing homes, and the elderly usually live with their children. While there is no study investigating the quality of elderly care in a family environment, the deficiency of elderly care at a society level has been acknowledged. In our study, the presence of a subset of the elderly visiting the emergency department due to abnormal clinical findings may indicate problems with in-house care.

Urogenital diseases tend to occur more commonly in older people than in younger people due to a number of reasons (24). In our study, urogenital diseases were the sixth most common cause. Studies have reported urogenital diseases among the five most common causes of the emergency department visits by the elderly (range, 8.5%–13.5%) (9,15); however, our study, in contrast to other studies, showed a lower incidence for urogenital diseases. One reason for this outcome may be the transfer of patients to another hospital due to lack of a dialysis unit at our hospital.

Finally, the majority of elderly visiting our emergency department were either discharged or transferred. The literature review revealed that 39%–93% of the elderly received outpatient treatment (8,25). Internal medicine, surgery, cardiology and intensive care services were the most frequently utilized services by hospitalized patients (8,18). In our study, the mortality among the elderly was very low; again, we predict that one primary reason was the transfer of more complex cases to other health care facilities.

In summary, the need for emergency services will grow with the increase in the elderly population. In our study, circulatory system problems were the most common cause of visits to the emergency department, at a rate that appeared to be considerably higher than that reported in other studies. Therefore, public awareness for the protection and prevention from circulatory system diseases should be increased, and emergency medical service planning should be prioritized accordingly. Finally, relevant protocols should be developed, and appropriate staff training should be provided.

Disclosure Statement

The authors declare that they have no conflict of interests.

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RESEARCH

EFFICACY AND TOLERABILITY OF CHEMOTHERAPY IN ELDERLY PATIENTS WITH METASTATIC GASTRIC CANCER

ABSTRACT

Introduction: Elderly patients are under-represented in the clinical trials of patients with metastatic gastric cancer (GC); therefore, the efficacy and tolerability of palliative chemotherapy are unclear in these patients. We aimed to assess the efficacy and tolerability of first-line palliative chemotherapy in elderly patients (age ≥70 years) with metastatic GC.

Materials and Method: From 2005 to 2014, 89 patients with metastatic GC who were 70 years and older and were treated with at least two cycles of systemic chemotherapy as first-line treatment were included retrospectively. Disease and patient characteristics, prognostic factors, treatment response, grade 3–4 toxicity related to treatment, progression free survival (PFS), and overall survival (OS) were evaluated.

Results: Of the 89 patients, 65 (73%) were males; median age was 74 (70–84) years. The median follow-up period was 7 months (min–max: 2–57 months), median PFS was 5 months (95% CI: 3.7–6.3), and median OS was 7 months (95 % CI: 5.2–8.9). The disease was controlled in 43.8% patients, whereas progression was observed in 56.2% patients. Univariate analysis showed that the Eastern Cooperative Oncology Group (ECOG) performance status, number of chemotherapy cycles, and response to the first line chemotherapy had a significant effect on PFS and OS; liver metastasis had an effect only on PFS; lung metastasis had an effect only on OS.

Conclusion: Fewer chemotherapy cycles, lung metastasis, liver metastasis, and poor ECOG performance scores were found to be poor prognostic factors.

Key Words: Stomach Neoplasms; Neoplasm Metastasis; Aged; Drug Therapy.

ARAŞTIRMA

METASTATİK MİDE KANSERLİ YAŞLI HASTALARDA KEMOTERAPİNİN ETKİNLİĞİ VE TOLERABİLİTESİ

ÖZ

Giriş: Yaşlı hastalar klinik çalışmalara alınmadığından metastatik mide kanseri (MK) olan hastalarda kemoterapinin etkinliği ve tolerabilitesi konusunda bilgiler yetersizdir. Bu çalışmada 70 yaş ve üstü metastatik MK hastalarında ilk seride verilen palyatif kemoterapinin etkinliğini ve tolerabilitesini araştırmayı amaçladık.

Gereç ve Yöntem: 2005-2014 yılları arasında, ≥70 yaş, ilk seride en az iki kür kemoterapi alan 89 hasta retrospektif incelendi. Hasta özellikleri, prognostik faktörler, tedavi cevabı, grad 3-4 toksisite, progresyonsuz-sağkalım (PSK) ve genel-sağkalım (GS) değerlendirildi.

Bulgular: 89 hastanın 65 (%73)'i erkekti ve medyan yaş 74 (70-84)'dü. Medyan takip süresi 7 ay (min–max:2–57ay), PSK 5 ay (%95GA:3,7–6,3) ve GS 7 ay (%95GA:5,2–8,9)'dı. Hastalık kontrolü %43,8'inde sağlanmasına rağmen %52,2'sinde progresyon görüldü. Tek değişkenli analizde Eastern Cooperative Oncology Group (ECOG) performans skoru, kemoterapi siklusu ve alınan cevap etkindi. Karaciğer metastazı PSK'da, akciğer metastazı ise GS'da etkindi.

Sonuç: Düşük kemoterapi siklusu, akciğer veya karaciğer metastazı ve kötü performans skoru olumsuz prognostik faktörlerdi.

Anahtar Sözcükler: Mide kanseri; Metastaz; Yaşlı; Kemoterapi.

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Introduction

Gastric cancer (GC) is the second leading cause of cancer-related death worldwide and is usually diagnosed at advanced stages. The number of patients aged 65 years and above diagnosed with GC is increasing, although the total incidence of GC is decreasing (1-3). The expected survival time with best supportive care (BSC) is limited to 4–5 months in advanced gastric cancer (AGC). Many combination chemotherapy regimens have been studied in randomized trials and a prolonged survival period up to 7–10 months has been reported for AGC (4-6).

Elderly patients have usually been excluded from or underrepresented in clinical trials; therefore, the efficacy and tolerability of palliative chemotherapy are unclear in these patients (7-9). While deciding the chemotherapy protocol in elderly patients, performance status, mental status, co-morbidity, medical fitness, basic activities of daily living, instrumental activities of daily life, concept of quality of life, home conditions, social support, nutrition, polypharmacy, and cognitive/psychosocial health should be evaluated (10). In planning medical treatment, the chronologic age of a patient does not reflect the physiological age. The assessment of the physiological age involves patient's tolerance to the planned treatment and the estimated life expectancy (11).

No gold standard combination regimen has yet been defined in patients with AGC. The superiority of combination treatments against single agent treatments in AGC patients is well- known (8). A study in 2003 reported that weekly cisplatin, leucoverin, and 5-FU (PLF) chemotherapy was safe and effective in elderly patients with AGC (12). Hematologic toxicities with combination chemotherapies (such as, docetaxel, cisplatin, and 5-FU regimen) are more frequent. In elderly patients, chemotherapy tolerance and safety is not similar to that of the patients under the age of 65; therefore, administration of full-dose combined chemotherapies is more difficult.

Here, we aimed to assess the efficacy and tolerability of first-line palliative chemotherapy in elderly patients (age ≥70 years) with AGC.

Materials and Method

Patients

A total of 89 patients received at least two cycles of systemic chemotherapy as first-line therapy at the Ataturk University Hospital, Erzurum, Turkey between 2005 and 2014 and were retrospectively evaluated.

Inclusion criteria consisted of patients diagnosed with pathologically proven metastatic GC, Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2, disease measurable by imaging, age 70 years and above, and at least two cycles of systemic chemotherapy received as first-line treatment.

Disease and patient characteristics, prognostic factors, treatment response, grade 3–4 toxicity related to treatment, progression free survival (PFS) and overall survival (OS) were evaluated.

Patients were categorized as per the ECOG performance status criteria. Chemotherapy regimens and dosages were adjusted according to the ECOG performance status, clinical findings, laboratory findings, and co-morbidities. All tumor measurements and treatment response evaluations were done after every two or three cycles of chemotherapy using imaging methods and other tests that were initially used to stage the tumor. The treatment response was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines. Toxicity was assessed according to the National Cancer Institute-Common Toxicity Criteria (NCI-CTC) version 3.0 toxicity scale.

We obtained a local ethics committee permission dated 16.10.2015 and number 16 for our study.

Chemotherapy Regimens

The chemotherapy regimens used in our study were weekly DCF (docetaxel 25 mg/m^2 i.v. on days 1, 8, and 15 + cisplatin 25 mg/m^2 i.v. on days 1, 8, and 15 + 5-FU 750 mg/m^2 i.v. on days 1, 8, 15, and every 21 days), modified DCF [docetaxel 40 mg/m^2 i.v. on day 1 + folinic acid (FA) 400 mg/m^2 i.v. on day 1 + 5-FU 400 mg/m^2 i.v. bolus followed by 2000 mg/m^2 46 hours infusion, cisplatin 40 mg/m^2 i.v. on day 3 and every 14 days], ECF (epirubicin 50 mg/m^2 i.v. on day 1 + cisplatin 60 mg/m^2 i.v. on day 1 + 5-FU l,200 mg/m^2 per day i.v. daily continuous infusion, every 21 days), capecitabine–cisplatin (capecitabine 625 mg/m^2 orally twice daily, day1-day21 (D1-D21) + cisplatin 75 mg/m^2 i.v. on day 1, every 21 days), FOLFIRI (irinotecan 180 mg/m^2 i.v. on day 1 + FA 400 mg/m^2 i.v. on day 1 + 5-FU 400 mg/m^2 i.v. bolus followed by 2400 mg/m^2 over 46 hours infusion, every 14 days), mFOLFOX-6 (oxaliplatin 85 mg/m^2 i.v. on day 1, FA 400 mg/m^2 i.v. on day 1 + 5-FU 400 mg/m^2 i.v. bolus followed by 2400 mg/m^2 over 46 hours infusion, every 14 days), XELOX (oxaliplatin 130 mg/m^2 i.v. on day 1 + capecitabine 1000 mg/m^2 oral twice daily, D1–D14, every 21 days), trastuzumab combination chemotherapy (trastuzumab 8 mg/kg



Table 1— Chemotherapy Regimens Used in the Study

	No. of Patients (%)	PFS (months)	95% CI	OS (months)	95% CI
wDCF and mDCF	30 (33.7)	4	1.8-6.1	7	5.9-8.1
DOF	16 (18)	3	0.1-5.8	5	0-12.8
Cisplatin+Capecitabine	8 (9)	4	1.5-6.5	6	4.6-7.3
XELOX	8 (9)	3	1.6-4.3	6	3.3-26
mFOLFOX-6	4 (4.5)	6	1.5-6.5	16	1-30.9
Cisplatin+5-FU	7 (7.9)	5	2.4-7.6	11	0-26
ECF	7 (7.9)			5	2.4-7.6
Trastuzumab combination chemotherapy	4 (4.5)	7	3-11	9	
Capecitabine	4 (4.5)	4	0-15	11	0-28.5
FOLFIRI	1 (1.1)	8		10	

wDCF: weekly Docetaxel, cisplatin, Fluorouracil; mDCF: modified DCF; XELOX: Capecitabine, oxaliplatine; FOLFOX: Oxaliplatine, folinic acide, fluorouracil; ECF: Epirubicine, cisplatine, fluorouracil; FOLFIRI: Irinotecan, folinic acide, fluorouracil.

loading dose and 6 mg/kg maintenance dose with cisplatin 80 mg/m^2 on day 1, plus capecitabine 1000 mg/m^2 orally twice daily, D1–D14, every 21 days or with 5-FU 800 mg/m^2 on D1-D5, every 21 days) (Table 1)

Statistical Analysis

Descriptive statistics were used to describe the demographical and clinical characteristics of the patients, treatment outcome, and incidence of toxicity. χ^2 test was used to determine the relation between categorical variables. PFS was defined as the time from the date of the first administration of chemotherapy to the date of progressive disease or death from any cause. OS was defined as the time from the date of diagnosis to the date of death from any cause. PFS and OS analyses were all estimated using the Kaplan–Meier method. Survival difference was analyzed using the log-rank test.

Multivariate analyses using the Cox proportional hazard regression model were performed to assess the impact of the following variables on PFS and OS: ECOG performance status, metastatic site, and number of chemotherapy cycles. The statistical data were obtained using an SPSS software package (SPSS 22.0 Inc., Chicago, IL, USA) and p values of <0.05 were accepted as significant.

Results

Of the 89 patients, 65 (73%) were males. The median age was 74 (70–84) years. Three patients (3.4%) had diabetes mellitus and 24 (27%) had hypertension. The last date of follow-up was May 1, 2015; till this date, 77 patients (86.5%) had died and 12 patients (13.5%) were still alive. Demographical and clinical characteristics of the patients are shown in Table 2.

Four patients (4.5%) received single drug therapy, 24 patients (27%) received two-drug combination therapy, and 61 patients (68.5%) received three-drug combination therapy as first-line chemotherapy. Chemotherapy regimens are shown in Table 2. The most administered combination was docetaxel, cisplatin, and 5-FU (33.7%).

The median follow-up period was 7 months (min–max: 2–57 months), median time to progression was 5 months (95% CI: 3.7–6.3) and median OS time was 7 months (95% CI: 5.2–8.9). Complete response was observed in one patient (1.1%); partial response and stabilization were observed in 31.5% and 11.2% patients, respectively. The disease was controlled in 43.8%, whereas progression was observed in 56.2% of the patients. In patients with ECOG performance status 0, chemotherapy was more effective compared to those with ECOG performance status 1 and 2, in terms of PFS and OS ($p = 0.001$ and $p = 0.001$, respectively). There was no significant difference between the chemotherapy regimens in terms of PFS and OS ($p = 0.74$ and $p = 0.59$, respectively), hematological toxicities ($p > 0.05$ for all), and response rates ($p = 0.88$). Furthermore, there was no significant difference between dublets and triplet drugs in terms of hematological toxicities ($p > 0.05$ for all) and response rates ($p = 0.93$).

In univariate analysis, ECOG performance status, number of chemotherapy cycles, and response to the first-line chemot-

Table 2— Demographical and Clinical Characteristics of the Patients

	No. of patients (n=89)	%
Gender		
Male	65	73
Female	24	27
ECOG		
0	7	7.9
1	48	53.9
2	34	38.2
Age		
70-74	52	58.4
74-79	23	25.8
≥80	14	15.7
Location		
Cardia	52	58.4
Corpus	11	12.4
Antrum	16	18.0
Diffuse	10	11.2
History of operation		
Yes	12	13.5
No	77	86.5
History of adjuvant chemotherapy		
Yes	6	6.7
No	83	93.3
Metastasis		
Liver	59	66.3
Lung	18	20.2
Bone	8	9.0
Peritoneal	29	32.6
Brain	1	1.1
Metastatic lesions		
1	66	74.2
2	20	22.5
3	3	3.4
Chemotherapy cycles		
2-3	35	39.3
4-6	48	53.9
<6	6	6.7
Chemotherapy regimen		
One drug	4	4.5
Two drugs	24	27
Three drugs	61	68.5
Response to chemotherapy		
Complete response	1	1.1
Partial response	28	31.5
Stable disease	10	11.2
Progressive disease	50	56.2
Last status		
Dead	77	86.5
Alive	12	13.5

herapy had an effect on PFS and OS, whereas liver metastasis effected only on PFS and lung metastasis effected only on OS (Table 3).

Multivariate analysis revealed that PFS and OS were not significantly associated with ECOG performance status (p=0.122 and p=0.747, respectively). Decreased PFS was significantly associated only with decreased number of chemotherapy cycles (p < 0.001), whereas decreased OS was significantly associated with lung metastasis and decreased number of chemotherapy cycles (p=0.003 and p<0.001, respectively) (Table 4).

Among patients with grade 3–4 toxicity; 19.1% had neutropenia; 12.4% had anemia; and 4.5% had thrombocytopenia and non-hematologic toxicities, including renal toxicity (2.2%), neuropathy (2.2%), cardiotoxicity (2.2%), and allergic reactions (1.1%) (Table 5).

Discussion

Gastric cancer is usually diagnosed at advanced stages and 60% of the patients are above 65 years of age (13). The elderly population has been increasing in recent years, and treatment responses are not well-known, particularly in patients aged 70 years and above who have metastatic GC. Randomized trials have shown that combined systemic chemotherapy is superior to BSC in patients with metastatic GC (4-6). However, these studies included patients younger than 65 years of age.

The prevalence and the incidence of adenocarcinoma of the lower esophagus and of the stomach increase with age. The biology of these tumors may not change with age, but due to an increased risk of treatment-related complications and a reduced life expectancy, the benefits of chemotherapy may decline. It was recommended that the treatment of patients aged ≥70 years with these malignancies be personalized based on the risk of complications and life expectancy (14).

In our study, median age of patients was 74 (70-84) years. Age groups were not associated with PFS and OS, which was similar to the literature findings of Z. Lu et al. (15) on patients with advanced or metastatic GC among the elderly population.

In our study, palliative chemotherapy was at least as effective as to those in the medical literature in patients less than 65 years old; OS was 1–2 months shorter, but PFS was similar. OS was longer than that of patients who received BSC as reported in literature findings (4, 16). Toxicity was generally mild in all the study patients.



Table 3— Univariate Analysis of Clinicopathological Factors and Treatments in Elderly Patients with Metastatic Gastric Cancer (PFS and OS)

PFS (months)		95% CI	p	OS (months)	95% CI	p	
Gender							
	Male	5	3.8-6.2	0.36	7	5.9-8.1	0.38
	Female	6	2.6-9.4		8	2.1-14	
ECOG							
	0	13	0-31.5	**0.001**	24	8-40	**0.001**
	1	6	4.2-7.8		10	7.1-13	
	2	3	2.3-3.7		6	4.4-7.6	
Age							
	70-74	5	2.7-7.3	0.51	9	4.9-13	0.21
	74-79	4	1.8-6.2		6	4.6-7.4	
	≤80	2	0.5-3.5		4	0-8.9	
Location							
	Cardia	4	2.7-5.3	0.6	7	4.9-9.1	0.99
	Corpus	7	2.7-11		7	0-14.9	
	Antrum	3	0-8.9		6	0-15.8	
	Diffuse	3	0.8-5.9		8	0.3-16	
History of operation							
	Yes	3	0-6.4	0.74	4	0.6-7.4	0.13
	No	5	3.7-6.3		8	5.1-7.4	
History of adjuvant chemotherapy							
	Yes	3	0-9	0.54	4	0-10	0.44
	No	5	3.8-6.2		7	4.3-9.7	
Metastasis							
	Liver	4	2.9-5.1	**0.036**	7	5.1-8.7	0.48
	Lung	4	1.5-6.5	0.62	5	2.2-7.8	**0.01**
	Bone	7	3.4-11	0.49	8	2.1-14	0.73
	Peritoneal	6	2.7-9.3	0.13	12	5.9-18	0.27
	Brain	3	3	0.38	6	6	0.52
Metastatic lesions							
	1	5	3.5-6.5	0.52	8	5.5-11	0.37
	2	3	0-6.1		5	2.1-7.9	
	3	2	0.4-3.6		2		
Chemotherapy cycles							
	2-3	2	1.5-2.5	**<0.0001**	4	3.3-4.7	**<0.0001**
	4-6	8	6.7-9.3		12	9.9-14	
	<6	8	1.3-15		16	8.5-23	
Chemotherapy regimen							
	One drug	4	0-15.7	0.38	7	0-28	0.19
	Two drugs	4	2.2-5.8		6	4.8-7.2	
	Three drugs	5	3-7		8	5.6-10	
Response of chemotherapy							
	Complete response	26	26	**<0.0001**	57	57	**<0.0001**
	Partial response	13	10-16		13	1.4-10	
	Stable disease	6	0.8-11		14	9.8-18	
	Progressive disease	3	2.3-.37		5	3.8-6.2	

Table 4— Multivariate Analysis of Clinicopathological Factors and Treatments in Elderly Patients with Metastatic Gastric Cancer (PFS and OS)

	PFS		OS	
	HR (95% CI)	p	HR (95% CI)	p
ECOG				
0	1 (reference)	0.122	1 (reference)	0.747
1	2.008 (0.697-5.783)		1.104 (0.423-2.884)	
2	2.903 (0.947-8.899)		1.329 (0.476-3.714)	
Metastasis				
Liver	1.198 (0.716-2.005)	0.49		**0.003**
Lung			2.387 (1.332-4.281)	
Chemotherapy cycles				
2-3	1 (reference)	<0.001	1 (reference)	**<0.001**
4-6	0.138 (0.070-0.269)		0.216 (0.121-0.386)	
6<	0.112 (0.038-0.325)		0.152 (0.044-0.528)	

Table 5— Grade 3-4 Hematologic and Non-hematologic Toxicities (National Cancer Institute Common Toxicity Criteria, Version 3.0)

	No. of patients (%)
Hematologic toxicities	
Neutropenia	17 (19.1)
Anemia	11 (12.4)
Thrombocytopenia	4 (4.5)
Febrile neutropenia	1 (1.1)
Non-hematologic toxicities	
Renal toxicity	2 (2.2)
Neuropathy	2 (2.2)
Cardiotoxicity	2 (2.2)
Allergic reactions	1 (1.1)

Various chemotherapy agents (single or combination) have been studied in patients with AGC since 1970; however, the median survival still remains between 6 and 9 months (17). In a study performed by Choi IS et al. (18) in 2007, oxaliplatin 100 mg/m^2, FA 100 mg/m^2 and 5-FU 2400 mg/m^2 (46 hours infusion) every 2 weeks regimen in elderly patients with AGC showed an overall response rate of 41.2%, a PFS of 5.7 months (95% CI: 4.2–6.3 months), and an OS of 9.8 months (95% CI: 4.4–12 months). Also grade 3–4 neutropenia was observed in 8.1% of the patients. They suggested that oxaliplatin/5-FU/FA had good efficacy and acceptable toxicity profile in this group.

Similarly, Zhao et al. (19) showed that the modified FOLFOX regimen is well-tolerated for elderly patients older than 65 years as first-line chemotherapy for AGC. The overall response rate was 45.6% (95% CI: 31–61%), median time to progression was 6.2 months (95% CI: 4.6–7.8), and median OS was 9.8 months (95% CI: 8.2–11.4). Grade 3 toxicity included neutropenia (8.7%), vomiting (4.3%), nausea (4.3%), and diarrhea (2.2%). In a phase II study by Santini et al. (20) comprising 42 chemotherapy-naïve patients aged 70 years or above who had locally advanced and metastatic GC, a regimen of weekly oxaliplatin 40 mg/m^2, 5-FU 500 mg/m^2, and FA 250 mg/m^2 was used. The response rate was 45.2%, the median time to disease progression was 5.0 months, and the median survival time was 9.0 months. Grade 3–4 neutropenia was 4.8% and the regimen was well-tolerated. In addition, Liu et al. (21) showed similar results with modified FOLFOX-4 regimen, and they declared that this was a well-tolerated and an active combination for elderly patients with AGC who were ≥65 years old.

In a study by Dong et al. (22), it was shown that XELOX was active and well-tolerated by elderly patients. Thus, it may be a good therapeutic option as first-line chemotherapy in AGC because of its easy administration. Median follow-up period was 9.5 months, median time to progression was 5.6 months (95% CI: 4.6–6.6), and OS was 9.8 months (95% CI: 7.4–12.2). Grades 3–4 adverse events included neutropenia (13.6%), thrombocytopenia (11.4%), anemia (2.3%), diarrhea (13.6%), hand-foot syndrome (9.1%), nausea, and vomiting (4.5%).



The phase III V325 trial comparing cisplatin and 5-FU with DCF as a first-line therapy showed that DCF should be reserved only for fit elderly patients because of a higher incidence of toxicity in AGC (23). In our study, the toxicity profile was found to be similar to that of other chemotherapy regimens because none of the patients had received standard DCF.

Elderly patients' have specific clinicopathological characteristics. Lu et al. (24) reported that body mass index, Karnofsky performance score, number of metastatic lesions, ascites, tumor differentiation grade, lactate dehydrogenase (LDH) activity, chemotherapy, and local treatment were independent prognostic factors. Serum LDH activity was superior to the serum carcinoembryonic antigen level for the prognosis of advanced or metastatic GC in elderly patients. Body mass index, Karnofsky performance score, and a well-differentiated histopathology were the factors favoring longer survival, whereas a greater number of metastatic lesions and elevated serum LDH activity were associated with poor prognosis among the studied elderly patients.

Univariate analysis of our study showed that ECOG performance status, number of chemotherapy cycles, and response to first-line chemotherapy had an effect on PFS and OS. We found that in patients with ECOG performance status 0, OS was longer than the patients with ECOG status 1 and 2. Moreover, liver metastasis was associated with poorer PFS, whereas having lung metastasis was associated with poorer OS. Multivariate analysis showed that decreased PFS was significantly associated with decreased number of chemotherapy cycles only, whereas decreased OS was significantly associated with both lung metastasis and decreased number of chemotherapy cycles.

While deciding chemotherapy administration in patients with metastatic GC who are ≥70 years old, parameters of physiological age, such as ECOG performance status, should be considered rather than the chronological age. It is reported that combined chemotherapy regimens are superior to single agents in patients younger than 65 years old. However, in our study, we found that preferred treatment regimen, drug numbers, and dose reduction had no effect on OS. This might be due to the low number of patients in the chemotherapy groups. While planning chemotherapy in patients aged ≥70 years, physiological age and co-morbidities of the patient should be considered. The treatment should be personalized based on the risk of complications and life expectancy. Possible minimally toxic single or combined regimens can be administered with dose reductions if necessary.

Main limitations of our study are its retrospective origin, low number of patients in the chemotherapy groups, and having no comparative control groups.

Conclusion

We found that PFS time and tolerability in our geriatric population was similar to those reported in the previous studies conducted among populations less than 70 years of age. Having fewer cycles of chemotherapy, lung metastasis, liver metastasis, and ECOG performance status 1 and 2 were found to be poor prognostic factors. We believe that physiological rather than the chronological age of the patient is the main factor to be considered during treatment planning in a geriatric population. In future, large phase III clinical trials should be designed for elderly patients taking into account their various physiological profiles.

Compliance With Ethical Standards

Disclosure of Potential Conflicts of Interest: The authors declare that they have no conflict of interests.

Ethical Approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. We have obtained a local ethics committee permission dated 16.10.2015 and number 16 for our study.

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RESEARCH

HEMATOLOGIC PARAMETERS IN GERIATRIC PATIENTS WITH IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

ABSTRACT

Introduction: To assess the validity of complete blood count (CBC) parameters in the diagnosis and prognosis of idiopathic sudden sensorineural hearing loss (ISSNHL) in geriatric patients.

Material and Method: Sixty-two patients (women, 36; men, 26; mean age of all patients, 51±19 years) with ISSNHL were included in our study, and 49 healthy volunteers (women, 33; men, 16; mean age of all volunteers 48.6 ± 16.2 years) with no history of audiologic complaints or diseases formed the control group. Subjects in both the control and study groups were further divided into two groups according to their ages (<65 years and ≥65 years). CBC results were evaluated. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated.

Results: NLR and PLR values in patients diagnosed with sudden hearing loss were much higher compared to those in the control group. However, in geriatric patients, there was no difference in NLR and PLR between the study and control groups. There was also no difference in mean platelet volume (MPV) levels between the control and study groups at all ages. Red cell distribution width (RDW) was higher in both geriatric and non-geriatric patients with ISSNHL compared with the control group. When NLR, LPR, MPV, and RDW of patients with ISSNHL were compared between those who responded and those who did not respond to the standard treatment, there was no significant difference between the groups.

Conclusion: NLR, PLR, and RDW are increased in ISSNHL patients aged <65 years but only RDW is increased in geriatric patients with ISSNHL.

Key Words: Geriatrics; Hearing Loss, Sudden; Lymphocyte; Mean Platelet Volume; Neutrophils; Erythrocyte Indices.

ARAŞTIRMA

ANİ İDİOPATİK SENSORİNÖRAL İŞİTME KAYBI OLAN GERİATRİK HASTALARDA HEMATOLOJİK DEĞERLER

ÖZ

Giriş: Ani idiopatik sensorinöral işitme kaybı olan geriatrik hastaların tanı ve prognozunu değerlendirimede tam kan sayımı değişkenlerinin geçerliliğini belirlemek

Gereç ve Yöntem: Ani idiopatik sensorinöral işitme kaybı olan 62 hasta (36 kadın, 26 erkek; yaş ortalaması: 51±19) çalışma grubu ve tamamen sağlıklı, herhangi bir odyolojik şikayeti ve hastalığı olmayan 49 gönüllü (33 kadın, 16 erkek; yaş ortalaması: 48,6±16,2 yaş) kontrol grubunu oluşturmak üzere araştırmamıza katıldı. Çalışma ve kontrol grubunda yer alan katılımcılar yaş aralıklarına göre (<65 yaş ve ≥65 yaş olmak üzere) iki gruba daha ayrıldı. Tam kan sayımı sonuçları değerlendirildi. Nötrofil lenfosit oranı (NLR) ve Platelet lenfosit oranı (PLR) hesaplandı.

Bulgular: Çalışma grubundaki hastalarda kontrol grubuna oranla NLR ve PLR oranlarında belirgin bir artış gözlenmiştir. Ancak; geriatrik hastalarda NLR ve PLR sonuçlarında çalışma ve kontrol grubu sonuçlarında farklılık gözlenmemiştir. Ortalama platelet hacmi (MPV) seviyelerinde de kontrol ve çalışma grubu sonuçları bütün yaş gruplarında karşılaştırıldığında farklılık görülmemiştir. Kırmızı hücre dağılım genişliği (RDW) ise geriatrik ve geriatrik olmayan ani idiopatik işitme kayıplı hastalarda kontrol grubuna oranla yüksek bulunmuştur. Çalışma grubunda NLR, PLR, MPV ve RDW sonuçları tedaviye cevap veren ve vermeyen hastalarda karşılaştırıldığında faklılık bulunmadı.

Sonuç: NLR, PLR ve RDW değerleri ani idiopatik sensorinöral işitme kaybı olan <65 yaş olan hastalarda yüksek bulundu; ancak sadece RDW değeri ani idiopatik sensorinöral işitme kaybı olan geriatrik hastalarda yüksek bulundu.

Anahtar Sözcükler: Geriatri; İşitme Kaybı; Lenfosit; MPV; Nötrofil; RDW.

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Introduction

Sudden sensorineural hearing loss (SSNHL) is defined as sensorineural hearing loss of 30 decibels (dB) or more, over a minimum of 3 consecutive audiometric frequencies, occurring within a 72-hour period (1,2). It has been shown to affect 0.005%–0.02% of the population per year (3). SSNHL with no identifiable cause despite adequate investigations is termed idiopathic sudden sensorineural hearing loss (ISSNHL) (2).

Neutrophils, lymphocytes, and platelets are important blood cell elements. Platelets are crucial for coagulation, thrombosis, inflammation, and atherosclerosis (4). MPV (mean platelet volume) is a blood marker related to the function and activation of platelets (5) and is also a marker of atherosclerosis, suggesting that it is an important prophylactic and diagnostic tool in thrombotic and prothrombotic cases (6).

The red cell distribution width (RDW) is a routine laboratory parameter that indicates the variability in the size of circulating erythrocytes. The main area in which RDW is used is in the differential diagnosis of microcytic anemia. It has been defined as a prognostic tool in different clinical conditions, such as cardiovascular diseases and pulmonary artery hypertension (7). It has also been reported as an important predictor of mortality in the general population and older adults (8).

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been defined as novel markers of inflammation and thrombotic events, which can be easily measured from the complete blood count (CBC) (9). SSNHL, Bell's palsy, and vestibular neuritis are certain pathological conditions that have been found to be related to NLR and PLR in otolaryngological practice (10-12). However, some studies have confounding results about this issue (13).

In the literature, we did not come across any study delineating the correlation between inflammatory and thrombotic parameters of CBC such as NLR, PLR, MPV, and RDW with the diagnosis and prognosis of ISSNHL in geriatrics. For this reason, we grouped ISSNHL patients and healthy volunteers according to their ages (<65 years old and >65 years old) and compared their CBC results.

Materials and Method

The present study was approved by the Institutional Review Board of the Ufuk University Medical School with decision number 30042015-7. All patients signed informed consent forms before participating in the study.

Patient Selection

Patients with a decrease in hearing ≥30 dB, affecting at least 3 consecutive frequencies within a 72-hour period or less, were considered as having SSNHL. Patients having vestibular schwannoma, stroke, malignancy, recent acoustic trauma, history of migraine, severe head trauma, usage of ototoxic medications, type 1 or 2 diabetes mellitus, hypertension, renal failure, or vertigo at the beginning of the disease were excluded from study. Patients with fluctuating hearing loss, isolated low frequency hearing loss were also excluded from study.

These patients and age- and sex-matched healthy volunteers were then divided into two groups according to their ages. Patients and healthy volunteers aged ≥65 years old formed the geriatric group while participants aged <65 years old formed the non-geriatric group.

Subjects were divided into four groups according to their ages: Group 1 comprised patients with ISSNHL aged <65 years old (36 patients; mean age 37.1±11.8 years); Group 2 comprised patients with ISSNHL aged ≥65 years (26 patients; mean age 70.2±5.8 years); Group 3 comprised healthy volunteers <65 years (32 patients; mean age 38.2±8.7 years); and Group 4 comprised healthy volunteers ≥65 years (17 patients; mean age 68.3±2.5 years). Groups 1 and 2 formed the study groups, while groups 3 and 4 formed the control groups.

All study participants underwent the tests outlined below.

Laboratory Measurements

Blood samples for biochemical parameters were taken after a minimum of an 8-hour overnight fast. CBC parameters of the blood samples were simultaneously measured and analyzed with a hematology analyzer (CELL-DYN Ruby Hematology System, Illinois, USA). Hemoglobin, erythrocyte, leukocyte, neutrophil, lymphocyte, RDW, platelet counts, and MPV results of all the participants were evaluated by obtaining the samples of all patients included in the study before the treatment. Subsequently, NLR (neutrophil-to-lymphocyte ratio) and PLR (platelet-to-lymphocyte ratios) values were calculated.

Audiological Examination

After middle ear pathologies were excluded by otologic examination and tympanometry (AZ 26 Clinical Audiometer; Interacoustics, Assens, Denmark), pure tone audiometry was performed (AC 33 Clinical Audiometer; Interacoustics, Assens, Denmark) in a totally isolated cabin between 250–8000 Hz frequencies. Pure tone average (PTA) was established as the simple arithmetic mean for frequencies of 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz. The speech



discrimination scores (SDS) were also obtained. SDS measured by 50 selected monosyllabic words at an easily detectable hearing level and the percentage of words correctly identified was calculated.

Hearing thresholds were noted at the onset of treatment and in the second week and the sixth month of treatment. Improvement of hearing (recovery) was defined as return to within 10 dB of the unaffected ear or >10dB improvement in PTA or 15% recovery in SDS. "No recovery" was defined as <10 dB improvement in PTA (2).

Pretreatment audiograms were categorized into four sensorineural types: upsloping, downsloping (falling curve), mid-frequency (flat or U-shaped curve), and profound loss (a flat audiogram with a threshold shift >90 dB in all frequencies). The upsloping (raising) curve was not included in this study because patients with upsloping curves also had vertigo at onset of ISSNHL.

Treatment Strategy

Oral prednisone (1 mg/kg; maximum dose 60 mg/day) in a single dose for 14 days was administered as the initial therapy for patients with ISSNHL[2]. Hyperbaric oxygen therapy was offered to patients with ISSNHL if there was no response to treatment within 3 months.

Statistical Analysis

The analysis of the results was performed using IBM SPSS Statistics (Armonk, New York, USA) version 21.0 software for Windows. Data were tested for normal distribution using the Kolmogorov–Smirnov test. To investigate the differences between groups, Mann–Whitney U test was used for two groups and Kruskal–Wallis H test for >2 groups. Chi-square test was performed for categorical variables. Post-hoc comparisons with Conover's multiple comparison test was used. Statistical significance was defined as $p<0.05$.

Results

Subjects

After 18 patients were excluded (3 patients had vertigo at the onset of hearing loss, 2 had a history of previous sudden hearing loss, 2 had bilateral sudden hearing loss, 6 had diabetes mellitus, and 5 had atherosclerotic vascular disease), 62 patients [36 (58.1%) women; mean age of all patients 51±19.0 years (range: 21–83 years)] were included in this study. Forty-nine healthy volunteers [33 (67.3%) women; mean age of all volunteers 48.6±16.2 years (min–max: 26–72 years)] who had no history of audiologic complaints or diseases formed the control group. There was no significant difference between the study and control groups in terms of gender and age ($p=0.32$ and $p=0.52$, respectively).

The demographics of the study and control groups are shown in Table 1.

Table 1— Demographics, Hemogram, Plasma Lipid Profiles, C-reactive Protein (CRP), Erythrocyte Sedimentation Rates (ESR), NLR, and PLR Values of the Study and Control Groups.

	Study Group [mean(sd)] (n=62)	Control Group [mean(sd)] (n=49)	p
Gender M/F (Female %)	26/36 (58.1 %)	16/33 (67.3 %)	0.32
Age	51 (19)	49 (16.2)	0.519
Cholesterol (mg/dL)	198 (46.6)	193.3 (46.6)	0.601
LDL (mg/dL)	120.4 (36)	116.6 (35.6)	0.585
HDL (mg/dL)	45.3 (11.7)	48.8 (11.2)	0.115
TG (mg/dL)	139.2 (79)	117.5 (59)	0.103
CRP (mg/dL)	3 (3.3)	3.1 (3.3)	0.820
ESR	2 (1.1)	2.3 (1.3)	0.267
Hb (g/dL)	14 (1.6)	14.3 (1.6)	0.389
White Blood Cell (10^3/µL)	7.2 (1.4)	7 (1)	0.127
Neutrophil (10^3/µL)	5 (1.8)	4 (1.5)	0.002
Lymphocyte (10^3/µL)	2 (0.8)	2.1 (0.6)	0.298
Platelet (10^3K/ µL)	234 (53.5)	236 (39)	0.840
Mean Platelet Volume (fL)	8.1 (1.2)	8.4 (1.2)	0.172
RDW (%)	13.4 (1.8)	14.7 (2.2)	0.001
NLR	3.1 (2.4)	2 (0.8)	0.002
PLR (10^3)	143 (83)	118 (31.2)	0.032

(LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; Hb: Hemoglobin; CRP: C-reactive protein; RDW: Red cell distribution width)

Table 2— NLR and PLR Values of Young Patients (<65 years old) in the Study (Group 1) and Control (Group 3) Groups.

	Group 1 [mean(sd)] (n=36)	Group 3 [mean(sd)] (n=32)	p
Gender M/F (Female %)	16/20 (55.6 %)	9/23 (71.9 %)	0.164
Age	37 (11.8)	38.2 (8.7)	0.635
Cholesterol (mg/dL)	190.7 (46.9)	189 (45.9)	0.880
LDL (mg/dL)	117.3 (36.3)	111.1 (35.4)	0.479
HDL (mg/dL)	44.2 (11.4)	51.7 (12)	0.222
TG (mg/dL)	136.5 (89.2)	110.3 (55.5)	0.157
CRP (mg/dL)	2.9 (3.8)	3.4 (3.9)	0.561
ESR	1.9 (1)	2.3 (1.3)	0.161
Hb (g/dL)	14.2 (1.9)	14.2 (1.6)	0.962
White Blood Cell (10^3/μL)	7.4 (1.4)	6.7 (0.7)	0.001
Neutrophil (10^3/μL)	5.2 (1.9)	3.8 (0.8)	< 0.001
Lymphocyte (10^3/μL)	1.9 (0.8)	2 (0.5)	0.954
Platelet (10^3K/ μL)	241 (56)	238 (33)	0.829
Mean Platelet Volume (fL)	7.9 (1.3)	8.3 (1.2)	0.162
RDW (%)	13.5 (2.03)	14.6 (2.2)	0.04
NLR	3.3 (2.8)	2.7 (2.2)	0.010
PLR (10^3)	149 (63)	137 (64)	0.042

(LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; Hb: Hemoglobin; CRP: C-reactive protein; RDW: Red cell distribution width)

Audiologic Test Results

Audiologic test results in terms of PTA and SDS in control and study groups before treatment are shown in Table 2. In the study groups, 35 (56.5%) patients had ISSNHL in the left ear and 27 (43.5%) in the right ear. Pretreatment audiogram types in the study groups were as follows: type 1 (upsloping) in 4 (6.5%) patients; type 2 (downsloping) in 10 (16.1%) patients; type 3 (U shaped) in 38 (61.3%) patients; and type 4 (profound loss) in 10 (16.1%) patients. There was no statistically significant difference between the study and control groups with respect to the side affected and type of audiograms (p=0.50 and p=0.13, respectively).

Laboratory Measurement Results

Hemogram, plasma lipid profiles, C-reactive protein (CRP), erythrocyte sedimentation rates (ESR), RDW, MPV, NLR, and PLR values and demographics are shown in Table 1, 2 and 3. In young patients, NLR, PLR and RDW significantly differed between ISSNHL and control groups (Table 2) while only RDW was significantly higher in ISSNHL group in elderly patients (Table 3).

Treatment Response Results

In the study groups (Groups 1 and 2), 26 (41.9%) patients were responsive to oral steroid treatment, and 7 (19.4%) of 36 patients who were unresponsive to oral steroids were responsive to hyperbaric oxygen treatment. Thus, in the study groups, 29 patients (46.8%) were unresponsive to treatment, while 33 (53.2%) patients were responsive to treatment. In addition, response and non-response to oral steroid therapy was evaluated among the two age groups of ISSNHL patients. In Group 2 (elderly group), 10 (38.5%) patients were responsive to oral steroid treatment, while 16 (61.5%) patients were not responsive. In Group 1, 44% of patients were responsive to oral steroid therapy, while 56% were unresponsive. When ages of patients with ISSNHL were compared between those responsive and unresponsive to both oral steroid and hyperbaric oxygen treatments, no significant difference was found between groups (p=0.14).

Treatment response did not change based on the side of the ear with hearing loss (p=0.85). However, there was a relationship between the audiogram type and response to treatment; 68.4% of patients with U-shaped audiograms were responsive to treatment, but no patient with profound hearing loss was responsive to treatment (p=0.001).



Table 3— NLR and PLR Values of Elderly Patients in the Study (Group 2) and Control (Group 4) Groups

	Group 2 [mean(sd)] (n=26)	Group 4 [mean(sd)] (n=17)	p
Gender M/F (Female %)	16/10 (61.5 %)	10/7 (58.8 %)	0.565
Age	70 (5.8)	68.3 (2.5)	0.923
Cholesterol (mg/dL)	208 (41.9)	201.5 (48.1)	0.969
LDL (mg/dL)	124.7 (35.8)	127.1 (34.7)	0.996
HDL (mg/dL)	47 (12.1)	43.4 (7.2)	0.750
TG (mg/dL)	144.1 (63.5)	130.8 (64.6)	0.932
CRP (mg/dL)	3.1 (2.5)	2.6 (1.4)	0.950
ESR	2.2 (1.1)	2.2 (1.3)	0.981
Hb (g/dL)	13.8 (1.3)	14.4 (1.4)	0.577
White Blood Cell (10^3/µL)	6.8 (1.4)	7.4 (1.2)	0.404
Neutrophil (10^3/µL)	4.5 (1.6)	4.4 (2.2)	0.997
Lymphocyte (10^3/µL)	2 (0.8)	2.3 (0.5)	0.341
Platelet (10^3 K/ µL)	224 (49)	230 (49)	0.976
Mean Platelet Volume (fL)	8.2 (1.2)	8.4 (1.2)	0.960
RDW (%)	15 (2.4)	13.2 (1.5)	0.015
NLR	2.7 (1.8)	2 (1)	0.562
PLR (10^3)	134 (84)	103 (28)	0.409

(LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; Hb: Hemoglobin; CRP: C-reactive protein; RDW: Red cell distribution width)

When NLR, LPR, MPV, and RDW of patients with ISSNHL were compared between the patients responsive and unresponsive to both oral steroid and hyperbaric oxygen treatments, no significant difference was found between groups (p=0.96; p=0.22; p=0.45; p=0.98, respectively).

Discussion

The major finding of this prospective clinical study is that in geriatric ISSNHL patients, only RDW values were increased and were significantly different from those of healthy volunteers. NLR and PLR values did not differ between the geriatric populations of both the control group and ISSNHL patients. Moreover, none of the parameters including NLR, PLR, MPV, and RDW predicted the prognosis of the disease in geriatric patients.

The etiopathogenesis of ISSNHL is not yet clearly understood, although many theories including infections, blood disorders, vascular pathologies, immune disorders, ototoxic drugs, and metabolic conditions have been reported to explain the pathophysiology of ISSNHL (14). Therefore, both inflammatory and thrombotic markers are being investigated to explain the cause of ISSNHL and to plan treatment strategy.

NLR is an easily available and inexpensive method of diagnosing inflammatory diseases in geriatric patients. A recent study in which 43 patients over 65 years of age were recruited revealed higher NLR values that were related with acute appendicitis (15). In addition, in 242 geriatric patients with type 2 diabetes, Ozturk et al. showed that increased NLR values were associated with microvascular complications (16). A larger study with 507 patients has shown that geriatric patients with coronary artery disease have higher NLR values (17). There are many studies pertaining to ISSNHL disease in non-geriatric patients showing that NLR values were significantly higher in sensorineural hearing loss than in the control group. Similarly, mean NLR was higher in non-responsive patients when compared with responsive patients. A significant correlation was observed between NLR values and the severity of hearing loss, indicating the presence of inflammation (7,13).

Similarly, PLR is also an inflammatory marker that is inexpensive to study. NLR and PLR are among the laboratory markers introduced into clinical practice for the purpose of evaluating systemic and subclinical inflammation (18). Previous studies showed that in various diseases, PLR value could be used as an inflammatory marker and correlated with poor prognosis (19). Besides cardiovascular diseases, the studies about ISSNHL showed similar findings (20). However, some authors believe there is not enough evidence and that

these results may be affected by other patient comorbidities and the inflammatory process of the disease (14). However, there was no study in the literature about PLR in geriatric patients.

MPV reflects the size of platelets and can be used as a marker for high platelet activity, which plays an active role in the pathophysiology of thrombosis, coagulation, and atherosclerosis. Previous studies have controversial results about MPV values in ISSNHL patients. The studies conducted by Karlı et al. (5) and Kum et al. (7) found no significant difference in MPV between the study and control groups in contrast to the findings of Ulu et al. (21) and Sagit et al. (22). However, no study has been reported concerning MPV in geriatric patients as yet.

To our knowledge, our study is the first study in the literature which assessed NLR, PLR, and MPV in geriatric ISSNHL patients. In this study, we did not find any difference in NLR, PLR, and MPV in geriatric patients with ISSNHL. These findings could have been affected by the exclusion of patients with comorbidities, such as diabetes mellitus and hypertension, which could influence the results. In addition, we found higher NLR and PLR values in the study group than in the control group in the younger population in this study, and this was similar to the results of some other manuscripts in the literature (12,13). This difference between young and old patients in NLR and PLR values may be explained by the increased incidence of atherosclerosis in elderly patients without any known disease. As asymptomatic atherosclerosis may also change the inflammatory parameters, the increase in these parameters in ISSNHL group may be masked by the presence of asymptomatic atherosclerosis in the control group. Another explanation to our findings may be the altered inflammatory response of the elderly patients to different conditions, i.e. ISSNHL in our study.

In the current study, we did not find relationship between NLR, PLR, MPV values and treatment response, and we assume that the cause of this finding could be the small sample size of our study.

Increased RDW values have been reported to be related with underlying chronic inflammation which promotes red blood cell membrane deformability and changes in erythropoiesis (23). However, RDW can be considered as a dynamic variable with rapid changes associated with acute disease states, such as acute myocardial infarction and acute decompensated heart failure (24). Wen et al. believe that RDW is associated with the presence of carotid plaque and carotid intima–media thickness (IMT) and is therefore related with stroke (25). In the literature, only Yasan et al. studied RDW in ISSNHL; they did not find any difference between the study and control groups. It must be noted that the control group of the study included patients with indication for septoplasty, and hence, the RDW results of the control group may not represent healthy individuals. In this study, higher RDW levels were observed in ISSNHL patients than in controls for all ages. The singular parameter which could be used in the diagnosis of ISSNHL in geriatric patients was RDW. The mechanism of the association between increased RDW and ISSNHL is unclear; however, some theories, such as inflammatory and thrombotic processes, causing impaired erythropoiesis could be postulated. However, studies about the relationship between SSNHL and RDW must be conducted to precisely determine the mechanisms involved.

There are several limitations of the study. First of all, the sample size of the study was small because it was a single-center study. In addition, it was a prospective study conducted over a relatively short period. Besides, other parameters related with inflammatory and thrombotic involvement may be studied to explore the significant findings; however, studying these parameters may increase incur higher expenses.

In conclusion, we investigated CBC parameters in the diagnosis and prognosis of geriatric ISSNHL patients in the current study. The single parameter of CBC count affected in geriatric patients was RDW, and the other parameters, including NLR, PLR, and MPV, should not be used for diagnosis in geriatric ISSNHL patients.

Conflict of Interest

All authors have no conflict of interest to declare.

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TREATMENT OF INTERTROCHANTERIC FRACTURES IN AMBULATORY ELDERLY; BIPOLAR HEMIARTHROPLASTY OR PROXIMAL FEMORAL NAIL ?

ABSTRACT

Introduction: The management of intertrochanteric fractures in elderly is challenging because of difficult anatomical reduction, poor bone quality and difficulty in weight bearing. Various internal fixation devices can be used for this type of fractures, and primary arthroplasty is also an option for treatment. This retrospective study compares bipolar hemiarthroplasty (BHA) with proximal femoral nail (PFN) in ambulatory elderly patients, focusing on functional results and return to premorbid level of activity.

Materials and Method: The study included 136 patients who underwent operations to treat AO 31-A type intertrochanteric fractures. Patients who were not ambulatory before having fracture were excluded from the study. Of the 78 patients with 31-A1 fractures; 40 were treated with BHA, 33 were treated with PFN and 5 were treated with dynamic hip screw (DHS). Forty patients had 31-A2 type fractures; 24 were treated with BHA, 7 were treated with PFN, 5 were treated with DHS and 4 were treated with different plate-screw systems. Eighteen patients had 31-A3 type fractures; 2 were treated with BHA, 15 were treated with PFN, and 1 was treated with a plate-screw system. Patients with BHA (mean age 80.61 years; range 68-98 years) and PFN (mean age 77.59 years; range 58-94 years) were compared in the final evaluation if they had at least 1 year of follow up documented postoperatively.

Results: Total perioperative blood loss was significantly lower in patients treated with PFN (590 to 390 ml). Time to surgery (4.1 vs 3.9 days), postoperative weight bearing time (2 vs 2 days), and mortality rates (16.66 % vs 18.18%) did not differ between patients treated with BHA and PFN, respectively. Total complication rate (22.4 % vs 28.2 %) was lower, and the duration of surgery (52.8 vs 82.5 min), the time to return to the premorbid daily activity (6.2 vs 8.5 weeks), Harris score (85.8 vs 81.3) and Postel Merle D'Aubigne (PMA) score (14.1 vs 12.2) were significantly better with BHA .

Conclusion: Hemiarthroplasty is not associated with greater postoperative mortality compared with osteosynthesis, although the perioperative blood loss is significantly higher. However, the complication rates are lower and functional results are better; thus, hemiarthroplasty can safely be the first choice of treatment for the intertrochanteric fractures of ambulatory elderly patients.

Key Words: Hip Fractures; Geriatrics; Hemiarthroplasty, Bone Nails; Fracture Fixation, Intramedullary.

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ARAŞTIRMA

İNTERTROKANTERİK KIRIKLARIN AMBULATUVAR YAŞLILARDA TEDAVİSİ; BİPOLAR HEMİARTROPLASTİ YA DA PROKSİMAL FEMORAL ÇİVİLEME?

Öz

Giriş: Yaşlı hastalarda intertrokanterik femur kırıklarının tedavisi anatomik redüksiyonun kolay olmayışı, kemik kalitesinin zayıflığı ve yük vermenin güçlükleri nedeniyle zordur. Bu tip kırıklar için çeşitli internal tespit cihazları kullanılabilir ve birincil artroplasti de tedavi yöntemlerinden biridir. Bu retrospektif çalışma ambulatuvar yaşlı hastalarda bipolar hemiartroplasti ile proksimal femoral çivilemeyi özellikle fonksiyonel sonuçlar ve hastanın kırık öncesi aktivite düzeyine dönüş süresi açısından karşılaştırmaktadır.

Gereç ve Yöntem: Çalışma AO 31-A tipi intertrokanterik kırığı olan 136 hastayı içermektedir. Kırık öncesi ambulatuvar olmayan hastalar önceden çalışmanın dışında bırakıldı. 31-A1 tipi kırığı olan 78 hastanın 40'ı bipolar hemiartroplasti (BHA), 33'ü proksimal femoral çivileme (PFN) ile ve 5'i dinamik kalça çivisi (DHS) ile tedavi edildi. 31-A2 tipi kırığı olan 40 hastanın 24'ü BHA ile, 7'si PFN ile, 5'i DHS ile ve 4'ü değişik plak-vida sistemleri ile tedavi edildi. 31-A3 tipi kırığı olan 18 hastanın 2'si BHA, 15'i PFN ve 1'i plak-vida sistemi kullanılarak tedavi edildi. Son karşılaştırmaya yalnızca BHA (ortanca yaşları 80.61, 68 ile 98 arasında) ve PFN (ortanca yaşları 77,59, 58 ile 94 arasında) kullanılarak ameliyat edilen ve cerrahi sonrası en az 1 yıllık kontrolü bulunan hastalar alındı.

Bulgular: Perioperatif toplam kan kaybı (cerrahi sırasındaki kan kaybı ile cerrahi sonrası drenajdan gelen kanın toplamı) PFN ile tedavi edilen hastalarda anlamlı olarak daha azdı (590'a karşı 390 ml). Ameliyata kadar geçen süre (4,1'e karşı 3,9 gün), postoperatif yük verme süresi (2'ye karşı 2 gün) ve mortalite değerleri (%16,66'ya karşı %18,18) BHA ve PFN arasında farklı değildi. Total komplikasyon yüzdesi (%22,4'e karşı %28,2) BHA de daha düşük, ameliyat süresi (52,8'e karşı 82,5 dakika), cerrahi öncesi günlük aktivite düzeyine dönüş süresi (6,2'ye karşı 8,5 hafta), Harris skoru (85,8'e karşı 81,3) ve Postel Merle D'Aubigne (PMA) skoru (14,1'e karşı 12,2) BHA için anlamlı olarak daha iyi idi.

Sonuç: Hemiartroplasti uygulanan hastalarda perioperatif kan kaybının anlamlı olarak daha fazla olmasına rağmen postoperatif mortalite hızı daha yüksek değildir. Buna karşın hemiartroplasti ile komplikasyon yüzdeleri daha düşük, işlevsel sonuçlar daha iyi olduğu için ambulatuvar yaşlı hastaların intertrokanterik kırıklarının tedavisinde güvenle ilk tedavi seçeneği olabilir.

Anahtar Sözcükler: İntertrokanterik Kırıklar; Geriatri; Hemiartroplasti; Proksimal Femur Çivisi.

Introduction

Hip fracture in elderly patients with osteoporosis is a frequent injury, and constitutes a major source of morbidity and mortality. An estimated 1.66 million hip fractures occurred worldwide in 1990. This worldwide annual number is rising rapidly with an expected incidence of 6.26 million by the year 2050; the number of these fractures is on the rise due to increased life expectancy of the population and associated osteoporosis (1). The majority of hip fractures result from relatively low energy trauma due to combination of weaker reflexes to cushion the impact of a fall and bones weakened by the osteoporosis. Unstable intertrochanteric fracture in elderly patients are associated with a high rate of mortality (up to 20%) during the first postoperative year (2,3). The treatment of such unstable intertrochanteric fractures remains controversial, despite published reports of randomized trials and comparative studies (4-10). The traditional goal of the treatment is rigid internal fixation of the fragment and early mobilization (3).

We believe that postoperative early mobilization and patients' return to the premorbid daily activities should be the primary objectives of the treatment of such fractures. Thus, the time to return to daily activity levels before fracture is accepted as the most important criterion when evaluating results. The aim of this study was to identify the most appropriate method of treatment with regard to this criterion.

Materials and Method

The retrospective study included patients who had undergone surgery to treat intertrochanteric femoral fractures in the Division of Orthopaedics and Traumatology between January 2011 and December 2013. Because of the aim of this study, the ambulatory status of the patients was very important; thus, patients with associated fractures that may have significantly affected the functional outcome or systemic problems preventing their ambulation, patients that were non-ambulatory or ambulatory with a wheel chair before injury, patients who had spontaneous or non-traumatic fractures, and patients with psychiatric disorders and mental problems were excluded. All patients were independent community ambulators prior to trauma.

Patients whose fractures were classified as 31-B (femoral neck fractures) and 31-C (femoral head fractures) according to AO proximal femoral fracture classification were also excluded. Only patients with AO 31-A type (femur trochanteric region) fractures were included in this study.

A total of 136 patients were identified [mean age 76.67±5.3 years (range 58–98 years)]. Seventy-eight patients had AO 31-A1 type fractures; 40 of these patients were treated with bipolar hemiarthroplasty (BHA), 33 were treated with proximal femoral nail (PFN), and 5 were treated with dynamic hip screw (DHS). Forty patients had AO 31-A2 type fractures; 24 of these patients were treated with BHA, 7 were treated with PFN, 5 were treated with DHS, and 4 were treated with other plate-screw systems. Eighteen patients had AO 31-A3 type fractures; 2 of these patients were treated with BHA, 15 were treated with PFN, and 1 was treated with a plate-screw system. Patients who were treated with implants other than bipolar prosthesis or PFN were also excluded from the study.

The remaining patients were followed up with regular visits. Sixty-six patients who underwent BHA were compared with 55 patients who underwent PFN. At least 1 year of follow-up was required when the study was planned; therefore, the authors also attempted to contact patients who were operated at least 12 months previously but did not attend regular follow-up control visits. Eleven of the patients (16.66%) who had undergone BHA died within 1 year postoperatively, and 8 patients (12.12%) did not attend regular follow-up control visits or could not be contacted at their known addresses. Ten of the patients (18.18%) who had undergone PFN died within 1 year postoperatively and 6 patients (10.90%) did not attend regular follow-up control visits or could not be contacted at their known addresses. Therefore, the final evaluation compared 49 patients who had undergone BHA and 39 patients who had undergone PFN.

All surgical procedures were performed by surgical teams experienced in the application of hemiarthroplasty and PFN. The operations were performed as quickly as possible, and bleeding controls were used meticulously before wound closure. Acceptable closed reduction was achieved in all PFN cases.

The patients were mostly elderly (>75 years of age) in both groups. They had independent mobility before sustaining the fracture. Preoperative data included age, sex, fracture type, and preoperative comorbid conditions that may affect the final outcome. Perioperative data included time to surgery, operative time, amount of blood loss, and number of units of blood transfused. Postoperative data included time to full weight bearing, duration of hospital stay, and postoperative complications such as pulmonary problems, deep vein thrombosis (DVT), cardiac problems, infection (superficial and deep), pressure sores, fixation failure, varus displacement, protrusion, prosthetic dislocation, and mortality.



In the hemiarthroplasty group, the operations were performed using the posterolateral approach in a lateral decubitus position. Meticulous care was taken to preserve the integrity of the greater trochanter, abductor muscles, all vascularized bone fragments, and to maintain the leg length and femoral neck off-set. The greater trochanter was reduced and stabilized using tension band technique, cerclage cables, or heavy sutures when needed.

In the internal fixation group, the operations were performed under flouroscopy in a supine position. The aim was to obtain closed reduction in an optimum position with the correct angle between the femoral neck and shaft or a slight valgus position. Distraction of the fragments, varus position, or lateral displacement of the shaft was avoided. Antirotation nails, which are highly recommended for unstable fractures, were used if necessary. They are used to enhance the stability of the fixation and lower the mechanical implant-associated complication rates (9,11).

The independent samples T test for equality of means was used for statistical analysis; p values <0.05 were considered to be significant.

Results

All patients had unilateral closed intertrochanteric fractures. The fractures were due to traffic accident in 2 patients (4.1%) in the hemiarthroplasty group and in 3 patients (7.7%) in the PFN group. The remaining patients sustained fractures of the hip after falling from a low height.

In the hemiarthroplasty group, the average age at operation was 80.61± 6.55 years (range 68–98 years). There were 21 men (42.8%) and 28 women (57.2%). Fracture classification was AO 31-A1 in 32 (65.3%) patients, AO 31-A2 in 15 patients (30.6%), and AO 31-A3 in 2 (4.1%) patients.

The patients underwent surgery in an average of 4.14±1.93 days (range 0–8 days) after the fracture. The average time for duration of the surgery was 52.82±10.57 min (range 42–69 min), total perioperative blood loss was an average of 590.12±115.04 mL (range 350–720 mL), and the amount of blood transfused was an average of 1.10±0.66 units (range 0–2 units).

The mean postoperative time to weight bearing was 2.21±0.52 days (range 1–3 days), and the mean postoperative hospital stay was 3.22±0.44 days (range 2–5 days). The mean time to return to the premorbid daily activity was 6.24±2.12 weeks (range 4–11 weeks).

The total complication rate was 22.4%. There were 3 patients with <0.5 cm protrusion of the femoral stem, 2 patients with delayed union of the greater trochanter, 3 patients with shortening of the limb by >1 cm, 1 patient with a deep wound infection (which was surgically debrided and subsequently healed), and 2 patients with superficial wound infections. No revision surgery was necessary except one surgical debridement.

The mean Harris score at the last follow-up visit was 85.79±7.14 (excellent in 15 (31%) patients, good in 22 (45%) patients, fair in 10 (20%) patients, and poor in 2 (20%) patients). The mean Postel Merle D'Aubigne (PMA) score (modified by Charnley) at the last follow-up visit was 14.10±1.74 (range 8–17), mean pain score 5.1, motion 4.8, and gait 4.3.

In the PFN group, the average age at operation was 77.59±5.58 years (range 58–94 years). There were 16 men (41.0%) and 23 women (59.0%). Fracture classification was AO 31-A.1 in 25 (64.1%) patients, AO 31-A.2 in 4 patients (10.3%), and AO 31-A.3 in 10 (25.6%) patients.

The patients underwent the operation in an average of 3.95±1.86 days (range 0–7 days) after the fracture. The mean duration of the surgery was 82.53±20.71 min (range 49–110 min), the mean total perioperative blood loss was 390.15±89.28 mL (range 100–510 mL), and the mean amount of blood transfused was 0.77±0.21 units (range 0–2 units).

Postoperative weight bearing time was a mean 2.75±0.86 days (range, 1–4 days), postoperative hospital stay was average 3.51±1.22 days (range 1–5 days). The average time to return to the pre-fractured daily activity was 8.54±2.73 weeks (range, 5–12 weeks).

The total complication rate was 28.2%. There were 4 patients with secondary varus displacement <10°, 3 patients with delayed union of the intertrochanteric fracture, 2 patients with trochanteric tip calcification, and 2 patients with superficial wound infection. All healed in acceptable measures without revision.

Harris score at the last follow-up visit was 81.28±7.75 [excellent in 7 (18%) patients, good in 15 (38%) patients, fair in 12 (31%) patients, and poor in 5 (12%) patients]. The mean PMA score at the last follow-up visit was 12.21±2.03 (range 5–16), pain score 4.1, motion 4.3, and gait 3.8.

Bipolar hemiarthroplasty was cemented in four patients (8.1%), because the implant did not appear to be rigidly fixed. Three of these patients had calcar replacement and 1 had a collar in the femoral stem. Forty-five (91.8%) of the patients

Table 1— Complications (number of patients).

	Protrusion	Delayed Union	Limb Shortening	Displacement	Deep wo. inf.	Superf. wo. inf	Troch Tip Calc.
BHA	3	2	3	-	1	2	-
PFN	-	3	-	4	-	2	2

had undergone cementless hemiartroplasty, while 29 (64.4%) of these implants had a collar with 4/5 porous coating, 13 (26.6%) had 1/3 porous and/or HA coating, and 4 (8.9%) had calcar replacement. Proximal femoral nails were applied through the trochanteric tip in all but 3 cases, in which fossa piriformis was used. The type of implant was selected by the surgeon performing the operation in all cases.

All patients received standard postoperative care, including low-molecular-weight heparin for DVT prophylaxis and antibiotics for infection prophylaxis. Twenty-two patients with hemiarthroplasty (45%) stayed an average of 2.1 days in the intensive care unit postoperatively and 19 patients with PFN implantation (49%) stayed 2.3 days in the intensive care unit postoperatively as requested by the anesthesiologist. The accompanying systemic diseases were similar in both groups.

Radiological evaluations were made in standard anteroposterior and lateral x-rays. In the PFN group, union of the fracture, loss of reduction, implant migration, varus displacement, and cut-out of the screw were assessed; in the BHA group, loosening of the stem, protrusion, dislocation, and stem ingrowth to the femur was assessed.

In the BHA group, 11 patients (16.66%) died within 1 year postoperatively and 8 patients (12.12%) did not attend regular follow-up control visits. In the PFN group, 10 patients (18.18%) died within 1 year postoperatively and 6 patients (10.90%) did not attend regular follow-up control visits. We have no reliable data about the cause of death of these patients; therefore, we cannot determine how many (perhaps none) have died because of surgical complications. Finally, 49 patients with BHA and 39 patients with PFN were compared for the evaluation of this study.

Discussion

The management of unstable osteoporotic intertrochanteric fractures in the elderly is challenging because of difficult anatomical reduction, poor bone quality, and sometimes, a need to protect the fracture from the stress of weight bearing. Internal fixation in these cases usually involves prolonged bed rest or limited ambulation to prevent implant failure secondary to osteoporosis. This might result in higher chances of complications such as pulmonary embolism, DVT, pneumonia, and decubitus ulcer. The mechanism of injury is mostly trivial trauma for intertrochanteric femoral fractures. Low energy trauma (fall < 1 m) caused 53% of all fractures in patients ≥50 years of age. In patients >75 years of age, low energy trauma caused >80% of all fractures (2). Most of these patients are osteoporotic, with a low level of bone mineral density; after sustaining a fracture, the mortality risks are extremely elevated even in the best peroperative and postoperative conditions (3).

Stable fractures can be easily treated with osteosynthesis with predictable results. However, the management of unstable intertrochanteric (AO 31-A2.2 and 2.3 type) fractures is a challenge because of the difficulty in obtaining anatomical reduction. In the past, fixed nail-plate devices used for the fixation of these fractures had higher rates of cut-out and fracture displacement. In addition, a period of restricted mobilization is suggested in elderly patients with unstable osteoporotic fractures, which may cause complications such as atelectasis, bed sores, pneumonia, and DVT (1,3). Therefore, early and full weight bearing is very important, and requires a very stable and rigid fixation. There are several studies comparing different types of internal fixation devices such as DHS, proximal femoral plate, gamma nail for intertrochanteric femoral fractures, and almost all state the superiority of PFN in the stability of fixation, healing time, Harris hip score, and total complication rate in the treatment of these fractures (5-13).

In elderly patients, the aim must be early mobilization to prevent complications and facilitate the patient's returning to premorbid status as quickly as possible to prevent mortality.

There was no difference between the average age of the patients in the two groups (80.61 vs 77.59, p=0.06). The sex distribution in our study is different from almost all studies reported about intertrochanteric fractures. In other studies, female patients represent approximately 80% of the included patients, while they represent approximately 58% of our population. This likely resulted from the exclusion of non-ambulatory, multiple-fractured patients with systemic diseases, the majority of whom were women.



The fracture distribution was mostly AO 31-A1 in both groups (65.2% vs 64.1%) and appeared highly comparable (p=0.38); it is almost always the most challenging problem to compare the same type of fractures in orthopedic studies. AO 31-A2 fractures were the second most common type (30.6%) in BHA patients, while 31-A3 was the second most common type (25.6%) in PFN patients.

The average time to surgery from admission was 4.14 and 3.95 days, respectively (p=0.32); thus, this factor cannot differently effect the mortality rate in both groups. This delay resulted from the policy of the anesthesiology division. They asked for a "ready" intensive care unit bed according to the patient's American Society of Anesthesiologists (ASA) criteria and physical condition; therefore, there was typically a wait for an available bed preoperatively.

The average duration of surgery was shorter in BHA patients compared with PFN patients (52.82 min vs 82.53 min) and the difference was significant (p=0.0001). The same difference was noted by several authors (5-7,14-18). The perioperative blood loss (blood lost during surgery plus postoperative surgical drainage) was significantly less (p<0.005) in the PFN group (590.12 mL vs 390.15 mL), which was also congruent with the literature as internal fixation was almost always achieved with closed intramedullary nailing (5,15-20). Kim et al. reported longer surgery time and more bleeding with cemented calcar replacement arthroplasty (21). Blood loss in the BHA group in our study may also be altered because of cementless hemiarthroplasty. However, units of blood transfused (1.10 units vs 0.77 units respectively) were significantly different (p=0.036) although we did not prefer blood transfusion if the hemoglobin value was ≥9 g/dL.

Postoperative hospital stay (3.22 vs 3.51 days) and postoperative weight bearing time (mean 2 days in both groups) were not different (p=0.31). Patients were encouraged to walk from the first postoperative day in both groups unless there was any doubt about the rigidity of the fixation.

The mean follow-up time was similar in both groups (16 months for BHA and 17 months for PFN).

The total complication rate was lower with BHA (22.4% vs 28.2%). Dong et al. reported significantly lower complication rates with PFN (5). Almost all other authors reported lower complication rates with hemiarthroplasty (4,10,13,18). Geiger compared dislocation rates with internal fixation and hemiarthroplasty and found 12% to 0% rates, respectively (10). Hohendorff observed a 31.7% complication rate with PFN (13). In our study, there were only a small number of mechanical complications in the BHA group, although we largely preferred cementless fixation. This is believed to be due to the ambulatory and less osteoporotic status of the patients. Femoral cortexes were thick enough to rigidly hold the femoral stems. There were 3 patients with <0.5 cm protrusion of the femoral stem, 2 patients with delayed union of the greater trochanter, 3 patients with shortening of the limb >1 cm, 1 patient with a deep wound infection (which was surgically debrided), and 2 patients with superficial wound infections. Highly experienced surgical teams aiming real "rigid" fixation probably lowered mechanical complication rates with arthroplastic procedures.

Mechanical complications are reported more with osteosynthesis (4,10,14-16,18-20). In the PFN group, there were 4 patients with secondary varus displacement <10°, 3 patients with delayed union, 2 patients with trochanteric tip calcification, and 2 patients with superficial wound infections. Although the total complication rate was significantly higher than the BHA group, it was still lower than expected for locked intramedullary nailing systems; e.g., "cut-out of lag screws" did not occur (12,13).

In our series, no pressure sores were observed in either group. Because most of the patients were out of their beds on the second day postoperatively and the recumbancy time was minimal, there were also no symptomatic chest complications or DVT findings in our series. Haentjens et al. showed a significant reduction in the incidence of pneumonia and pressure sores in those undergoing prosthetic replacement because their implant group had delayed weight bearing due to the rigidity of fixation (16).

Eleven of the patients (16.66%) who underwent BHA died within 1 year postoperatively, and 8 patients (12.12%) did not attend regular follow-up control visits or could not be contacted at their known address. Ten of the patients (18.18%) who underwent PFN died within 1 year postoperatively, and 6 patients (10.90%) did not attend regular follow-up control visits or could not be contacted at their known address. The difference in mortality rates was not significant (p=0.058). Because we do not know the fate of the patients who missed their control visits at 1 year postoperatively, 19 patients (38.7%) with BHA and 16 patients (41.0%) with PFN may be considered as "lost," the difference of which is still not significant (p=0.34). Kim et al. found a doubled 1-year mortality rate with arthroplasty and stated that there was no surgical benefit (21). Many other authors found no significant difference between these two groups in terms of mortality rate in the first year (4,10,14,21,22).

Functional results were evaluated using Harris and Postel Merle d'Aubigne (modified by Charnley) scores. Both functional evaluation scores were significantly better in the arthrop-

lasty group. The Harris hip score at the last follow-up control visit was significantly higher (p=0.004) in the BHA group (85.79 vs 81.28, respectively). The hip score was found to be 75% excellent to good in the BHA group, while it was 56% excellent to good in the PFN group. Hohendorff et al. found unsatisfactory functional results with PFN in elderly patients, observing normal ambulation in only 33.8% of patients and only 64.6% free of pain (13). Dong et al. reported better Harris scores with hemiarthroplasty, and Sancheti et al. reported 71% excellent to good fair (91% excellent to fair) functional results with hemiarthroplasty in osteoporotic fractures (AO 31-A2.2 and A-2.3) with a mean patient age of 77.1 years (1,5). In a study of primary bipolar hemiarthroplasty for unstable intertrochanteric fractures in 37 elderly patients, Rodop et al. observed 17 (45%) excellent and 14 (37%) good results after 12 months according to the Harris hip-scoring system (23). In a comparative study investigating cone hemiarthroplasty versus internal fixation, Kayali et al. reached the conclusion that the functional results of both hemiarthroplasty and internal fixation groups were similar. Hemiarthroplasty patients were allowed full weight bearing significantly earlier than the internal fixation patients (24). Broos et al. concluded that the operative time, blood loss, and mortality rates were comparable between the two groups, with a slightly higher percentage (73% vs 63%) of those receiving prosthesis considered to be pain free (25). Kim et al. compared the calcar replacement prosthesis with intramedullary nailing in a prospective study involving two groups of 29 patients. They did not find any significant difference concerning the functional outcomes (21). Sinno et al. found significantly higher Harris hip scores (80.35 vs 68.17) in patients who underwent hemiartroplasty than internal fixation (18).

The mean PMA score at the last follow-up control visit was significantly better (p=0.0001) in the BHA group (14.10 vs 12.21, respectively). Bonnevialle et al. also reported better PMA and Parker scores with arthroplasty at the last follow-up control visit (14).

The mean time to return to the premorbid daily activity was 6.24±2.12 weeks and 8.54±2.73 weeks in the BHA and PFN groups, respectively; this difference was significant (p<0.001). It was challenging to determine the exact time of the patient's return to daily activities before fracture; thus, we asked for help from the relatives. Sinno et al. reported that the time to independent full weight bearing and return to the prefracture level of activity was significantly earlier in patients who underwent bipolar arthroplasty (1.26±0.68 weeks) compared with the internal fixation group (9.6±2.28 weeks; p<0.0001) (18). We believe that this is the most important criteria to evaluate results with elderly patients because there is no standard assessing value for individuals with various activity levels. The baseline should be the patient's premorbid daily activity level. The results showed that elderly patients had better functional results with hemiarthroplasty in intertrochanteric fractures because they could more quickly "go back" to their lives despite having more blood loss during surgical procedure. This may also be the main reason of lower complication rates with BHA.

Conclusion

The typical attitude in trochanteric fracture is internal fixation, because it spares head vitality and osteogenesis ensures repair as long as the osteosynthesis assembly is secure: a large majority of traumatologists adopt this option. Because of the rate of mechanical failure and the necessary caution in resuming weight bearing, several authors recommended hip arthroplasty (16,19,20,22). However, when newer implants such as PFN are used, these problems are minimized and early weight bearing is possible.

The present study showed better results with hemiarthroplasty than with intramedullary locked nailing in unstable trochanteric fracture in patients >75 years of age, in terms of associated complications, functional scores, and time to re-

Table 2— Evaluation of the Results

	BHA	PFN	p
Age (years)	80.61±6.55	77.59±5.58	0.06
Fracture Distribution (AO 31-A1)	65.2 %	64.1 %	0.38
Duration of Surgery (minutes)	52.82±10.57	82.53±20.71	0.0001
Perioperative Blood Loss (mL)	590.12±115.04	390.15±89.28	0.0001
Harris Score at the last visit	85.79±7.14	81.28±7.21	0.004
Modified PMA Score at the last visit	14.10±1.75	12.21±2.03	0.0001
Return to Premorbid Activities (weeks)	6.24±2.12	8.54±2.73	0.004



turn to the prefracture daily activity. It can be emphasized that hemiarthroplasty was not associated with greater postoperative mortality than osteosynthesis and can safely be the first choice of treatment for such fractures among ambulatory elderly patients.

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Case Report

MYCOSIS FUNGOIDES AND MANTLE CELL LYMPHOMA: A CASE REPORT

Abstract

Mycosis fungoides (MF) is the most common type of primary non-Hodgkin cutaneous T-cell lymphoma and typically presents with a patch or plaque lesion with variable progression to tumors and extracutaneous involvement. Epidemiological studies have indicated that patients with MF are at a high risk for the development of secondary lymphomas.

However, although some of these studies have reported an increased risk for NHL, Hodgkin disease (HD) remains the most common type of secondary lymphoma in patients with MF in other studies.

In this report, we describe a 76-year-old male patient with MF (stage IA) who was concomitantly diagnosed with mantle cell lymphoma (MCL). Histopathologic and immunophenotypic features as well as cyclin D1 oncogene and chromosomal aberrations were subsequently identified.

Key Words: Aged; Mycosis Fungoides; Lymphoma, Mantle-Cell.

Olgu Sunumu

MİKOZİS FUNGOİDES VE MANTLE CELL LENFOMA BİRLİKTELİĞİ: OLGU SUNUMU

Öz

Mikozis fungoides (MF) en sık görülen primer T hücreli non-Hodgkin kutanöz lenfoma olup, tipik olarak yama, plak ve tümörler ile, nadiren de ekstrakutanöz organ tutulumuyla karakterizedir. Epidemiyolojik çalışmalar MF tanısı alan hastalarda sekonder lenfoma gelişme riskinin artmış olduğuna dikkat çekmektedir.

Bu çalışmalardan bazılarında MF'ye eşlik eden en sık görülen sekonder lenfoma tipi Hodgkin lenfoma (HL) iken, diğer çalışmalar özellikle non-Hodgkin lenfoma (NHL) için risk artışı olduğunu bildirmektedir. Bu olgu sunumunda Mantle cell lenfoma (MCL) tanısı alan evre IA MF nedeni ile takip edilen 74 yaşındaki erkek hastanın histopatolojik, immünfenotipik, cyclin D1 onkogen ve kromozomal değişiklik özellikleri tanımlanmıştır.

Anahtar Sözcükler: Yaşlı; Mikozis Fungoides; Mantle Cell Lenfoma.

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Introduction

Mycosis fungoides (MF) is the most common type of primary non-Hodgkin cutaneous T-cell lymphoma and typically presents with a patch or plaque lesion with variable progression to tumors and extracutaneous involvement (1). The association between MF and both non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma has been rarely reported and studies have indicated that patients with MF are at a high risk for the development of secondary lymphomas (2-7).

In this report, we describe a patient with MF (stage IA) who was concomitantly diagnosed with mantle cell lymphoma (MCL). Histopathologic and immunophenotypic features as well as cyclin D1 oncogene and chromosomal aberrations were subsequently identified.

Case Report

A 74-year-old man with a two-year history of pruritic eruption on the back was referred to our dermatology department. During physical examination, patches and plaques that were consistent with the symptoms of MF were observed. Skin biopsy showed classical features of MF with prominent epidermotropism (Figure 1), and immunohistochemical staining; T cells were predominant and mostly expressed CD2, CD3, CD 7, and CD5; CD8 and CD4 expression was noted, although, it was comparatively less predominant. Staining for CD30 and CD20 showed negative results.

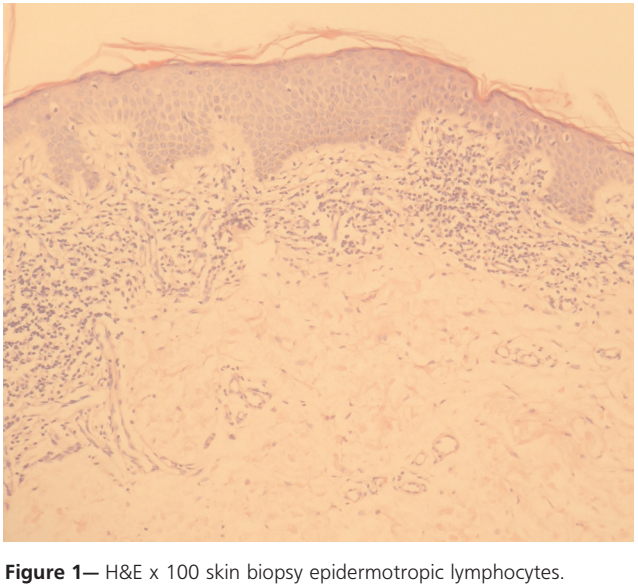


Figure 1— H&E x 100 skin biopsy epidermotropic lymphocytes.

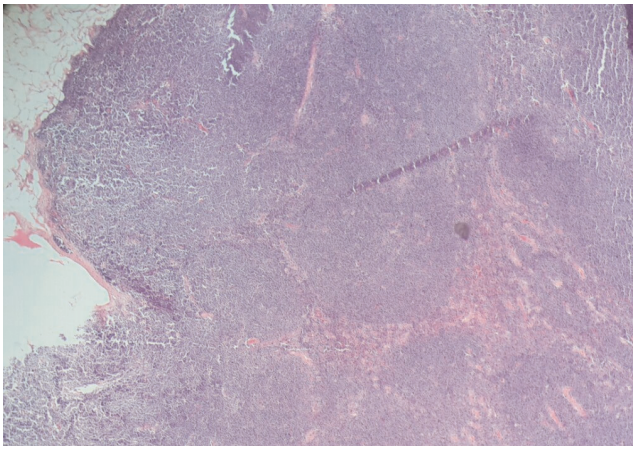


Figure 2— H&E x 400 lymph node biopsy showed small lymphoid cell infiltration.

Hematological studies showed a hemoglobin level of 10.4 g/dL [normal range (NR): 13.2–17.2 g/dL], a platelet count of 60 x 10^3 cells/µL (NR: 150–450 x 10^3 cells/µL), and a white blood cell (WBC) count of 2.55 x 10^3 cells/µl (NR: 4.8–10.8 x 10^3 cells/µL).

Bilateral axillary, inguinal, submandibular, and cervical lymphadenopathy as well as splenomegaly were detected on ultrasound examination. Computed tomography scanning of the thorax and abdomen revealed paratracheal, aortopulmonary, paraesophageal, mesenteric, and retroperitoneal lymphadenopathy and splenomegaly. The lymph node biopsy showed small lymphoid cell infiltration (Figure 2), which stained heterogenously with CD79a, CD20 (Figure 3), CD43, CD5, Bcl2, CD3, CD4, CD8, and CD23. Cyclin D1 staining was negative (Figure 4).



Figure 3— x200 lymph node biosy, CD20 positivity.

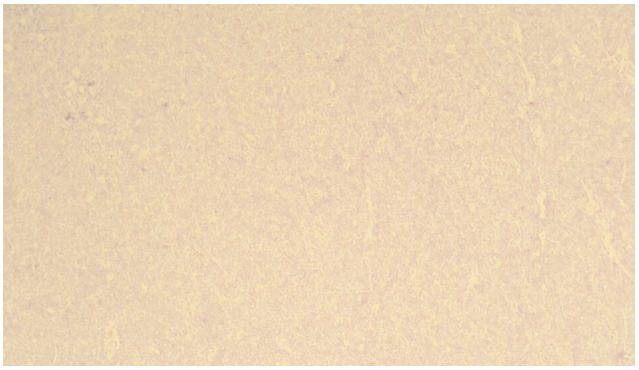


Figure 4— x100 lymph node biopsy cyclin D1 negativity.

Lymphoid cell infiltration of up to 90% was seen on bone marrow aspiration. Flow cytometric analysis revealed CD5, CD19, CD22, CD23±, CD20, CD79b, FMC7, CD25, CD43, and lambda positivity. On Fluorescence in situ hybridization analysis of MCL cells, which was performed for differential diagnostic purposes, extra copies of the t(11;14) translocated chromosomes were detected. On the basis of these results, the patient was diagnosed with concomitant MCL and MF. The hematology department planned chemotherapy for the patient as he was not suited for autologous stem cell transplantation. In January 2013, he received six cycles of the rituximab–cyclophosphamide-vincristine-prednisolone combination therapy. However, because he did not positively respond to this regimen, chemotherapy was resumed in October 2013, which was discontinued after the third cycle upon his request. The patient is presently being followed up.

Discussion

The coexistence of both MF and B-cell malignancies in the same patient is extremely rare. Previous epidemiological studies that investigated the association between MF and secondary malignancies have consistently reported an increased risk for secondary lymphoid neoplasms (2, 5-8). However, although some of these studies have reported an increased risk for NHL (5, 8), Hodgkin disease (HD) remains the most common type of secondary lymphoma in patients with MF in other studies (2, 6). In one of these studies, no case of HD was found. The authors explained that this may be due to the lesser prevalence of HD in their population, approximately four times less than that of NHL (8).

There are several hypotheses for the coexistence of two different lineages of lymphomas in the same patient other than the possibility of the coincidental development of two different types of lymphomas. One of the overemphasized explanations is that immunodeficiency due to the primary neoplasm or treatment regimens for the primary neoplasm can facilitate development of secondary malignancies (8). Gniadecki (9) hypothesized a common neoplastic stem cell origin or genetic predisposing event for the development of different cell lineages. In addition, exposure to common viruses and carcinogens that affect B- and T-cell precursors have been suggested (8). Apart from all these possible explanations, several epidemiological studies have supported the increased risk of secondary neoplasms in lymphoma patients. MCL, a type of NHL that is characterized by small-to-medium-sized lymphocytes, has an aggressive clinical course and occurs because of the overexpression of a cyclin D1 (bcl-1) proto-oncogene, which is generally associated with the t(11;14) chromosomal translocation (10). Nevertheless, cyclin D1 staining can be negative in rare instances, as demonstrated in our case. The importance of normal immune system functions in the MF course is well known. Immunosuppression after the initiation of chemotherapy for second lymphoma can induce aggressive progression of early-stage MF. We have thus been closely following up our patient, who refused to complete his chemotherapy, at frequent intervals.

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Case Report

FACIAL BURN ASSAULT OF A GERIATRIC WOMAN: A CASE REPORT

Abstract

Violence against women is a social, developmental, economic, legal, educational and human rights issue. Regardless of culture, religion, education level or financial status of those involved and the country's level of development, violence against women has been identified as a serious public health problem. It is a preventable cause of morbidity and mortality in women. Violence against women may also be observed in geriatric patients. In these patients burning and/or an attempt at burning as a physical assault can cause serious problems.

Geriatric patients, usually defined as those older than 65 years, comprise approximately 10% of the major burns population. Burn injuries continue to be among the most serious and devastating health threats for human beings, with a long and permanent effect on the patients' health and quality of life

Worldwide, burns caused by criminal acts mostly concern women and are acts of domestic violence.

In this case report; a 68-year-old female patient who had facial burns due to an assault by her husband and who had been followed up at a burn intensive care unit has been presented.

Key Words: Violence; Burns; Aged.

Olgu Sunumu

BİR GERİYATRİK KADIN HASTAYA UYGULANAN ŞİDDET SONUCU YÜZ YANIĞI: OLGU SUNUMU

Öz

Kadına uygulanan şiddet sosyal, ekonomik, hukuki, eğitimsel ve insan haklarını ilgilendiren bir konudur. Kültür, din, eğitim düzeyi ve finansal durumdan ve ülkenin gelişmişlik düzeyinden bağımsız olarak kadına yönelik şiddet ciddi bir halk sağlığı problemi olarak belirlenmiştir. Bu durum kadınlarda önlenebilir morbidite ve mortalite nedenidir. Kadına yönelik şiddet geriatrik hastalarda da görülebilmektedir. Bu hastalarda fiziksel şiddet amaçlı yakma ve/veya yakma girişimi oldukça ciddi problemlere neden olabilir.

Geriatrik hastalar genellikle 65 yaş üstü hastalar olarak tanımlanırlar ve toplumdaki majör yanıkların %10'unu oluştururlar. Yanık hasarları insanlar için hastaların sağlıkları ve yaşam kaliteleri üzerinde uzun ve kalıcı etkileri ile en ciddi ve en yıkıcı sağlık tehdidi olmaya devam etmektedir.

Tüm dünyada kriminal etkilerle oluşan yanıklar en sık kadınları ilgilendirmektedir ve aile içi kadınlara yönelik şiddete bağlı oluşmaktadır.

Bu olguda kocası tarafından şiddete maruz kalması sonucu yüz yanığı oluşmuş ve yanık yoğun bakım ünitesinde takip edilmiş 68 yaşında bir kadın hasta sunulmuştur.

Anahtar Sözcükler: Şiddet; Yanıklar; Yaşlı.

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Introduction

Violence against women by intimate partners is an important conditioning factor for female health (1). Overall 35% of women worldwide have experienced physical intimate partner violence (2).

For physical assault against women combustible materials are frequently used. Geriatric patients, usually defined as those older than 65 years, comprise approximately 10% of the major burns population (3). In particular, elderly burn patients suffer from greater morbidity and mortality than younger patients with similar extent of burns.

In general, burns covering >30% of the total body surface area in the elderly have a very poor prognosis. Reasons for the increased mortality rate are concomitant medical disease, burn wound sepsis and multisystem failure (4).

Case

A 68-year-old Syrian patient was admitted to our burn centre after an assault by her husband with flaming oil at refugee camp. She was admitted at our emergency department 6 hours after the incident by a helicopter ambulance and at her first examination we found erythema and edema which encompassed her entire face, scalp, left eyelid and both shoulders (Figure 1).

When tachypnea and oxygen desaturation (SpO_2<91%) occurred she was immediately intubated orotracheally and pressure support mechanical ventilation was started. The wounds were covered with 0.5% chlorhexidine acetate and petrolatum gauze. After the initial dressing, the patient was taken to the intensive care unit. Central venous catheterization from the right femoral vein and arterial, urinary, and nasogastric catheterizations were performed. With sedation and analgesics mechanical ventilation with SIMV-P mode was started. Fluid resuscitation was maintained after calculating the body surface area. Blood, urine and tracheal culture samples were drawn from the patient. Leucocyte counts in blood and CRP, lactate and procalcitonin levels were measured for follow up infection.



Figure 1— Erythema and edema.

Altogether, 35% of the total body surface area (TBSA) was burned by flame (2nd- 3rd degree). The regions affected were the face, anterior neck, right anterosuperior trunk and right upper extremity. After sedation with midazolam and ketamine the burned areas were scrubbed with distilled water and 7.5% povidione iodine in our burn unit washroom.

Fluid resuscitation was completed using the Parkland formula (4 ml/kg/ %TBSA) in relation to urine output as 1.5-2 ml/kg/day after the first 24 h follow up (5). Albumin, erythrocytes and colloids were administered to the patient for the treatment of acidosis.

Pseudomonas aeruginosa was isolated from the blood culture on day 7. Appropriate antibiotic therapy using a sensitive antibiotic was performed. Oral nutritional support solutions were commenced. Caloric replacement was estimated using the Currieri formula (6) (25 kcal/kg actual BW+40 kcal/%TBSA burn).

We assessed the patient's hypotensive state on day 10 and therapy with an inotropic agent was initiated. After 4 days inotropic therapy was terminated. On day 13 of hospitalization, mechanical ventilation was terminated. During hospitalization, dressings were changed daily under sedation. The patient was hospitalized for a total of 30 days after which she was discharged upon completion of treatment (Figure 2).

Discussion

Violence against women is a phenomenon that persists worldwide. It is a major contributor to the ill health of women. No country in the world is free from violence against women. It is known that combustible materials causing burns are used in physical assaults against women. In particular, violence against women still exists in our society too. However, burn assaults by throwing flaming oil on women are very rare.



Figure 2— After the treatment.

Unfortunately, burn injuries rank fourth among the causes of injury-related deaths in the geriatric age group (7). In geriatric patients, pre-morbid conditions, such as chronic obstructive pulmonary disease and coronary artery disease may lead to longer hospital stays, increased ventilation requirements and elevated complication rates. The mortality rate also increases owing to an impaired response to infection and sepsis, in addition to a decreased ability to tolerate prolonged stress and physiological insult (8).

Mortality in young adults with an 80% TBSA burn is 50%, whereas in adults aged 60-70 years with a 35% TBSA burn is 50% (9). The deficient nutritional state observed in geriatric burned patients may also cause impaired wound healing. Co-morbid factors are responsible for this increase in morbidity and mortality. Elderly people have thinner skin, poorer microcirculation, and increased susceptibility to infection. In addition, rates of inhalation injury, pulmonary pathology, septicaemia and renal failure are higher than those in younger people (10).

Geriatric people have decreased pulmonary reserves for gas exchange and lung mechanics and they are prone to pulmonary failure, which is a major cause of death in all burn patients (11). Facial burns found in our patient are generally considered severe. This is due to the possibility of respiratory complications. Although there were no signs of inhalation injury, no respiratory failure was observed in our patient after fast respiratory support.

In geriatric patients the severity and extent of the burn lesions and the duration of hospitalization of the patients are defined as the main prognostic factors (11). In geriatric burn patients fluid resuscitation is also important. Fluids should be administered to patients with burn >5% TBSA burns. Resuscitation solutions should be initiated at a rate of 3- 4 ml/kg/%TBSA. Adequacy of resuscitation should be maintained at; 30- 50 ml/h urine output, clear mentation, and appropriate blood pressure (12).

Wound healing is of great concern in geriatric people. There are significant changes in the skin with ageing that are responsible for the greater percentage of deep burns in the elderly, including the progressive thinning of the dermis and epidermis. Many factors contribute to a higher proportion of deep burns and a decrease in healing rates. These factors include decrease in epidermal turnover and the amount of skin appendages, vascularity, collagens and matrices, fibroblasts, and macrophages (13).

These factors cause a delay in epithelialization, an increase in burn depth, particularly in second-degree burn areas, and healing complications at the donor site.

One such problem, protein energy malnutrition, has been reported to be present in at least one-third (30% -60%) of elderly patients admitted to hospital. By giving our patient a high-energy, calorie-rich diet 1 day after burn injury we prevented her from developing a state of protein energy malnutrition. As in other diseases age is an important factor affecting the treatment outcomes of burns (13).

Kartal Dr. Lutfi Kırdar Training and Research Hospital's Burns Unit is the biggest and best equipped burn centere in Turkey. It functions in a multidisciplinary manner. It has 6 intensive care unit beds, 16 burn service beds and 2 separate operating rooms all housed in one building. It has a helicopter landing field and it accepts patients from every region of the country and from neighboring countries. The present case is unusual because it involves an assault against a geriatric woman who is part of the refugee population in our country.

Conclusion

The government policy makers, program planners and other nongovernmental organizations should establish an appropriate strategy to prevent and control violence against women. Although burn treatment has improved during the past decade, the prognosis remains poor for older adult patients. With early respiratory support, fluid resuscitation, infection challenge and early surgery, it is possible to decrease the high mortality and morbidity rates in geriatric patients.



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Case Report

SPINAL DURAL ARTERIOVENOUS FISTULA: A RARE CAUSE OF PROGRESSIVE PARAPARESIS

Abstract

Spinal dural arteriovenous fistula (dAVF) is a rare and disabling but potentially treatable vascular malformation of the spine. The lesion is more common in men over the age of 50 years and affects the thoracic and lumbar spine. These patients usually present with slow and progressive paraparesis with both upper and lower motor neuron lesion findings, which hinders the clinical differentiation of spinal dAVF from polyneuropathies and other causes of myelopathies. Available treatment includes endovascular embolization and microsurgical techniques. Because a patient's prognosis is strongly correlated with the time of the diagnosis and early treatment, spinal dAVF should always be considered in the differential diagnosis of patients with paraparesis. A 65-year-old male patient was admitted to our clinic with a 3-month history of progressive bilateral lower extremity weakness. Neurological examination revealed hypoesthesia in the L4 dermatome bilaterally, and the strength in the bilateral hip flexors and knee extensor muscles was 4/5. On contrast magnetic resonance imaging, vascular structures surrounding the dural sac were prominent in the lumbar and thoracic regions. In angiography a spinal dAVF was detected. Following the worsening of the patient's paraparesis, endovascular embolization was applied to the fistula. Patient's clinic completely restored after the procedure.

In this report, it has been aimed to present a male patient who admitted with progressive paraparesis and diagnosed as subsequent lumbar dAVF in the light of updated literature.

Key Words: Arteriovenous Fistula, Spinal Dural; Paraparesis; Aged; Rehabilitation.

Olgu Sunumu

SPİNAL DURAL ARTERİOVENÖZ FİSTÜL: NADİR BİR PROGRESİF PARAPAREZİ NEDENİ

Öz

Spinal dural arteriovenöz fistüller (sdAVF) omurganın nadir görülen, sekel bırakabilen ancak tedavi edilebilir vasküler malformasyonlarındandır.Genellikle 50 yaş üstü erkek hastalarda lomber ve torakal omurgada gözlenir. Hastalar genellikle yavaş ve progresif seyirli üst ve alt motor nöron lezyonları ile seyreden paraparezi kliniği ile başvururlar ki bu, spinal dAVF'nin diğer polinöropati ve miyelopati nedenlerinden ayırtedilmesini zorlaştırır. Mikrocerrahi teknikleri ve endovasküler embolizasyon mevcut tedavi secenekleridir. Hastanın prognozu tanı zamanı ve erken tedavi ile yakın ilişkili olduğundan spinal dAVF paraparezili hastaların ayırıcı tanısında mutlaka göz önünde bulundurulmalıdır. 65 yaşında erkek hasta kliniğimize 3 aydır devam eden alt ekstremitelerinde güçsüzlük şikayeti ile başvurdu. Nörolojik muayenesinde her iki L4 dermatomunda hipoestezi vardı ve her iki kalça fleksiyon ve diz ekstansiyon kas güçleri 4/5 idi. Kontrastlı manyetik rezonans görüntülemede lomber ve torasik omurgada dural sakı çevreleyen vasküler yapılarda belirginleşme ve anjiografide spinal dAVF saptandı. Hastanın paraparezisinin ağırlaşmasını takiben fistüle endovasküler embolizasyon uygulandı. İşlem sonrasında hastanın kliniği tamamen düzeldi.

Bu yazıda alt ekstremitelerinde progresif güçsüzlük ile başvuran ve spinal dAVF tanısı alan erkek bir hastanın güncel literatür ışığında sunulması amaçlanmıştır.

Anahtar Sözcükler: Spinal Dural Arteriyovenöz Fistül; Paraparezi; Yaşlı; Rehabilitasyon.

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Introduction

Spinal dural arteriovenous fistula (dAVF) is a rare and disabling but potentially treatable vascular malformation of the spine. The resultant venous hypertension decreases spinal cord perfusion, leading to ischemia and edema, which results in slowly progressive myelopathy, sensory disturbances, and bowel and bladder dysfunction. The lesion is more common in men over 50 years of age. It usually affects the thoracic and lumbar spine (1).

Few cases of this vascular malformation have been reported in the literature (2,3). Clinical symptoms and imaging findings are non-specific and can be easily confused with other causes of myelopathy. However, early diagnosis and treatment of patients with dAVF is crucial for prognosis (4).

Here, we describe the case of a male patient who presented with gradually progressive bilateral lower extremity weakness with subsequent lumbar dAVF diagnosis and a literature review.

Case Report

A 65-year-old male patient was admitted to our clinic with a 3-month history of progressive bilateral lower extremity weakness with periods of recovery. There was no history of trauma, weight lifting, lower back pain, or neuropathic pain. The patient did not complain of bladder and bowel problems or sexual dysfunction.

On admission, neurological examination revealed hypoesthesia in the L4 dermatome bilaterally, and the strength in the bilateral hip flexors and knee extensor muscles was 4/5. There was no spasticity. Hyperactive deep tendon reflexes were noted bilaterally in the lower extremities. Babinski's response was also positive. Evaluation on admission showed the following findings: Functional Ambulation Scale (FAS), category 5 (independent ambulation) and Functional Independence Measure (FIM) score, 125 (18–126).

Antinuclear antibodies (ANA), anti-phospholipid antibodies, anti-double-stranded DNA antibodies, human immunodeficiency virus, and markers for hepatitis infection were negative on laboratory tests. Erythrocyte sedimentation rate, thyroid stimulating hormone and parathyroid hormone were in normal limits.

Cranial and spinal magnetic resonance imaging (MRI) were planned because of the inconsistent course of paresis and reflex abnormalities. Spinal MRI revealed multiple disc protrusions and an extruded hernia at the level of the T8–9 vertebrae. The diameter of the spinal canal was within normal limits. On contrast imaging, vascular structures surrounding the dural sac were prominent in the lumbar and thoracic regions. Spinal cord edema was observed (Figure 1). Cranial MRI was normal. The patient was evaluated at the Interventional Radiology Clinic and angiography was performed with the suspicion of arteriovenous malformation. A spinal dAVF was detected. It originated from the bilateral lumbar arteries and was supplied with a large number of small arteries at the level L1–2. The spinal dAVF was drained to the inferior vena cava by the spinal perimedullary veins.



A B

Figure 1— A) T2 weighted sagittal MRI shows intramedullary increased signal in the distal spinal cord without associated expansion as well as signal void serpingious structures (arrows) around the spinal cord representing dilated vessels. **B)** Postcontrast T1 weighted sagittal image with fatsat shows contrast enhancement of the dilated vessels.

Patient was scheduled for endovascular embolization at the Interventional Radiology Clinic. After the patient's muscle weakness worsened to 1/5 bilaterally, with complete loss of

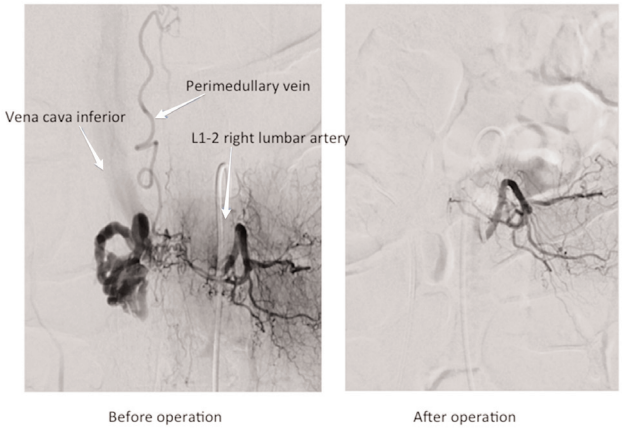


Figure 2— The spinal dural arteriovenous fistula in angiography images; feeding from right lumbar artery at L1-L2 level, draining to perimedullary vein and vena cava inferior.

sensation in the lower extremities, an emergent angiography was performed. Preoperative FAS was 0 (non-functional ambulation) and FIM was 63. Under general anesthesia, the iliac veins and inferior vena cava were accessed by entering from the right common femoral vein. The fistula was also viewed with arterial catheterization. After passing the level of the fistula transvenously, the perimedullary vein was catheterized. Starting at this level, the venous system and fistula were closed with a fluid embolization agent. Control angiography did not reveal any finding of dAVF (Figure 2). No complications were observed after angiography. According to the clinical condition of the patient, a rehabilitation program was planned, which included passive and active-assistive range of movement (ROM) exercises, neuromuscular electrical stimulation, progressive resistance exercises, balance and coordination exercises, lower limb robotic rehabilitation, and progressive ambulation training.

Before embolization, the patient was paraplegic; however, he showed a significant improvement in the first month of rehabilitation. At discharge, the patient's lower extremity muscle strength returned to normal. He had minimal hypoesthesia in the L5/S1 dermatomes and did not have any gait disability. FAS was 5 (independent ambulation) and FIM was 123. The patient was scheduled for follow up after 2 months.

Discussion

Spinal dAVF is a cause of vascular-related spinal cord injury (5). The incidence is estimated to be approximately 5–10 cases per million. The lesion is more common in men over the age of 50 years and affects the thoracic and lumbar spine (1). These patients usually present with slow and progressive myelopathy. Trauma, infection, surgery, and syringomyelia are all considered as alternative diagnoses because the exact etiology is often unclear. The pathological lesion is a shunt between the radicular artery and vein, which causes venous hypertension in the spinal cord (1). Vascular steal and spinal cord compression have also been suggested as the mechanism for damage. However, the current theory is that shunting of arterialized blood causes increased venous pressure in the coronal venous plexus and leads to congestion, edema, and eventually ischemic injury in the affected region of the cord (6).

Although it is a treatable cause of myelopathy, spinal dAVF is rarely considered and is usually diagnosed late. This is because it is so infrequently encountered in daily practice and the clinical presentation is non-specific (1). Gait disability is usually the first symptom. Progression to full-blown myelopathy or paraplegia is slow. Intermittent paresthesia and symptoms of sensory loss, suggestive of peripheral nerve lesions, may be observed (4). Bladder dysfunction, intestinal dysfunction, and impotence may also be observed (6). Our patient had a history of difficulty in walking and motor symptoms; however, he did not have any bladder or intestinal dysfunction until he was completely paraplegic.

Physical examination may reveal upper motor neuron lesion findings, such as increased muscle tone and increased deep tendon reflexes, as well as early lower motor neuron lesion findings, and this can complicate the diagnosis. The average time between the onset of the symptoms and the diagnosis ranges from 12 to 44 months (4). Our patient was symptomatic for 3 months, and, although he described paraparetic episodes, the physical findings were ambiguous. Unnecessary interventions, surgeries, and misdiagnosed cases have been reported in the literature (4,7).

In the differential diagnosis, the causes of non-traumatic progressive myelopathy, which are extensive, should be considered (8). Patients with a more rapid progression should primarily be investigated for compressive lesions, such as metastatic neoplasms and spinal dural abscesses, which require immediate intervention. Also, cervical spondylosis, which is the most common cause of quadriparesis, and lumbar disc steno-



sis should be considered (9). Aortic dissection, postoperative ischemia, vascular embolism, or systemic hypotension can cause similar clinical manifestations by creating spinal cord ischemia (5). Inflammatory myelopathies can have acute, subacute, or chronic onset. They can be isolated or be a component of multiple sclerosis, and, rarely, may be associated with chronic infections [e.g., acquired immunodeficiency syndrome (AIDS), syphilis, etc.], and rheumatic or connective tissue diseases, such as systemic lupus erythematosus (SLE) and anti-phospholipid syndrome (10). The other causes of myelopathy, such as anterior horn motor neuron disease, paraneoplastic syndromes, radiation or electrical injury, and nutritional etiologies, especially in patients with gastrointestinal disease and gastric bypass operations, should also be considered (8).

Family history, duration of symptoms, patient age, comorbid diseases, systemic symptoms, and thorough questioning for peripheral nervous system symptoms are helpful in the diagnosis. Mass lesions, discopathy, and inflammatory myopathies can be excluded through imaging modalities and cerebrospinal fluid analysis (8). Early symptoms, such as paresthesia and lower motor neuron findings, can also suggest polyradiculopathies. Upper extremity symptoms are rarely seen in spinal dAVF, and the absence of glove-like sensory loss, asymmetry, and bladder dysfunction may help to exclude polyneuropathies (4).

A spinal dAVF is seen as a hyperintense lesion on T2-weighted MRI images, and often a corresponding hypointense signal can be found on T1-weighted images. These findings are secondary to the cord ischemia and edema. Additional MRI findings include prominent intradural veins, spinal cord enhancement and enlargement, and scalloping and irregular cord surface. However, these findings are non-specific and must be confirmed by the gold standard imaging method of angiography (11). In our patient, on spinal MRI, there were no degenerative findings, discopathy, or stenosis to explain the clinical symptoms. Due to the edema and the expansion of the vascular structures at the thoracic and lumbar regions of the cord, an angiography was performed to investigate vascular lesions.

Endovascular embolization and microsurgical techniques are available as treatments for spinal dAVF. Our patient was treated with endovascular embolization. Hessler et al. stated that there is no consensus as yet for the optimal treatment of dAVF, and surgery can be performed on patients with failed embolization (2). The level of healing is thought to be related to the degree of spinal lesion caused by spinal venous congestion (7). Prognosis and success of treatment have been reported to be better in younger patients with fewer symptoms. Pre-operative severe neurological clinical signs are one of the major factors that worsen the prognosis (12,13).

Early diagnosis is strongly correlated with a better prognosis. Better treatment outcomes have been shown in early-diagnosed patients who were treated with either embolization or surgery (13). Micturition, pain, and muscle spasms often have a worse response to treatment compared to gait disability (4,13). Our patient was symptomatic for 3 months when he underwent embolization. Due to the early intervention, he showed rapid improvement after the treatment and did not have gait or any serious disability on discharge. In most of the case series in the literature, data on the time between the onset of rehabilitation and fistula treatment are limited (14). However, in most cases, it has been reported that if the intervention is delayed, even prolonged rehabilitation does not change the grave prognosis (15).

In conclusion, spinal dAVF is an important and treatable condition with slow clinical progression and non-specific symptoms. Because a patient's prognosis is strongly correlated with the time of diagnosis, spinal dAVF should be considered in the differential diagnosis of patients who present with paresis and plegia in daily practice. Embolization and surgery are available treatment options and should be supported with appropriate rehabilitation programs.

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LETTER TO THE EDITOR

RADIATION INDUCED DIFFUSE CUTANEOUS BASAL CELL CARCINOMA (BCC) IN A RETIRED RADIOLOGY TECHNICIAN

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To the editors,

Basal cell carcinoma (BCC), the major histological type of non-melanoma skin cancers with an 80% prevalence, is the most frequently diagnosed malignancy in the fair-skinned population worldwide (1,2). The American Cancer Society reported that skin cancers consist of approximately half of all cancers diagnosed in the USA (2). Skin cancers, including BCC, are the first solid cancers associated with radiation (3). Radiologists and radiology technicians were the first working population in which radiation-induced skin cancers were recognised (3). Rogers et al. reported a 4.2% incidence of non-melanoma skin cancers among the health care population in their research, analysing the years between 1992 and 2006 (4). We aim to raise all of our colleagues' awareness with our one-patient letter.

An 81-year-old male patient observed a spontaneously formed scar on his nose approximately 4 years ago. He applied different dermatologic treatments in an attempt to heal it; however, 5–6 months before our examination, he detected another lesion on the left half of his upper lip and was referred by a dermatologist. After applying additional dermatologic treatments, punch biopsies were sampled from both of the lesions. Pathology reported BCC and he was consulted by our clinic. A history of working as a radiology technician for over 50 years, preparing radioactive materials and solutions for imaging devices with bare hands, particularly in the first decade of his occupational lifetime, was noted as remarkable in the anamnesis. In contrast, he mentioned that he had never had similar complaints before, particularly during his occupational life. Excisional biopsies were planned for the lesions (Figure 1). Lesions on the nasal dorsum and left nasolabial groove were excised *en block*. All of the scars healed without complication. The pathology department reported BCC for the lesions and dermatologic follow up was coordinated for the patient. At month 2 of his follow up, multiple dermatologic nodular lesions with irregular borders and telangiectasia on the chest wall and bilateral shoulders were observed (Figure 2). Excision was performed and BCC (superficial spreading) was reported again. Dermatologic follow up continued. Three months later, he was examined with multiple lesions on posterior cervical, left preauricular, left anterolateral femoral and left lumbar sites and the dorsum of the trunk (Figure 3). Excisional biopsies were reported as nodular BCC for posterior cervical lesions. Others were of the superficial spreading form again (Figure 4). After scar healing without complications, the patient declared that he rejected to proceed with his follow up. His follow up ended 6 months after his first examination.

Objectively, detecting BCC in a patient who worked with radioactive materials and radiologic imaging devices without enough protection for more than 50 years was not an unexpected clinical situation. However, ignoring sun exposure as one of the main factors would be a bias after considering the patient's age and localizations

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Figure 1— Scar on the nose.

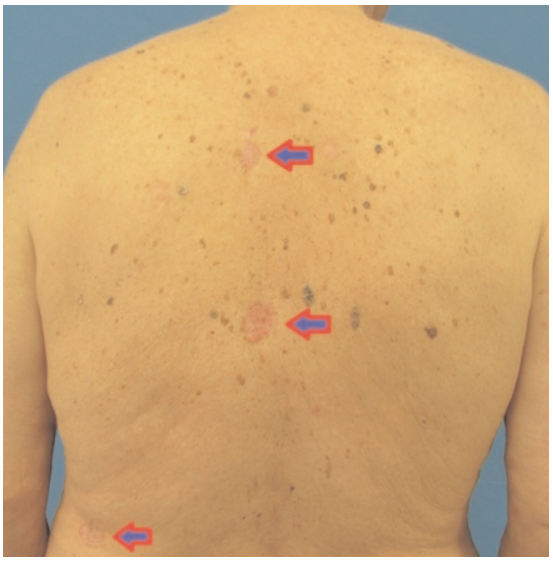


Figure 3— Multipl lesions.

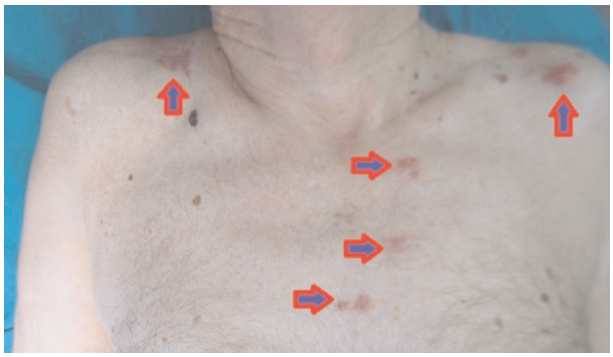


Figure 2— Noduler lesions.



Figure 4— Superficial spreading.

of the first excised lesions (nasal dorsum and nasolabial groove). On the other hand, most of the lesions detected on follow up were under clothed areas. If we add the aggressiveness of BCC and literature data on record, the rational for a radiation-induced BCC diagnosis is strengthened. In addition, the patient had been a retired individual for 15 years. There was quite a long lag period before the first lesions were detected. Eventually, it was a misfortune that the patient chose to end his follow ups voluntarily.

Scientific studies on radiation and its effects on health are progressing exponentially. Moreover, radiation-induced diseases still present challenging situations. Clearly, we are not proficient enough in some cases. Almost all branches of medicine need to work with radiology or radiologic materials today. We hope to remind our colleagues about radiation-induced BCC with this letter.

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