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Prognostic Significance of Nuclear Factor Kappa B and CD9/Motility-related Protein-1 in Stage II-III Rectal Cancer Patients Treated with Postoperative Chemoradiotherapy

Postoperatif Kemoradyoterapi ile Tedavi Edilen Evre II-III Rektum Kanseri Olgularında Nükleer Faktör Kappa B ve CD9/Motility Related Protein-1'in Prognostik Önemi

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ABSTRACT

Objective: The aim of this study is to investigate the prognostic significance of nuclear factor kappa B (NFkB) and CD9 (MRP-1) proteins in stage II-III patients with rectum cancer treated by surgery and adjuvant chemoradiotherapy.

Material and Methods: Between May 2003 and April 2008, 5 µm sections were taken from paraffin-embedded tissue samples of 45 patients diagnosed with rectal cancer and treated with radiotherapy and 5FU-based chemotherapy at our clinic. Immunohistochemical staining with CD9 and NFkB was performed. The effects of CD9 and NFkB positivity on local-regional recurrence, disease-free survival, and overall survival were investigated. Statistical analyses were performed using the SPSS 15.0 software package.

Results: A statistically significant difference was found in the CD9 positive group in terms of five-year local control (p=0.026). However, no statistically significant difference was found in 5-year disease-free survival and overall survival between CD9 positive and negative cases (p=0.223, p=0.205). No statistically significant difference was found in 5-year disease-free survival, overall survival and local control between NFkB positive and negative cases (p=0.794, p=0.362 and p=0.805, respectively).

Conclusion: It was thought that CD9 positivity may have prognostic significance in terms of local-regional recurrence in our rectal cancer cases. The prognostic significance of CD9 positivity or negativity in terms of 5-year disease-free and overall survival in rectal cancer cases could not be demonstrated. The prognostic significance of NFkB positivity or negativity in terms of 5-year disease-free survival, local control, and overall survival in rectal cancer cases could not be demonstrated.

Keywords: CD9, NFkB, stage II-III rectum cancer, adjuvant chemoradiotherapy

ÖZ

Giriş: Bu çalışmada; postoperatif kemoradyoterapi uygulanan evre II-III rektum kanserli hastalarda, nükleer faktör kappa B (NFkB) ve CD9 (MRP-1) proteinlerinin prognostik önemi araştırıldı.

Gereç ve Yöntemler: Mayıs 2003-Nisan 2008 tarihleri arasında kliniğimizde rektum kanseri tanısı ile radyoterapi ve 5FU temelli kemoterapi uygulanan 45 hastanın, parafin bloklanmış doku örneklerinden alınan 5 µm'lik kesitlere CD9 ve NFkB ile immünohistokimyasal boyama uygulandı. CD9 ve NFkB pozitifliğinin yerel-bölgesel yinleme, hastalüksüz sağkalım ve genel sağkalıma etkileri incelendi.

Bulgular: Beş yıllık lokal kontrol bakımından CD9 pozitif grupta istatistiksel olarak anlamlı fark bulundu (p=0,026). Ancak, CD9 pozitif ve negatif olgularda 5 yıllık hastalüksüz sağkalım ve genel sağkalım açısından istatistiksel olarak anlamlı fark saptanmadı (p=0,223, p=0,205). NFkB pozitif ve negatif olgularda 5 yıllık hastalüksüz sağkalım, genel sağkalım ve lokal kontrol açısından istatistiksel olarak anlamlı fark bulunmadı (sırasıyla; p=0,794, p=0,362 ve p=0,805).

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Sonuç: CD9 pozitifliğinin rektum kanserli olgularımızda yerel-bölgesel yineleme açısından prognostik önemi olabileceği düşünüldü. CD9'un pozitif veya negatif olmasının 5 yıllık hastaliksız ve genel sağkalım açısından rektum kanserli olgularda prognostik önemi gösterilemedi. NFKB pozitif veya negatif olmasının rektum kanserli olgularda 5 yıllık hastaliksız sağkalım, lokal kontrol ve genel sağkalım açısından prognostik önemi gösterilemedi.

Anahtar Kelimeler: CD9, NFKB, evre II-III rektum kanseri, adjuvan kemoradyoterapi

INTRODUCTION

While the prognosis of early-stage rectal cancer (RC) is favorable, outcomes worsen as the tumor extends distally within the rectum and progresses to a higher stage. Unlike in colon cancer, local and regional recurrences are particularly important in RC. Compared with colon cancer at the same stage, RC has higher rates of locoregional recurrence following treatment. Reasons include the lack of a serosal barrier (facilitating local invasion) and anatomical limitations that make it difficult to achieve wide tumor-free lateral (radial, circumferential) surgical margins even when proximal and distal margins are adequate (1).

Surgery is the primary treatment for RC. However, due to the high potential for local and systemic relapse in stage II-III cases, adjuvant treatment is necessary. Combined chemotherapy (CT) and radiotherapy (RT), either preoperatively or postoperatively, is the standard treatment for stage II-III RC. In a multidisciplinary setting, RT is usually applied as an adjuvant therapy, with or without CT, either preoperatively or postoperatively (2).

The CD9 antigen is a surface marker on leukemic and lymphohematopoietic cells. It is expressed on mature B lymphocytes and serves as a surface marker of leukemia arising from differentiating cells. It has also been demonstrated in a wide range of hematopoietic and non-hematopoietic tissues. CD9 is associated with cellular stimulation, growth, motility, adhesion, tumor metastasis, and nervous system development and protection. CD9 (MRP-1) is one of 20 members of the transmembrane 4 superfamily and is localized on chromosome 12 (12p13). It plays roles in cell growth, adhesion, and motility (3).

Nuclear factor kappa B (NFKB) regulates the expression of many genes responsible for cell growth, differentiation, regulation of apoptosis, cytokine production, and neoplastic transformation. Studies indicate that NFKB plays a role in preventing apoptosis in several cancer types (e.g., lung, gastric, and prostate cancers). However, it is also involved in regulating apoptosis (4).

The aim of this study was to evaluate the prognostic significance of the NFKB and CD9 (MRP-1) proteins in patients with stage II-III RC treated with postoperative CT-RT.

MATERIALS and METHODS

This study was conducted in the Departments of Radiation Oncology and Pathology in our university's Faculty of Medicine. Forty-five patients with locally advanced RC (T3-

T4 and/or lymph node-positive) who were admitted to our Oncology Hospital between May 2003 and April 2008 were retrospectively included in the study. Patients underwent abdominoperineal resection (APR), low anterior resection (LAR), anterior resection (AR), or total colectomy (TC). All patients received adjuvant concurrent CT-RT after curative surgery, followed by maintenance CT. Ethics committee approval was obtained from the Dean's Office of Erciyes University Faculty of Medicine in the presence of the professors (decision number: 142, date: 26.02.2010).

Radiotherapy Protocol

Pelvic RT included the tumor bed and the perirectal, internal iliac, external iliac, and presacral lymph node regions. A total dose of 45 Gy was delivered in 25 fractions (1.8 Gy/day, 5 days/week). After pelvic RT, a boost of 5.4 Gy was applied to the primary tumor bed.

Chemotherapy Protocol

Patients received weekly RT concurrently with 5-fluorouracil (425 mg/m²) and folinic acid (20 mg/m²).

Immunohistochemical Staining

Immunohistochemical staining for CD9 (MRP-1) and NFKB was performed on paraffin-embedded rectal carcinoma tissue samples using the streptavidin-biotin immunoperoxidase method.

CD9 (MRP-1) Staining

5 µm-thick sections were cut from paraffin-embedded tissue blocks and mounted on poly-L-lysine-coated slides. After deparaffinization at 60 °C for one hour and rehydration through graded alcohols (99%, 96%, 70%), endogenous peroxidase activity was blocked by incubation with 0.3% hydrogen peroxide for 10 minutes. The slides were washed in phosphate-buffered saline (PBS) and incubated overnight at 4 °C with primary CD9 antibody. The following day, sections were treated with biotinylated anti-mouse and anti-rabbit immunoglobulins, each for 10 minutes, followed by streptavidin-peroxidase conjugate for 10 minutes. After washing with PBS, diaminobenzidine (DAB) chromogen was applied for 10 minutes. Counterstaining was performed with Mayer's hematoxylin, after which the slides were washed, mounted with balsam, and covered with a glass coverslip.

NFKB Staining

Sections 5 µm thick were cut from paraffin-embedded tissue blocks and mounted on poly-L-lysine-coated slides. The slides were deparaffinized at 60 °C for one hour, then cleared

in xylene, rehydrated through decreasing concentrations of ethanol, and rinsed in distilled water. Antigen retrieval was performed using 10 nM citrate buffer (pH 6.0) in a microwave oven at 200 °C for 20 minutes. After cooling to room temperature, endogenous peroxidase activity was blocked with 0.3% hydrogen peroxide for 10 minutes. The sections were washed with PBS and incubated with the NFKB primary antibody for 30 minutes at room temperature. They were then treated with biotinylated anti-mouse and anti-rabbit immunoglobulin for 10 minutes, followed by streptavidin-peroxidase conjugate for 10 minutes. After washing in PBS, DAB chromogen was applied for 10 minutes, followed by rinsing in distilled water. Counterstaining was performed with iron hematoxylin, and the slides were washed, mounted with balsam, and covered with a glass coverslip.

Evaluation of Immunohistochemical Staining

Tissue-internal staining was used as the positive control. Tonsil tissue served as the positive control for CD9, and prostate tissue served as the positive control for NFKB.

CD9 (MRP-1) Evaluation

Cases showing cytoplasmic staining in more than 5% of tumor cells at 10× magnification were considered positive; others were considered negative.

NFKB Evaluation

Cytoplasmic staining in more than 10% of tumor cells at ×10 magnification was considered positive; cytoplasmic staining in less than 10% of tumor cells at ×10 magnification was considered negative.

Statistical Analysis

Data were analyzed using SPSS 15.0 for Windows (Statistical Package for the Social Sciences). The Shapiro-Wilk test was used to assess normality. Categorical variables were compared using the chi-square test, and survival analyses were performed using the Kaplan-Meier method. A p-value <0.05 was considered statistically significant.

RESULTS

The average age of the patients was approximately 56 (26-78) years. 23 (51%) male and 22 (49%) female patients were included in the study fifteen patients underwent APR, eight underwent AR, twenty-one underwent LAR, and one underwent TC surgery. Lymph node metastasis was present in 21 patients (47%). Forty-two of the patients were diagnosed with adenocarcinomas and three with signet-ring cell carcinomas. Vascular invasion and perineural invasion were each seen in 15 patients. The mean follow-up period for the patients was 37 months (range: 3-77 months), and distant metastases occurred during follow-up in the liver (9), lung (7), brain (2), mesentery (1), and inguinal lymph nodes (1). There were 15 (33%) patients who were NFKB-negative and

30 (67%) who were NFKB-positive. Sixteen (36%) patients were CD9-negative and 29 (64%) patients were CD9-positive. The mean overall survival, mean local control time, and mean disease-free survival time were 37±17.56, 36±16.87, and 36±18.11 months, respectively.

Among CD9-positive patients, the five-year disease-free survival, local control, and overall survival rates were 65%, 90%, and 82%, respectively. In contrast, these rates were 48%, 66%, and 46% in CD9-negative patients.

Although there was no statistically significant difference between CD9-positive and CD9-negative groups in terms of five-year disease-free survival or overall survival (p=0.223 and p=0.205, respectively), both parameters were numerically higher in the CD9-positive group. However, the five-year local control rate was significantly higher in the CD9-positive group (p=0.026).

In NFKB-positive patients, the five-year disease-free survival rate, local control rate, and overall survival rate were 60%, 84%, and 70%, respectively. In NFKB-negative patients, these rates were 56%, 75%, and 76%. There was no statistically significant difference between NFKB-positive and NFKB-negative groups in terms of disease-free survival, local control, or overall survival (p=0.794, 0.362, and 0.805, respectively).

DISCUSSION

In our study, patient characteristics and distribution by NFKB expression are shown in Table 1.

In a retrospective study by Zvieriev et al. (5), tumor specimens from 153 patients with head and neck tumors who received external beam RT were evaluated immunohistochemically for CD9 expression. CD9 positivity was found in 108 patients (71%), whereas 45 (29%) were CD9 negative. Five-year disease-free survival was significantly higher in CD9-positive patients.

Similarly, Wang et al. (6) investigated 40 patients with pancreatic cancer and reported CD9 positivity in 15 (38%) cases. One-year overall survival rates were lower among CD9-negative patients (0-25.5%) than among CD9-positive patients. Median survival time was also longer in CD9-positive patients (397 vs. 226 days) (7).

In another study by Guo et al. (8) increased NF-κB pathway activity leads to increased growth of breast cancer cells and an increased risk of breast cancer metastasis to bones, lymph nodes, lungs, and liver (9).

Lind et al. (10) evaluated 146 patients with stage III colon cancer and found CD9 positivity in 69 (47%) cases and negativity in 77 (53%) cases. Three-year overall and disease-free survival rates were significantly higher among CD9-positive patients (p<0.001).

Multiple studies in the literature including those on breast, lung, osteosarcoma, bladder, esophageal, and prostate cancers have demonstrated that CD9 positivity is associated with

Table 1. Distribution of patients according to NFKB expression			
Parameters		NFKB (-)	NFKB (+)
n		15 (33%)	30 (67%)
Age (years)		54 (26-76)	58 (26-76)
Gender	Female	7 (16%)	15 (33%)
	Male	8 (18%)	15 (33%)
Operation type	APR	4 (9%)	11 (25%)
	LAR	6 (13%)	15 (33%)
	AR	4 (9%)	4 (9%)
	TC	1 (2%)	0 (0%)
Histopathology	Adenocarcinoma	13 (29%)	29 (65%)
	Signet-ring cell carcinoma	2 (4%)	1 (2%)
Grade	Grade I	0 (0%)	5 (11%)
	Grade II	10 (22%)	20 (45%)
	Grade III	5 (11%)	5 (11%)
LVI	Present	5 (11%)	10 (22%)
	Absent	10 (22%)	20 (45%)
PNI	Present	3 (6%)	12 (27%)
	Absent	12 (27%)	18 (40%)
T stage	T3	12 (27%)	27 (61%)
	T4	3 (6%)	3 (6%)
N stage	N(-)	6 (13%)	18 (40%)
	N1	3 (7%)	9 (20%)
	N2	4 (9%)	2 (4%)
	N3	2 (4%)	1 (3%)

NFKB: Nuclear factor kappa B, LVI: Lymphovascular invasion, PNI: Perineural invasion, APR: Abdominoperineal resection, LAR: Low anterior resection, AR: Anterior resection, TC: Total colectomy

improved overall and disease-free survival (11).

Of 45 patients with RC in the present study, 29 (64%) were CD9 positive (Figure 1; Tables 2 and 3) and 16 (36%) were CD9 negative. As this is the first study on RC evaluating CD, 9 and NFKB expression together, our results were compared with findings from non-RC studies.

Our CD9 positivity rate (64%) was comparable to the 71% positivity reported by Guo et al. (8) CD9 release appears to increase the spread of some cancers, while in others it seems to restrict spread and the degree of invasion. Therefore, this pathway is interconnected with the cell structure, the

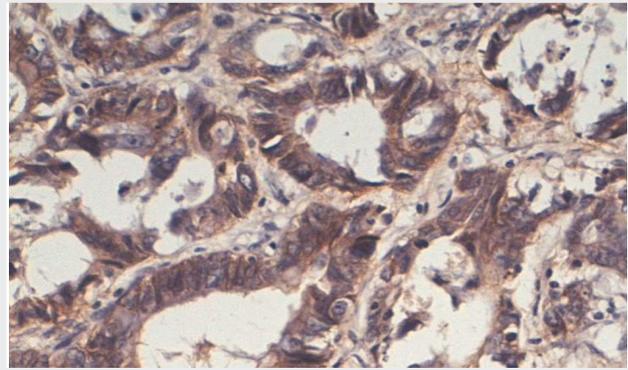


Figure 1. Positive CD9 staining in tumor tissue

Table 2. Distribution of patients according to CD9 expression			
Parameters		CD9 (-)	CD9 (+)
n		16 (36%)	29 (64%)
Age (years)		60 (26-76)	53 (26-78)
Gender	Female	9 (20%)	13 (29%)
	Male	7 (16%)	16 (36%)
Operation type	APR	4 (9%)	11 (24%)
	LAR	9 (20%)	12 (27%)
	AR	3 (7%)	5 (11%)
	TC	0 (0%)	1 (2%)
Histopathology	Adenocarcinoma	14 (31%)	28 (62%)
	Signet-ring cell carcinoma	2 (5%)	1 (2%)
Grade	Grade I	3 (6%)	2 (5%)
	Grade II	11 (24%)	19 (42%)
	Grade III	2 (5%)	8 (18%)
LVI	Present	4 (9%)	11 (24%)
	Absent	12 (27%)	18 (40%)
PNI	Present	3 (6%)	12 (27%)
	Absent	12 (27%)	18 (40%)
T stage	T ₃	13 (29%)	26 (59%)
	T ₄	3 (6%)	3 (6%)
N stage	N (-)	7 (16%)	17 (38%)
	N ₁	4 (9%)	8 (18%)
	N ₂	3 (6%)	3 (6%)
	N ₃	2 (5%)	1 (2%)

LVI: Lymphovascular invasion, PNI: Perineural invasion, APR: Abdominoperineal resection, LAR: Low anterior resection, AR: Anterior resection, TC: Total colectomy

Table 3. Comparison of survival according to CD9 and NFKB expression

Survival		CD9			NFKB		
		-	+	p	-	+	p
Disease-free survival	5-year	48%	65%	0.223	56%	60%	0.794
Local control	5-year	66%	90%	0.026	75%	84%	0.362
Overall survival	5-year	46%	82%	0.205	76%	70%	0.805

NFKB: Nuclear factor kappa B

microenvironment surrounding the cell, cell signaling, and the interaction of molecules involved. Consequently, CD9 serves as a reliable marker for leukemic cells, and its monitoring is particularly important in the diagnosis and control of acute lymphoblastic and myeloid leukemia (9,11,12). In our series, although five-year disease-free and overall survival rates were numerically higher in CD9-positive patients (65% vs. 48% and 82% vs. 46%, respectively), the differences were not statistically significant ($p=0.223$ and $p=0.205$). However, CD9-positive patients had significantly better local control (90% vs. 66%, $p=0.026$).

These findings are consistent with those of Wang et al. (6) activation of RelA, a member of the Rel/NF-kappaB transcription factor family, leads to the sustained activation of pancreatic adenocarcinoma cells. Inhibition of RelA in pancreatic tumor cells can reduce their potential for invasion and metastasis. In our study, the lack of statistically significant differences in disease-free and overall survival may be attributable to the small sample size.

No previous studies have directly evaluated the effect of CD9 expression on local control in RC. The observed improvement in local control without a corresponding increase in overall or disease-free survival might also be related to the limited number of patients.

In our study, Figure 2 and Table 3 show positive NFKB staining in tumor tissue.

Several investigators have suggested that NFKB activation plays a key role in tumor development and progression by regulating genes involved in cell-cycle control, invasion, metastasis, angiogenesis, and inhibition of apoptosis in cancers such as pancreatic, breast (13), colorectal, hepatocellular, prostate, and gastric carcinomas (14). Furthermore, NFKB activation has been associated with resistance to anticancer therapy. Inhibition of NFKB has been shown to sensitize tumor cells including those from fibrosarcoma, lymphoma, melanoma, bladder cancer, breast cancer, and squamous cell carcinoma to the cytotoxic effects of TNF, chemotherapy, and RT (13).

Yildiz et al. (13) studied 49 patients with gastric carcinoma who were treated with adjuvant chemoradiotherapy and reported NFKB negativity in 29 patients (59%) and positivity in 20 patients (41%). No significant difference was found in progression-free survival; however, overall survival was shorter in NFKB-positive patients ($p=0.033$).

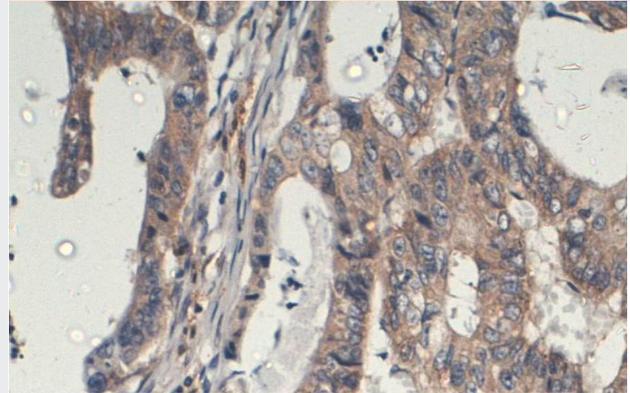


Figure 2. Positive NFKB staining in tumor tissue
NFKB: Nuclear factor kappa B

Eroğlu et al. (14) evaluated 28 patients with stage III non-small-cell lung cancer treated with concurrent chemoradiotherapy and reported NFKB negativity in 21 cases (75%) and NFKB positivity in 7 cases (25%). Eight-month progression-free survival was significantly higher in the NFKB-negative group (83% vs. 24%, $p=0.046$), while no significant difference was observed in 15-month overall survival (41% vs. 33%, $p=0.94$) (15).

Yamanaka et al. (15) studied 63 patients with gastric carcinoma, finding NFKB negativity in 42 patients (67%) and positivity in 21 patients (33%). Among 47 surgically treated patients, the NFKB-negative group had a significantly longer overall survival ($p=0.015$).

In our study, 15 patients (33%) were NFKB-negative and 30 patients (67%) were NFKB-positive. NFKB expression showed no significant impact on disease-free survival, overall survival, or local control rates in RC patients treated with postoperative concurrent chemoradiotherapy.

Kim et al. (16) demonstrated that high CD9 expression in rectal tumor cells was inversely correlated with tumor recurrence, particularly in left-sided colorectal cancer. However, they noted that it occupies a different position in immune cells regardless of the location of the primary tumor. In their review, Sadati et al (17) stated that the NF- κ B pathway plays a crucial role in the progression of colorectal cancer and that targeting this pathway may have therapeutic benefits.

Because our research was conducted in a single center with a relatively small sample size, the results should be interpreted with caution. We believe that larger, multicenter studies could provide more definitive conclusions. Future investigations incorporating molecular-level analyses may further elucidate the role of CD9 and NFKB in determining local recurrence and progression-free survival in RC and potentially guide the development of new therapeutic strategies.

CONCLUSION

Among stage II-III RC patients treated with surgery and adjuvant concurrent CT-RT, CD9 positivity was associated with significantly improved local control but did not affect disease-free or overall survival; NFKB positivity had no prognostic impact on survival or local control.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Dean's Office of Erciyes University Faculty of Medicine in the presence of the professors (decision number: 142, date: 26.02.2010).

Informed Consent: This study is a retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.K., O.G.Y., I.S., S.S., Concept: O.G.Y., I.S., S.S., Design: O.G.Y., I.S., S.S., Data Collection or Processing: S.K., I.S., Literature Search: S.K., I.S., Writing: S.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Evaluation of Cranial Gunshot Injuries with 3 Dimension Computed Tomography

Kraniyal Ateşli Silah Yaralanmalarının 3 Boyutlu Bilgisayarlı Tomografi ile Değerlendirilmesi

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ABSTRACT

Objective: Despite the widespread use of tomography in different forensic situations and gunshot injuries, the use of new radiological methods in patients receiving care at hospitals has lagged, and there are limited publications on the use of 3D imaging in gunshot injuries. This study aimed to investigate the findings obtained with 3D reconstruction in cranial gunshot injuries.

Material and Methods: Reconstructed 3D images produced by tomographic scanning of 12 sheep heads were used. Radiological images were obtained using a Vimago GT30 CT (Epica Animal Health, USA). Images recorded as DICOM were exported to digital media, then reconstructed and evaluated by two researchers using the HORUS apps.

Results: The location and size of the entry-exit wounds, the size and spread of bone fragments, the location and size of skull fractures, the integrity of the bones and joints forming the joints in the shooting region, and the damage in complex anatomical areas are shown using 3D reconstruction.

Conclusion: 3D reconstruction provides essential information to clinicians, surgeons, and radiology, and emergency professionals, including damage to the skin, the number, course, and length of skull bone fractures, the number and distribution of bone fragments, joint integrity, and the relationship between bone fragmentation and joint integrity, creating lifelike images without performing an autopsy. 3D reconstruction provides early, non-destructive, and critical information to legal authorities for forensic investigations, in cases under post-injury healthcare and a forensic autopsy is not possible. In cranial gunshot injuries, 3-dimension reconstruction should be part of the radiological evaluation.

Keywords: Computed tomography, 3D tomography, cranial gunshot injuries, firearm injury

ÖZ

Giriş: Tomografi farklı adli olgularda ve ateşli silah yaralanmalarında yaygın olarak kullanılmasına rağmen, hastanelerde tedavi gören hastalarda yeni radyolojik yöntemlerin kullanımı geride kalmış olup, ateşli silah yaralanmalarında 3D görüntülemenin kullanımına ilişkin sınırlı sayıda yayın bulunmaktadır. Bu çalışmada, kraniyal ateşli silah yaralanmalarında 3D rekonstrüksiyon ile elde edilen bulguların incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: On iki adet koyun kafasının tomografi görüntülerine 3D rekonstrüksiyon uygulandı. Radyolojik görüntüler Vimago GT30 CT (Epica Animal Health, ABD) kullanılarak elde edildi. DICOM olarak kaydedilen görüntüler dijital ortama aktarıldı, ardından iki araştırmacı tarafından HORUS uygulaması kullanılarak yeniden yapılandırıldı ve değerlendirildi.

Bulgular: Giriş-çıkış yaralarının yeri ve büyüklüğü, kemik parçalarının boyutu ve yayılımı, kafatası kırıklarının yeri ve büyüklüğü, atış bölgesindeki eklemleri oluşturan kemik ve eklemlerin bütünlüğü, kompleks anatomik bölgelerdeki hasarlar 3D rekonstrüksiyon ile gösterilmiştir.

Sonuç: 3D rekonstrüksiyon, klinisyenlere, cerrahlara, radyoloji ve acil servis çalışanlarına deri hasarı, kafatası kemiği kırıklarının sayısı, seyri ve uzunluğu, kemik parçalarının sayısı ve dağılımı, eklem bütünlüğü ve kemik parçaları ile eklem bütünlüğü arasındaki ilişki gibi temel bilgiler sağlayarak otopsi yapılmadan gerçekçi görüntüler oluşturur. 3D rekonstrüksiyon, yaralanma sonrası sağlık bakımı altındaki, adli otopsi yapılamayan olgularda adli makamlara adli soruşturmalar için erken, tahribatsız ve kritik bilgiler sağlar. Kraniyal ateşli silah yaralanmalarında 3D rekonstrüksiyon radyolojik değerlendirmenin bir parçası olmalıdır.

Anahtar Kelimeler: Bilgisayarlı tomografi, 3D tomografi, kraniyal ateşli silah yaralanması, ateşli silah yaralanması

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INTRODUCTION

Penetrating cranial gunshot injuries (GSIs) are forensic incidents associated with high morbidity and mortality, causing considerable damage to the scalp, skull, and brain parenchyma. Accurate and rapid assessment of medical injury severity and forensic clarification of the event necessitate the immediate determination of the location and size of entry-exit wounds, intracranial damage, and trajectory. Previous cases have demonstrated that radiological imaging performed promptly after initial intervention reduces morbidity and mortality (1-5). Cranial tomography (CT) provides critical findings about entry-exit wounds, Hounsfield unit values in different tissues, brain damage, intracranial gas, cranial bone fractures, distribution of bone fragments, bullet trajectory, foreign bodies, and bullet core residues (6-9). Cranial CT is an appropriate method for clinicians to guide medical or surgical treatment in emergencies, monitoring and clinical follow-up processes, and for forensic physicians in detecting gunshot wounds, determining the type of weapon and injury characteristics, investigation of death etiology, disaster victim identification, crime scenes reconstruction, and shooting reconstruction (10-14). Tomography has remarkable potential for rapid isotropic documentation, generation of 2D reformats, and 3-dimension reconstruction (3DR) (15-18).

3DR is a simulation software that enables comprehensive examination of the entire body or any of its parts, which is always accessible and repeatable. 3D imaging techniques have been accepted by Thali et al. (15) as an important part of the Virtopsy project. 3DR techniques have been reported in different forensic situations, such as GSIs, traffic accidents, explosions via virtual animation of the body, facial reconstruction, height estimation, gait analysis, crime scene reconstruction, determination of weapon type, and shooting reconstruction (19-23).

However, in cases with nonfatal injuries receiving medical care at advanced intervention centers, the use of new radiological methods has remained limited (24). Although CT is widely used in GSIs, there are limited publications regarding the use and benefits of 3D images. In this study, the aim was to investigate 3DR's findings in cranial GSIs.

MATERIALS and METHODS

Reconstructed 3D images produced through CT scanning of 12 sheep heads were used. CT images obtained from our previous CT study. Since it is the most used weapon in civilian injuries, a 9×19 mm caliber Canik Mete TP9 semi-auto handgun with 9×19 mm M822 type (Full Metal Jacket) ammunition was used. Shots were made to the frontal, temporal, and occipital regions from distances of 50 cm, 1m, 5m, and 10m. Radiological images were obtained using a Vimago GT30 CT (Epica Animal Health, USA). Images recorded as DICOM were exported to digital media, then reconstructed and evaluated

by two researchers using the HORUS apps. The final reports were written by consensus of the two researchers.

Ethical approval for the previous CT study was received from the Çukurova University Local Ethics Committee for Animal Experiments on (decision number: 6, date: 30.04.2024). Since no living organ, animal, or human tissue was used in this study, ethics committee approval was not required.

Statistical Analysis

Statistical methods were not used during image review and evaluation in this descriptive study.

RESULTS

As a result of the experiments performed with sheep skulls, the location and size of the entry-exit wound, the size and distribution of bone fragments, the location and size of skull fractures, the integrity of the bones forming the joints in the shooting area, and the damage occurring in anatomically complex regions were demonstrated using 3DR.

Shot characteristics and 3DR findings of sheep:

Sheep 1: The shot was taken 50cm from the frontal region. A well-defined, round, millimetric entry wound was detected on the skin in the frontal region, to the right of the midline. In the bone images, a bone defect measuring 90×88 mm corresponding to the entry wound was observed in the frontal bone, to the right of the midline, along with a 33×45 mm displaced, fragmented bone piece at the margin of the defect. In the posterior cervical region, to the right of the midline, an irregular-edged, large exit wound causing tissue loss in the muscle tissue, occipital bone, and C1 vertebra was detected.

Sheep 2: The shot was taken 50cm from the temporal region. A well-defined, round, millimetric entry wound was detected on the skin in the right temporal region, between the eyeball and the ear. In the bone images, an irregular-edged entry wound was observed in the temporal bone, with the first fracture line extending from the entry wound toward the occipital bone and another toward the eyeball. In contrast, the zygomatic bone and temporomandibular joint were intact. A bone defect corresponding to the exit wound was detected in the area close to the lateral wall of the orbit, between the left temporomandibular joint and the eyeball, and the temporomandibular joint was observed to be intact.

Sheep 3: The shot was taken 50 cm from the occipital region. There is no skin present in the shot area. In the bone images, an entry wound measuring 90×113 mm was detected in the occipital bone, along with four separate fracture lines originating from the entry wound. The millimetric nasal bone and skin defect at the exit wound, detected on CT, was not visualized in the 3DR images.

Sheep 4: The shot was taken 1m from the frontal region. On the skin, a well-defined, round, millimetric entry wound was detected in the frontal region, to the left of the midline. In the bone images, an entry wound measuring 130×90 mm,

involving the midline, was observed in the frontal bone, with a single fracture line extending from the entry wound toward the temporal bone. The Integrity of the occipital bone was disrupted due to a large exit wound containing multiple bone fragments around it, and a fracture line originating from the exit wound was seen extending toward the frontal bone.

Sheep 5: The shot was taken 1m to the temporal region. On the skin, a well-defined, round, millimetric entry wound was detected in the right temporal region, between the eyeball and the ear. In the bone images, a fracture in the mandible and damage to the temporomandibular joint associated with the entry wound were observed. Millimetric comminuted fractures were detected in the left temporal bone and zygomatic bone, and a skin defect corresponding to the exit wound was observed in the left ear.

Sheep 6: The shot was taken 1m to the occipital region. On the skin, a well-defined, round entry wound was detected in the occipital region. In the bone images, a well-defined bone defect measuring 1.8×1.4 cm was observed in the occipital bone, with one fracture line extending from the bone defect toward the left lateral side and two fracture lines extending toward the right lateral side. In the right frontal bone, to the right of the midline and adjacent to the nasal bone, an exit wound measuring 1.8×1.0 cm was detected, along with millimetric fragmented bone pieces around the exit wound.

Sheep 7: The shot was taken 5m from the frontal region. On the skin, a laceration area extending from the right frontal region toward the vertex and the occipital bone was observed. In the bone images, a wide, irregular-edged bone defect originating from the entry wound in the frontal bone was seen extending up to the exit wound in the occipital bone. Multiple bone fragments were scattered into and around the trajectory. In the occipital bone, a large exit wound was detected, with two separate fracture lines originating from the exit wound extending toward the right and left lateral sides.

Sheep 8: The shot was taken 5m to the temporal region. On the skin, a well-defined, round, millimetric entry wound was detected in the right temporal region, between the eyeball and the ear. In the bone images, the entry wound caused damage to the temporal bone and the temporomandibular joint, with a fracture line originating from the entry wound extending toward the occipital bone. In the left temporal bone, adjacent to the temporomandibular joint, an exit wound was observed, along with two fracture lines originating from the exit wound.

Sheep 9: The shot was taken 5m to the occipital region. On the skin, a well-defined, round entry wound measuring 5×5 mm was detected in the occipital region. In the bone images, a well-defined bone defect measuring 90×80 mm was observed in the occipital bone, with a single fracture line originating from the bone defect extending to the right frontal bone. The nasal bone was intact, and a 3×5 mm exit wound was observed on the skin between the nostrils.

Sheep 10: The shot was taken 10m from the frontal region.

On the skin, a well-defined skin defect measuring 4×3 mm was detected distal to the nasal bone, to the right of the midline. In the bone images, an irregular-edged defect measuring 1.1×1.0 cm was identified adjacent to the nasal bone in the frontal bone. A large exit wound causing damage to the lateral part of the occipital bone and the C1 vertebra, to the right of the midline, was observed.

Sheep 11: The shot was taken 10m to the temporal region. On the skin, a well-defined, round, millimetric entry wound was detected in the right temporal region, behind the eyeball. In the bone images, damage to the temporomandibular joint and a mandibular fracture were observed. In the left temporal region, behind the eyeball, a millimetric exit wound was detected, along with damage to the temporomandibular joint and a mandibular fracture.

Sheep 12: The shot was taken 10m to the occipital region. In the bone images, a large entry wound causing a bone defect in the corpus of the C1 vertebra, to the left of the midline, was detected. In the nasal bone, to the right of the midline, a wide, irregular-edged exit wound was observed, with fragmented bone pieces spreading outward from the exit wound.

DISCUSSION

As first stated by Thali et al. (15) in 2003, radiological methods have opened new horizons in the evaluation of forensic cases (16,17). Over the past 20 years, technological advancements in multi-slice CT scanners have enabled higher resolution and the acquisition of truly isotropic data sets. These data sets can be reconstructed in any desired plane, processed volumetrically, and restructured using various algorithms to obtain realistic 3D images. By integrating resolution and color information into sectional radiological methods, 3DR enables non-destructive, permanent documentation of findings in both living and deceased individuals, while providing detailed information and records about the incident and injury (22,25,26). Tomography is ideal for visualizing radiopaque materials and bone structures, yet it is limited in evaluating soft tissues and parenchymal organs. 3DR is a highly effective approach for demonstrating the damage caused by the bullet core on the skin in GSIs, overcoming the soft tissue limitations of CT and providing critical information for wound reconstruction. With 3DR, it is possible to visualize, preserve, and present the damage inflicted by the bullet core on the skin, as well as provide visual evidence regarding entry and exit wounds. In cases that reach advanced intervention centers after injury, the examination of entry and exit wounds is performed by the first physician evaluating the patient and is recorded in the forensic report. Radiological examination with 3DR reduces external examination errors dependent on personal experience and measurements, assists in distinguishing entry and exit wounds, enables visual presentation of the anatomical localization, size, and morphological characteristics of wounds, and ensures accurate recording of findings (20,24,27).

In patients receiving medical care, entry and exit wounds may undergo temporal changes during wound healing or due to medical treatments. However, thanks to the preservable and archivable nature of findings obtained with 3DR, wounds can be reassessed later and presented to legal authorities when necessary. Entry and exit wounds caused by the 9×19 mm pistol used during this study in various anatomical regions are shown in Figure 1.

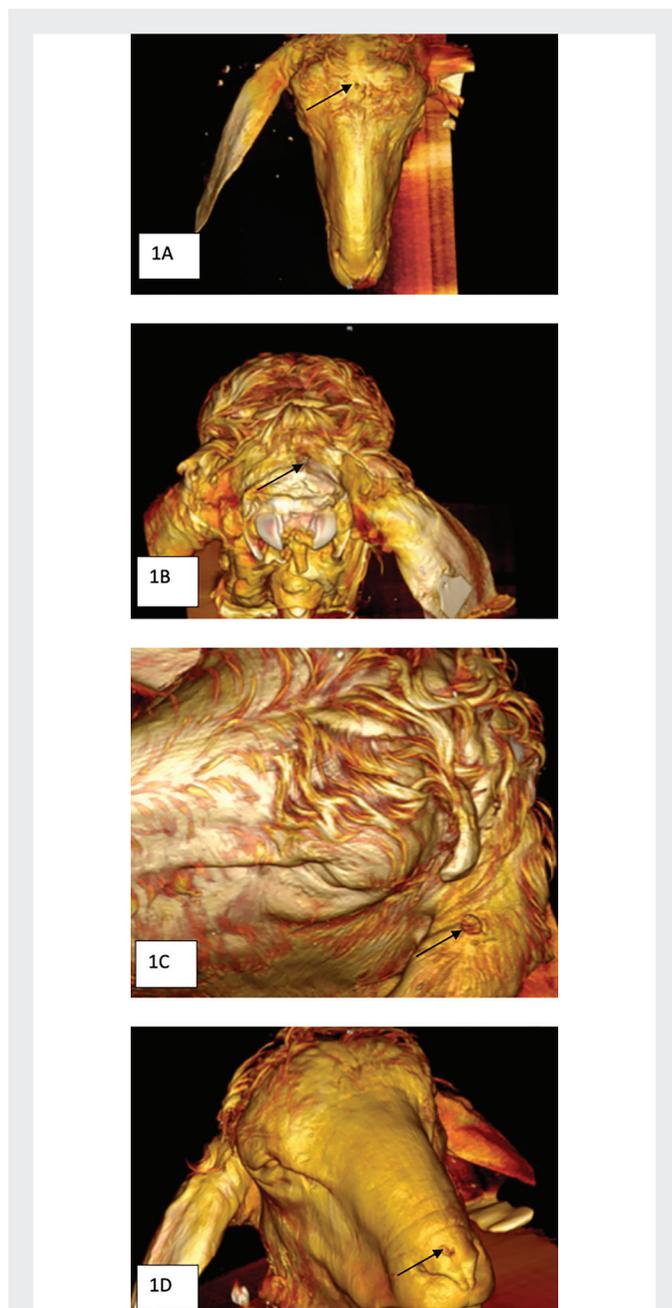


Figure 1: 1A: Entry wound (black arrow) observed on the skin in the frontal region (Sheep 1). 1B: Entry wound (black arrow) observed on the skin in the occipital region (Sheep 6). 1C: Exit wound (black arrow) located in the left ear (Sheep 5). 1D: Exit wound (black arrow) at the distal part of the nose, between the nostrils (Sheep 9).

Images processed with 3DR provide improved visualization of bullet damage through virtual rotation and color options (Figure 2). It illustrates in detail the relationships among bones, fracture fragments, and soft tissues, presenting health professionals with near-realistic images and contributing to decision-support systems. It offers surgeons the opportunity to conduct virtual simulations, assessments, and material selection before interventions. It also aids clinicians, surgeons, radiologists, and forensic physicians in understanding the interrelations of anatomical structures. In cases receiving health care after injury, where wound-related findings may change due to medical or surgical treatments, or when a forensic autopsy cannot be performed, 3DR enables early non-destructive acquisition of critical information essential for forensic investigation (20,24).

3DR presents the extent of damage caused by the bullet core as 3D images, non-destructively demonstrating the severity of the injury (28,29). Measurements can be taken using 3D models, such as in the stab wound case, the measurement of fracture height in the bones of the lower extremities, and the skull fracture lines (22). According to one study, skull fracture scores derived from the total length of fracture lines on 3D-CT VR images correlate with macroscopic evaluation. This score can be used as an index to assess fracture severity (30). In clinical and forensic radiology, initial assessments are primarily based on 2D sections. However, accurate interpretation of 2D images requires comprehensive anatomical knowledge, awareness of postmortem changes, understanding of treatment-related effects, spatial imagination, and 3D reasoning skills. For individuals working in non-medical fields, such as prosecutors, lawyers, judges, and police officers, who often lack this specialized expertise, understanding findings and incidents becomes challenging. Such information is generally presented through visual reports, including drawings, illustrations, and printouts. 3D models accurately reproduce spatial relationships between various elements, thereby visualizing the incident, the scene, and the injury (22,31). Figure 3, using 3DR, demonstrates the location and size of the entry and exit wounds, the course and distribution of skull fractures, and the trajectory.

3DR enables zooming, focusing, and measurements on images, allowing examination of suspicious areas in detail. Thus, it allows assessment of the relationship between entry and exit wounds, bullet trajectories, and joints in the shooting area, as well as damage to the bones forming the joints and joint integrity. While preserving the integrity of the structures within the shooting region, 3DR simultaneously facilitates measurements and analyses. The visual data it provides offers a simple and practical means of understanding, explaining, and reporting the extent of damage. It ensures the acquisition of objective, non-invasive, storable, portable, and presentable scientific data independent of the observer (25,32-34). Figure 4 illustrates findings on joint and bone integrity by zooming into the joint structures within the shooting area.

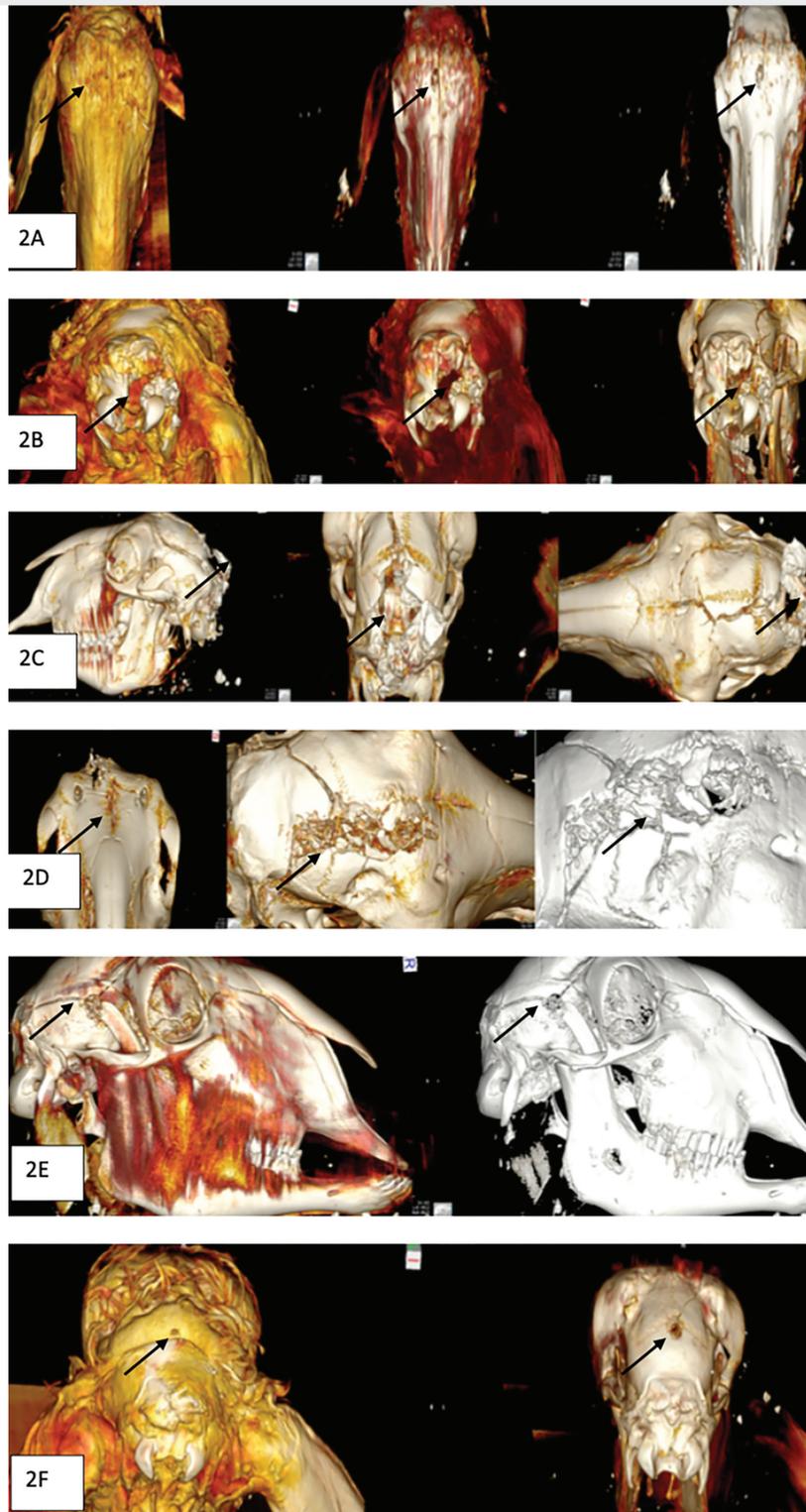


Figure 2. (A) Entry wounds (black arrows) in the frontal bone observed under different contrast levels (Sheep 1) (B) Large exit wound, occipital bone, and C1 vertebral damage (black arrows) observed under different contrast levels (Sheep 1) (C) Large exit wound and fragmented bone pieces (black arrows) in the occipital bone observed from multiple perspectives (lateral, posterior, and superior) (Sheep 4) (D) Large frontal bone defect (black arrows) between the entry and exit wounds observed under different contrast levels and angles (Sheep 7) (E) Bone defect and skull fractures originating from the entry wound (black arrows) in the temporal bone observed in different contrast levels (Sheep 8) (F) Entry wounds (black arrows) on the skin and in the occipital bone observed under different contrast levels (Sheep 9) (Sheep 9)

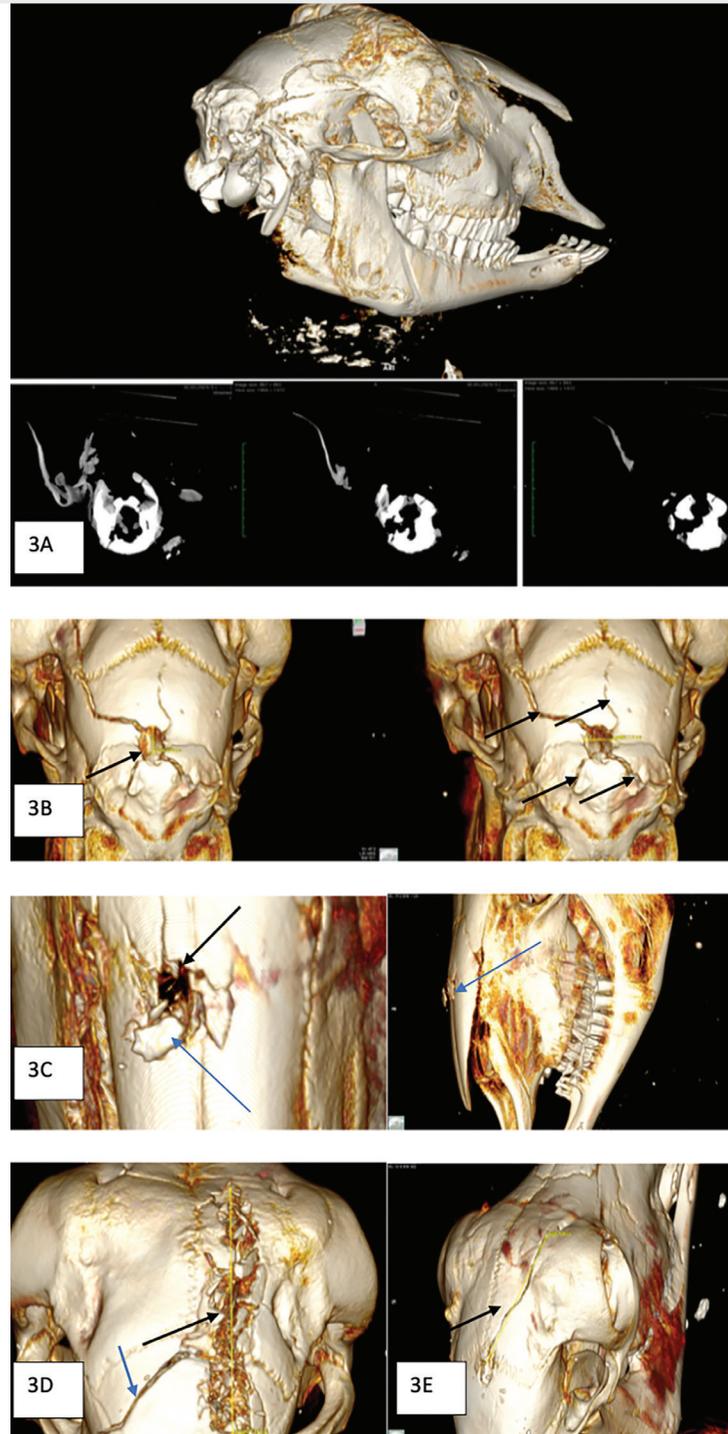


Figure 3. (A) In the upper image, a single skull fracture originating from the exit wound splits into two within the temporal bone; one fracture continues within the temporal bone, while the other extends to the frontal bone. In the lower images, the corresponding skull fractures are observed on CT images (Sheep 2) (B) In the first image, the entry wound (black arrow) is observed in the occipital bone, measuring 90×113 mm in diameter. In the second image, four skull fractures (black arrows) originating from the entry wound are observed (Sheep 3) (C) Exit wound (black arrow) and fragmented bone pieces (blue arrows) projecting toward the skin are observed in the nasal bone from different perspectives (anterior, lateral) (Sheep 12) (D) Multiple fractures of the frontal and occipital bones along the trajectory (black arrow), scattered bone fragments within and around the trajectory, and an additional skull fracture in the right occipital bone (blue arrow) are observed. The measured distance between entry and exit wounds is 72 mm (Sheep 7) (E) The skull bone fracture extending from the entry wound in the occipital bone to the frontal bone is measured as 6 cm (Sheep 9)

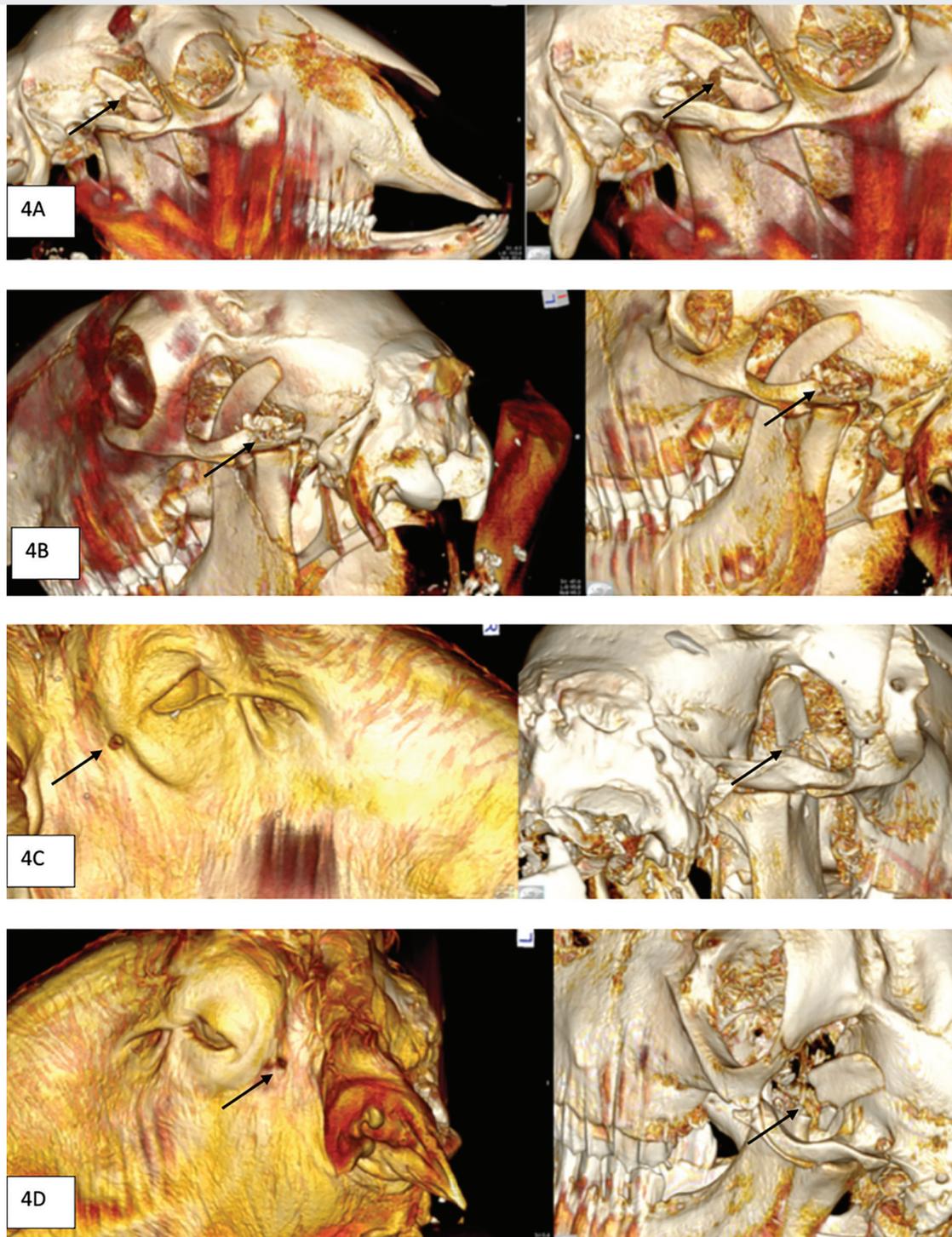


Figure 4. (A) In the first image, the entry wound (black arrow) is observed in the right temporal region. In the second image, a closer evaluation of the injury demonstrates damage to the temporomandibular joint and mandibular fractures (black arrow) (Sheep 5) (B) In the first image, the exit wound (black arrow) is observed in the left temporal region. In the second image, a closer evaluation demonstrates temporal bone damage and fractures of the zygomatic bone (black arrow) (Sheep 5) (C) In the first image, a millimetric entry wound (black arrow) is observed on the skin, posterior to the eyeball, in the right temporal region. In the second image, damage to the joint, complete fracture, and separation of the mandible (black arrow) are observed (Sheep 11) (D) In the first image, a millimetric exit wound (black arrow) is observed on the skin, posterior to the eyeball, in the left temporal region. In the second image, damage to the joint, complete fracture, and separation of the mandible (black arrow) are observed (Sheep 11)

Penetrating firearm injuries of the head and neck region are associated with high mortality, and the complex anatomical structures in this area, combined with the intricate nature of the injuries, require meticulous evaluation. Advanced 3D techniques and sectional radiological imaging can be used to detect injuries in soft tissues, parenchymal organs, and bones; to localize bullet cores and fragments; and to identify wound mechanisms and trajectories. CT and 3DR are fast and practical

tools for diagnosing fractures within the skeletal system (35-37). In our study, 3DR showed damage to the occipital bone and cervical vertebra. 3DR is a suitable method, especially for detecting anatomically difficult-to-reach areas (Figure 5). Our results indicate that 3DR is a fast, non-invasive, and non-destructive method for clinicians, surgeons, radiologists, and forensic medicine physicians in cranial firearm injury cases.

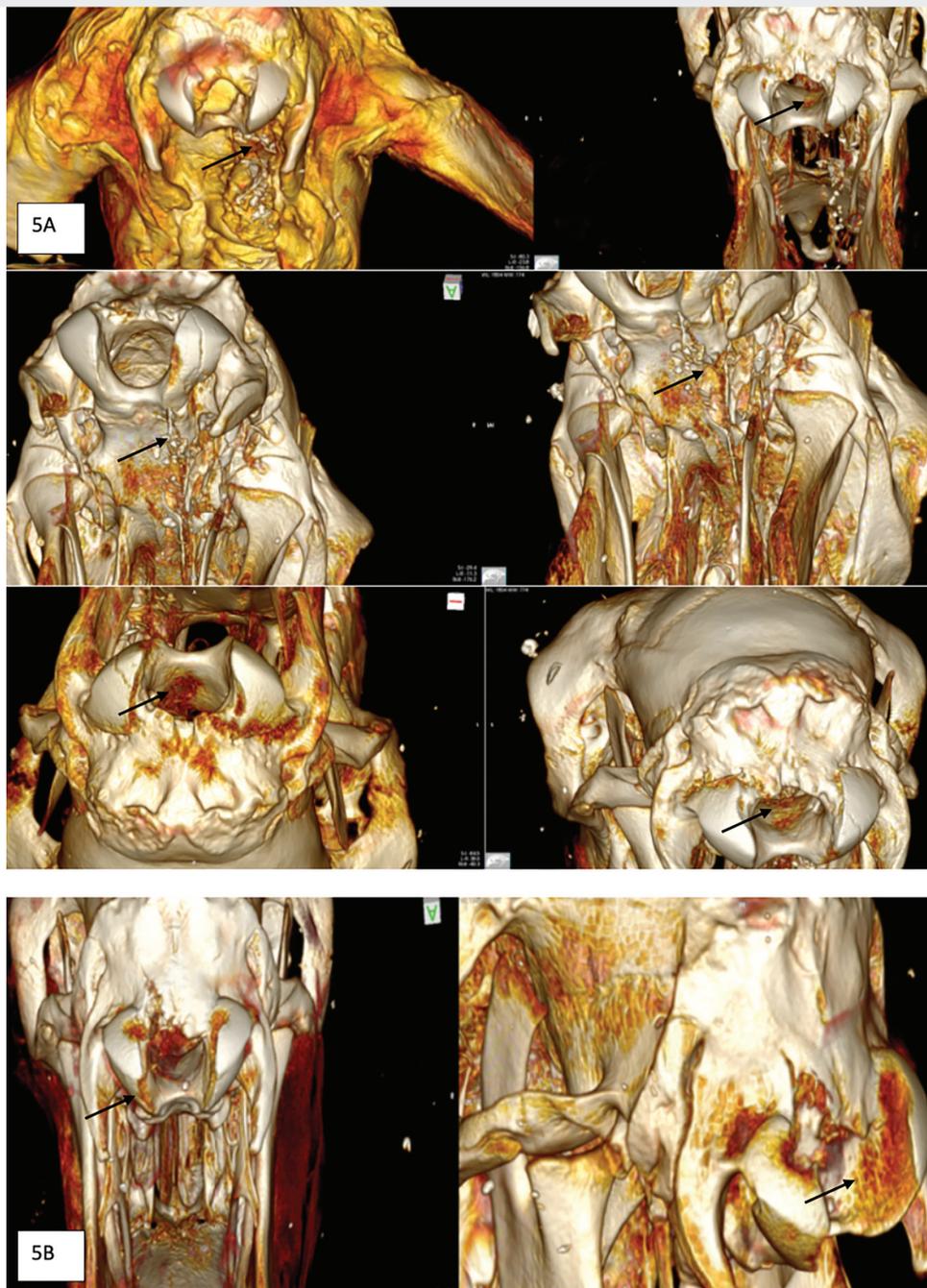


Figure 5. (A) In all images, the exit wound, occipital bone destruction, and C1 vertebral damage are observed under different contrast levels and from multiple angles (Sheep 10) (B) In the first image, a large entry wound (black arrow) is observed to the left of the midline in the C1 vertebra. In the second image, a large C1 vertebral defect (black arrow)

The 3DR findings obtained as a result of our study are listed below:

- The location of entry-exit wounds is determined.
- The diameter of the entry-exit wounds is measured.
- Bone damage in entry-exit wounds is determined.
- Bullet core trajectories are shown.
- The distribution of bone fragments is detected.
- The number, location, and course of skull bone fractures are detected.
- The length of skull fractures is measured.
- Bones forming the joint, and the Integrity of the joint are determined.
- Allows detailed examination of suspicious areas via zoom.
- Lesions in soft tissues such as skin are detected.
- Tissues can be examined at different contrasts.
- Anatomical areas that are challenging to reach, such as the skull, are evaluated.
- Objects can be rotated 360° on the X and Y axes. In this way, damaged areas are examined from different angles.

Although 3DR is a beneficial method in cranial firearm injuries, it has some disadvantages. CT is more effective than 3DR for showing parenchymal brain lesions. Equipment and application are required for reconstruction. However, the most significant issue is that accurate detection of pathological findings requires experience. This study can lead to the spread of using 3DR in cranial firearm injuries and lead to experienced authors.

Study Limitation

The limitation of the study is that it was conducted with a small number of decapitated sheep's heads. However, the results are not affected by its similarity to human anatomical structure.

CONCLUSION

The application of imaging methods for non-invasive documentation and analysis of findings in living persons has lagged behind the tremendous technical advancement in imaging methods. Whereas 3DR provides essential information to clinicians, surgeons, and radiology and emergency professionals, including damage to the skin, the number, course, and length of skull bone fractures, the number and distribution of bone fragments, joint integrity, and the relationship between bone fragmentation and joint integrity, creating lifelike images without performing an autopsy. In addition, in cases receiving health care after injury, where wound-related findings may change due to medical and surgical treatments and/or when a forensic autopsy cannot be performed, it enables the non-destructive acquisition of information critical for forensic investigation at an early stage. In cranial GSIs, 3DRs generated from CT images should be included in the radiological evaluation.

Ethics

Ethics Committee Approval: Ethical approval for the previous CT study was received from the Çukurova University Local Ethics Committee for Animal Experiments on (decision number: 6, date: 30.04.2024).

Informed Consent: This study is an animal experiment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: İ.A., G.İ.Ö., A.S.K., A.Y., Ç.A., Concept: İ.A., G.İ.Ö., Design: İ.A., G.İ.Ö., A.S.K., Data Collection or Processing: İ.A., G.İ.Ö., A.Y., Ç.A., Analysis or Interpretation: İ.A., G.İ.Ö., A.S.K., A.Y., Ç.A., Literature Search: İ.A., G.İ.Ö., Writing: İ.A., G.İ.Ö., A.S.K., A.Y., Ç.A.

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Assessment of Basic-instrumental Activities of Daily Living and Related Factors in Individuals Aged 80 and Over

Seksen Yaş ve Üzerindeki Bireylerin Temel-enstrümental Günlük Yaşam Aktiviteleri ve İlişkili Faktörlerin Değerlendirilmesi

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ABSTRACT

Objective: Chronic diseases, frailty, and external dependence may increase in elderly age. Therefore, age-specific assessment methods have been developed for the elderly. The aim of this manuscript is to investigate the cognitive status, daily living and instrumental daily living situations, and nutritional characteristics of individuals who can be included in the middle-aged and elderly age groups, and to determine their similarities and differences with other age groups.

Material and Methods: In this study, data from 222 participants aged 80-99 were retrospectively examined. The sociodemographic data, cognitive status, basic and instrumental daily living activities, and nutrition of participants were evaluated using the Mini Mental State test (MMST), Katz Index of Independence in Activities of Daily Living, Lawton-Brody Instrumental Activities of Daily Living scale, and Mini Nutritional Assessment test.

Results: The average age of the participants was 84.07, and 61.71% were female. The majority had comorbidities, with an average daily medication use of 4.27. The most common diseases are hypertension, diabetes mellitus, coronary artery disease, osteoporosis, gonarthrosis, and lumbar disc herniation. Participants scored an average of 5.58 out of 6 on the Katz Index of Independence in Activities of Daily Living, an average of 6.90 out of 8 on the Lawton-Brody Instrumental Activities of Daily Living scale, an average of 25.73 out of 30 on the MMST and an average of 11.99 out of 14 on the Mini Nutritional Assessment test. The success of the participants was influenced by age, gender, educational status, number of medications used and existing chronic diseases.

Conclusion: It should be noted that dependence increases, especially in individuals aged 80 and over, all basic and instrumental activities of daily living decrease, and compliance with the treatments to be given may decrease as a result. Assessing elderly adults using valid and reliable short scales can provide a more objective description of their health status.

Keywords: Aging, cognitive status, daily living activities, nutrition

ÖZ

Giriş: Yaşlılık döneminde kronik hastalıklar, kırılabilirlik ve dışa bağımlılık artabilir. Bu nedenle yaşlılarda yaşa özgü değerlendirme yöntemleri geliştirilmiştir. Araştırmanın amacı orta yaşlı ve ileri yaşlı grubuna dahil edilebilen bireylerin bilişsel durumlarını, günlük yaşam ve enstrümental günlük yaşam durumlarını, beslenme özelliklerini araştırarak diğer yaş gruplarıyla benzerlik ve farklılıklarını belirlemektir.

Gereç ve Yöntemler: Araştırmada yaş aralığı 80-99 olan 222 katılımcının verileri retrospektif olarak incelenmiştir. Katılımcıların sosyodemografik verileri, bilişsel durumları, temel ve enstrümental günlük yaşam aktiviteleri, beslenmeleri, standardize Mini Mental test (MMST), Katz Günlük Yaşam Aktivite ölçeği, Lawton Brody Enstrümental Günlük Yaşam Aktivite ölçeği, Mini Nutrisyonel Değerlendirme testi yardımıyla değerlendirilmiştir.

Bulgular: Katılımcıların yaş ortalaması 84,07 olup %61,71'i kadındı. Komorbid hastalıkları olanlar çoğunlukta idi, günlük ortalama 4,27 ilaç kullanımı mevcuttu. En sık karşılaşılan hastalıklar hipertansiyon, diabetes mellitus, koroner arter hastalığı, osteoporoz, gonartroz ve lumbal disk hernisidir. Katılımcılar Katz Günlük Yaşam Aktivite ölçeği'nde 6 üzerinden ortalama 5,58, Lawton Brody Enstrümental Günlük Yaşam Aktivite ölçeği'nden 8 üzerinden ortalama 6,90, MMST'ten 30 üzerinden ortalama 25,73 ve Mini Nutrisyonel Değerlendirme testi'nden 14 üzerinden ortalama 11,99 puan almışlardı. Katılımcıların başarıları yaş, cinsiyet, eğitim durumu, kullanılan ilaç sayısı ve mevcut kronik hastalıklardan etkilenmekteydi.

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Sonuç: Özellikle 80 yaş ve üzeri bireylerde bağımlılığın arttığı, tüm temel ve enstrumental günlük yaşam aktivitelerinin azaldığı, bunlara bağlı olarak verilecek tedavilere uyumun azalabileceği unutulmamalıdır. Yaşlı bireylerin geçerli ve güvenilir kısa ölççekler ile değerlendirilmesi yaşının sağlık durumunu daha objektif biçimde tanımlayabilir.

Anahtar Kelimeler: Yaşlılık, bilişsel durum, günlük yaşam aktiviteleri, nutrisyon.

INTRODUCTION

The distribution of diseases in aging populations differs from that in younger populations. Chronic diseases such as hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), osteoporosis, stroke, dementia, and malignancies are more common in the elderly population. In addition, frailty is greater in old age than in the younger population. Falls, immobility, incontinence, vision and hearing loss are common in frail elderly people (1). For all these reasons, age-specific assessment methods should be used in the follow-up of elderly patients.

According to the Turkish Journal of Geriatrics' definition, old age and age scale: 65-74 years old are young elderly, 75-84 years old are middle-aged elderly, and 85 years and older are elderly (2). According to this scale, people in the middle-aged and elderly age groups need a unique assessment that differs from other population groups.

In assessing aging, level of consciousness, participation in daily living activities, level of frailty, and nutritional status must be included alongside a comprehensive history and physical examination. Our research was planned with these reasons in mind.

The aim of this research is to examine the cognitive status, daily living and instrumental daily living conditions, and nutritional characteristics of individuals aged 80 and over, and to determine their similarities and differences with other age groups.

MATERIALS and METHODS

The research was conducted at the Healthy Aging Center of Adana Hospital. It is retrospective. All patients were 80 years of age and older. Ethical approval was obtained from the Scientific Research Ethics Committee of University of Health Sciences Türkiye, Adana Training and Research Hospital (decision number: 818, date: 23.10. 2025).

The data collected in the study consisted of five components: sociodemographic data, the Mini Mental State Examination (MMSE), the Katz Activity of Daily Living scale (Katz ADL), the Lawton Brody Enstrumental Daily Living Assessment scale (Lawton Brody EADL), and the Mini Nutritional Assessment test (MNT).

The MMSE was developed by Folstein et al. (3) in 1975 and is a widely used test worldwide for assessing cognitive status. A Turkish validity and reliability study was conducted by Güngen et al. (4). A Turkish validity and reliability study of the modified MMSE-education (E) form for untrained

groups was conducted by Babacan-Yıldız et al. (5). The MMSE consists of 11 questions, with a score range of 0-30. As the score obtained on the scale increases, it is concluded that the person's memory and cognitive level are better.

The Katz ADL was developed by Katz et al. (6). The Turkish validity and reliability study was conducted by Özkan Pehlivanoğlu et al. (7). Katz examines activities under 6 subheadings; 6 points indicate fully independent individuals, and 0 points indicate fully dependent individuals.

The Lawton Brody EADL was developed by Lawton and Brody (8). The Turkish validity and reliability study was published by Güzel et al. (9). The scale examines activities under 8 subheadings, the score range is 0-8, high scores indicate greater independence in instrumental daily living activities.

The MNT was developed and published by Rubenstein et al. (10). The Turkish validity and reliability study of the scale was conducted and published by Sarikaya et al (11). Scores in the MNT can range from 0 to 14. Higher scores indicate better nutritional levels, while scores of 7 and below favor malnutrition.

Data was collected through archival research, and no sample size was determined. All individuals who applied to the Healthy Aging Center of Adana Training and Research Hospital between October 1, 2023, and October 1, 2025, were included in the study.

Twenty-two hundred and fifty people applied to the Healthy Aging Center of Adana Training and Research Hospital between October 1, 2023, and October 1, 2025. When this number is accepted as the universe, the sample size was calculated as 143 with a 95% confidence level, 5% margin of error, and 95% power. In the calculation, the formula for calculating the sample size with a known population was used. However, the study reached the entire population and was conducted with 225 participants.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS 22.0 software package, and a significance level of $p < 0.05$ was accepted.

Descriptive statistics were determined using numbers, percentages, minimums, maximums, mean, and standard deviations. The normality of the distribution of numerical data was analyzed using the Kolmogorov-Smirnov test. The Kruskal-Wallis test and the Mann-Whitney U test were used to compare numerical data relative to a categorical variable. The Fisher's exact test was used to compare categorical data. The strength and direction of the relationship between 2 numerical variables were evaluated using Spearman's correlation analysis.

RESULTS

The total number of patients was 222, 61.71% (n=137) were female and 38.29% (n=85) were male. The age range was 80-99, with an average age of 84.07±3.28. The majority of patients had received primary education or less. 26.6% had never attended school, 30.2% were primary school graduates, 3.6% were secondary school graduates, 9.5% were high school graduates, and 10.8% were university graduates or higher.

The majority of patients had comorbidities. The most common diseases were HT, DM, CAD, osteoporosis, gonarthrosis, and lumbar disc herniation. The distribution is shown in Figure 1. The number of medications used varies between 0 and 13, with an average of 4.27±2.68.

The MMSE was administered differently to trained and untrained individuals. Those who answered the trained MMSE questions (n=196) scored an average of 25.73±3.24, while those who answered the untrained MMSE questions (n=26) scored an average of 22.8±5.13. Patients scored an average of 5.58±0.93 on the Katz ADL, 6.90±1.69 on the Lawton Brody ADL, and 11.99±2.03 on the MNT.

Positive scores were obtained on the following items of the Katz ADL: bathing 89.63% (n=199), dressing 91.44% (n=203), toilet use 97.30% (n=216), transfer 98.64% (n=219), incontinence 80.18% (n=178), and nutrition 99.54% (n=222).

The Lawton Brody EADL items were found to be successful in the following percentages: using a telephone 86.93% (n=193), shopping 73.87% (n=164), preparing meals 80.18% (n=178), cleaning the house 76.12% (n=169), doing laundry 83.33% (n=185), traveling 98.64% (n=219), taking medication regularly 95.04% (n=211), and managing finances 88.73% (n=197).

Patients scored an average of 1.72 points on the question “Has there been a decrease in nutrient intake from MNT?” 2.71 points on weight loss in the last 3 months, 1.83 points on physical activity, 1.89 points on emotional stress in the last 3 months, 1.79 points on neuropsychological problems, and 1.56 points on body mass index. High scores on all items indicate better nutrition.

The relationships between patients’ age, number of medications taken, and total scores on the scales were evaluated using Spearman’s correlation analysis. The results are shown in Table 1.

The average age of our patients according to gender, the number of medications they use daily, their MMSE score, Lawton Brody EADL score, and MNT score were all similar. The difference was not statistically significant; the p-values were 0.415, 0.784, 0.808, 0.871, and 0.507, respectively. In addition, male patients scored higher than female patients on the Katz ADL. Male patients scored an average of 5.75±0.61 points, while female patients scored 5.44±1.04 points (p=0.017).

When we evaluated the distribution of diseases according to the gender of the patients, we found that HT, osteoporosis, and gonarthrosis were more prevalent in female patients than in male patients. The p-values were 0.000, 0.000, and 0.048, respectively. However, there was no statistically significant difference between genders for DM, CAD, and lateral dysplasia of the heart. The p-values were 0.259, 0.413, and 0.483, respectively.

There was no statistically significant difference between the ages and educational levels of the patients (p=0.450). There was also no logarithmic relationship between the number of drugs used and the level of education. However, the group using the most drugs were middle school graduates, and

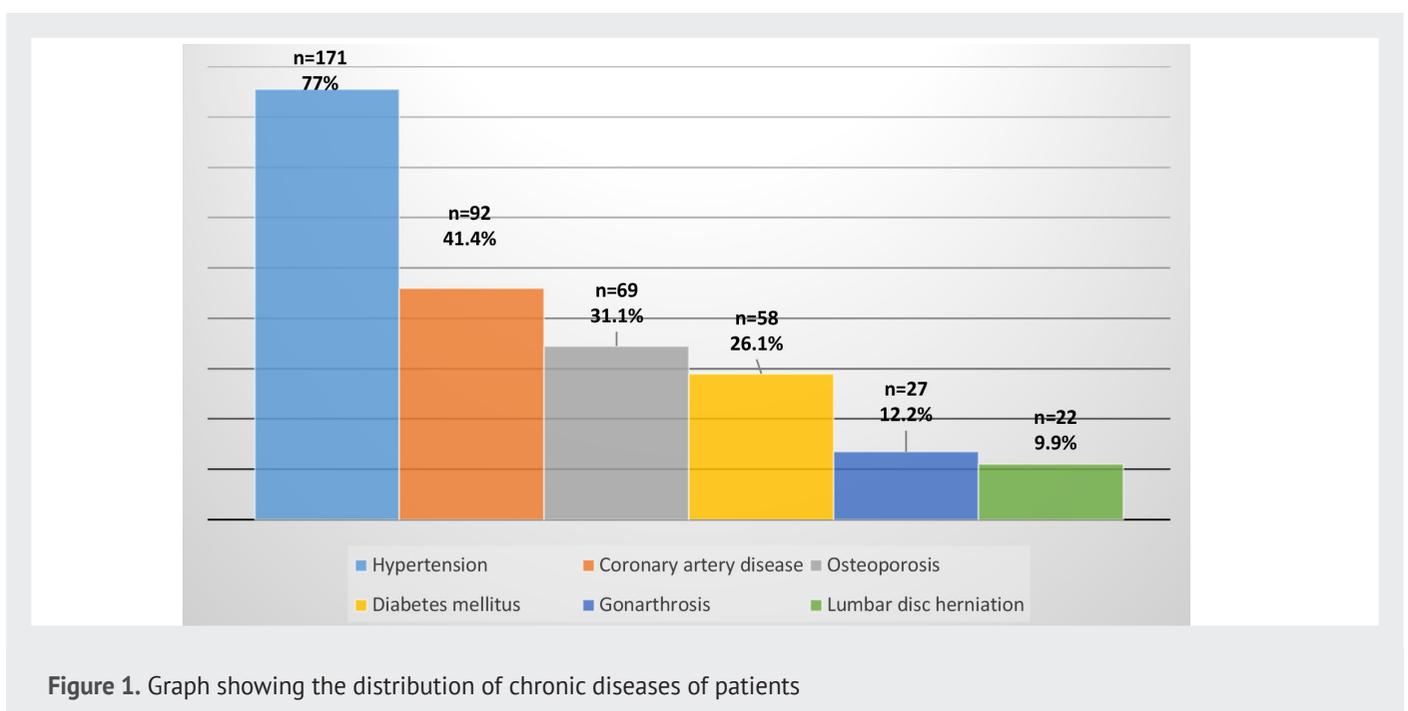


Figure 1. Graph showing the distribution of chronic diseases of patients

the group using the least drugs were university graduates (p=0.039).

The patients' education level statistically significantly affected all assessment tests. The distribution is shown in Table 2.

Tables 3-6 show the distribution of geriatric assessment tools used by patients according to the four most common diseases among them.

Table 3 shows the distribution according to HT. Patients with HT use more medication than those without HT, and they scored lower on the Katz ADL assessment. However, patients with HT have higher nutritional achievement than those without HT. The results are statistically significant (Table 3).

Table 4 shows the distribution according to the presence of CAD. Patients with CAD use more medication than those without. However, there are no statistically significant differences in the other parameters evaluated (Table 4).

Table 5 shows patients evaluated according to the presence of osteoporosis. Patients with osteoporosis were older, used more medications, and scored higher on the MMSE and MMSE-E. However, patients with osteoporosis scored lower on daily living, instrumental daily living, and nutrition assessments. None of the results were statistically significant (Table 5).

Table 6 evaluates the distribution according to DM. Accordingly, patients with DM are younger and use more medications. The results are statistically significant. However, cognitive assessment, activities of daily living, instrumental activities of daily living, and nutritional assessment do not show statistically significant differences according to DM (Table 6).

DISCUSSION

The aging can make people more vulnerable biologically, psychologically, and socially. There was a statistically

insignificant negative correlation between our patients' ages and their MMSE, Katz ADL, Lawton Brody ADL, and MNT scores (Table 1). Undoubtedly, there are many sociodemographic and clinical factors that contribute to this outcome. In our study, we evaluated some of these factors. Our results and some data from the literature are as follows:

In the research, the average age of our patients was 84.07, and female patients constituted 61.71%. Similarly, in a randomized controlled trial conducted with elderly people in Denmark, the average age was 78, and women were included in the study at a rate of 56% (12). In another study where the sample group was elderly individuals, 61% of the patients were women (13). Our sample group is similar in nature to the research in the literature that works with the elderly. This situation may be due both to the fact that women benefit more from health services and that women have a longer life expectancy at birth than men.

Of our patients, 26.6% had never attended school and 30.2% were primary school graduates. According to the Turkish Statistical Institute 2019 data, 32.8% of the elderly population in our country had never attended school while 45.5% were primary school graduates (14). Our patients were found to have received more formal education than the national average. We believe this difference may be due to the fact that the institution where we conducted the research is a tertiary hospital.

Chronic diseases are more common in older age groups. In our study, most of our patients had at least one chronic disease. The three most common chronic diseases we encountered were HT, CAD, and osteoporosis. In a study conducted with elderly people in China, the most common chronic diseases were cardiovascular diseases (15). Another study conducted in America also mentions an increase in chronic diseases

Table 1. Correlation distribution of elderly assessment tools according to age and number of medications

	Age	Number of medicines	MMSE	MMSE-E	Katz ADL	Lawton Brody EADL	MNT
Age	r	-0.021	-0.099	0.010	-0.111	-0.121	-0.023
	p	0.753	0.403	0.913	0.100	0.072	0.738
Number of medicines	r	-0.021	-0.065	-0.036	-0.100	0.074	0.071
	p	0.753	0.592	0.690	0.139	0.277	0.297
MMSE	r	-0.099	-0.065	.	-0.105	-0.098	-0.024
	p	0.403	.0592	.	0.377	0.410	0.840
MMSE-E	r	0.010	-0.036	.	-0.030	-0.154	0.124
	p	0.913	0.690	.	0.738	0.087	0.175
Katz ADL	r	-0.111	-0.100	-0.105	-0.030	0.479	0.089
	p	0.100	0.139	0.377	0.738	0.000	0.188
Lawton Brody EADL	r	-0.121	0.074	-0.098	-0.154	0.479	0.235
	p	0.072	0.277	0.410	0.087	0.000	0.000
MNT	r	-0.023	0.071	-0.024	0.124	0.089	0.235
	p	0.738	0.297	0.840	0.175	0.188	0.000

MMSE: Mini Mental State Examination, MMSE-E: Mini Mental State Examination education, Katz ADL: Katz Activity of Daily Living scale, Lawton Brody EADL: Lawton Brody Enstrumental Daily Living Assessment scale, MNT: Mini Nutritional Assessment test

Table 2. Distribution of elderly assessment tools according to educational status

	Education	Mean	Standard deviation	Effect size= ξ^2R^{**}	p-value [†]
MMSE	Primary school	24.82	3.627	0.242	0.001
	Secondary school	22.00	2.828		
	High school	26.47	2.366		
	University	27.50	1.745		
	No education	5.457	0.934		
Katz ADL	Primary school	5.343	1.162	0.188	0.027
	Secondary school	5.875	0.353		
	High school	5.904	0.300		
	University	5.875	0.337		
	No education	6.559	1.812		
Lawton EADL	Primary school	6.731	1.523	0.292	0.002
	Secondary school	7.750	0.462		
	High school	7.571	0.746		
	University	7.666	0.761		
	No education	11.932	1.680		
MNT	Primary school	12.149	1.860	0.162	0.048
	Secondary school	13.250	0.707		
	High school	12.047	3.057		
	University	12.708	1.160		

[†]Kruskal-Wallis test, ^{**}The formula for effect size in the Kruskal Wallis Test is as follows: Small ≥ 0.01 , medium ≥ 0.06 , large ≥ 0.14 . Ranges for is from 0 to 1, with higher values indicating a larger effect

MMSE: Mini Mental State Examination, Katz ADL: Katz Activity of Daily Living scale, Lawton Brody EADL: Lawton Brody Enstrumental Daily Living Assessment scale, MNT: Mini Nutritional Assessment test

Table 3. Distribution of hypertension and elderly assessment tools

	HT	Mean	Standard deviation	Effect size= Irl^{**}	p-value [†]
Age	No	83.255	2.441	0.00	0.902
	Yes	85.093	3.256		
Number of medicines	No	1.727	2.316	0.48	0.000
	Yes	4.924	2.388		
MMSE	No	25.69	3.146	0.00	0.839
	Yes	25.73	3.293		
MMSE-E	No	20.965	7.876	0.09	0.300
	Yes	23.389	3.854		
Katz ADL	No	5.851	0.658	0.15	0.021
	Yes	5.497	0.990		
Lawton Brody EADL	No	6.957	1.944	0.00	0.984
	Yes	6.871	1.636		
MNT	No	11.341	2.632	0.15	0.023
	Yes	12.152	1.824		

[†]: Mann-Whitney U test, ^{**}: The formula for effect size in the Mann-Whitney U test is as follows: $r = Z / \sqrt{N}$. Small $Irl \geq 0.1$, medium $Irl \geq 0.3$, large $Irl \geq 0.5$. Ranges for Irl is from 0 to 1, with 0 indicating no difference between groups. HT: Hypertension, MMSE: Mini Mental State Examination, MMSE-E: Mini Mental State Examination education, Katz ADL: Katz Activity of Daily Living scale, Lawton Brody EADL: Lawton Brody Enstrumental Daily Living Assessment scale, MNT: Mini Nutritional Assessment test

Table 4. Distribution of coronary artery disease and elderly assessment tools					
	CAD	Mean	Standard deviation	Effect size=lrl**	p-value*
Age	No	83.1154	3.215	0.11	0.101
	Yes	85.4348	3.362		
Number of medicines	No	3.3937	2.535	0.48	0.000
	Yes	5.4891	2.397		
MMSE	No	25.45	3.501	0.68	0.734
	Yes	26.03	2.965		
MMSE-E	No	22.6923	5.689	0.03	0.699
	Yes	22.9787	4.109		
Katz ADL	No	5.6154	0.935	0.00	0.331
	Yes	5.5326	0.931		
Lawton Brody EADL	No	6.9077	1.718	0.00	0.887
	Yes	6.8913	1.667		
MNT	No	11.8110	2.252	0.09	0.153
	Yes	12.2391	1.666		

*: Mann Whitney U test, **: The formula for effect size in the Mann-Whitney U test is as follows: $r = Z / \sqrt{N}$. Small lrl ≥ 0.1 , medium lrl ≥ 0.3 , large lrl ≥ 0.5 . Ranges for lrl is from 0 to 1, with 0 indicating no difference between groups
CAD: Coronary artery disease, MMSE: Mini Mental State Examination education, MMSE-E: Mini Mental State Examination education, Katz ADL: Katz Activity of Daily Living scale, Lawton Brody EADL: Lawton Brody Enstrumental Daily Living Assessment scale, MNT: Mini Nutritional Assessment test

Table 5. Distribution of osteoporosis and elderly assessment tools					
	Osteoporosis	Mean	Standard deviation	Effect size=lrl**	p-value*
Age	No	83.464	2.316	0.11	0.102
	Yes	85.434	2.987		
Number of medicines	No	4.146	2.740	0.07	0.273
	Yes	4.550	2.546		
MMSE	No	25.55	3.254	0.09	0.420
	Yes	26.28	3.250		
MMSE-E	No	22.597	5.830	0.00	0.833
	Yes	23.186	3.479		
Katz ADL	No	5.568	0.965	0.00	0.746
	Yes	5.608	0.861		
Lawton Brody EADL	No	6.895	1.810	0.00	0.725
	Yes	6.913	1.411		
MNT	No	11.986	2.029	0.00	0.730
	Yes	12.000	2.057		

*: Mann-Whitney U test, **: The formula for effect size in the Mann-Whitney U test is as follows: $r = Z / \sqrt{N}$. Small lrl ≥ 0.1 , medium lrl ≥ 0.3 , large lrl ≥ 0.5 . Ranges for lrl is from 0 to 1, with 0 indicating no difference between groups
MMSE: Mini Mental State Examination, MMSE-E: Mini Mental State Examination education, Katz ADL: Katz Activity of Daily Living scale, Lawton Brody EADL: Lawton Brody Enstrumental Daily Living Assessment scale, MNT: Mini Nutritional Assessment test

with age (16). Our data are consistent with the literature. Increased chronic diseases in old age can lead to a decrease in daily living activities, increased frailty (1) and make elderly individuals more dependent.

A negative correlation was found between the ages of our patients and the MMSE ($r=-0.099$), Katz ADL ($r=-0.111$), Lawton Brody ADL ($r=-0.121$), and MNT ($r=-0.023$) scores.

Age-related chronic diseases, increased frailty, family and environmental losses, falls, and depression can all lead to declines in cognitive abilities, daily living activities, and nutrition in old age (17-19). Our data is consistent with these predictions and the literature.

Our patients scored an average of 5.58 ± 0.93 on the Katz ADL. In another elderly assessment study covering 7 European countries, they scored 6.9 ± 1.67 on the Katz ADL (18).

Table 6. Distribution of diabetes mellitus and elderly assessment tools

	DM	Mean	Standard deviation	Effect size=lrl**	p-value*
Age	No	84.920	3.473	0.15	0.024
	Yes	81.689	4.837		
Number of medicines	No	3.711	2.498	0.36	0.000
	Yes	5.910	2.538		
MMSE	No	26.10	3.029	0.13	0.244
	Yes	24.96	3.593		
MMSE-E	No	23.206	4.274	0.03	0.624
	Yes	21.392	7.319		
Katz ADL	No	5.652	0.772	0.08	0.212
	Yes	5.379	1.268		
Lawton Brody EADL	No	6.884	1.556	0.03	0.606
	Yes	6.948	2.047		
MNT	No	12.055	1.976	0.03	0.630
	Yes	11.803	2.202		

*: Mann-Whitney U test, **: The formula for effect size in the Mann-Whitney U test is as follows: $r = Z / \sqrt{N}$. Small lrl ≥ 0.1 , medium lrl ≥ 0.3 , large lrl ≥ 0.5 . Ranges for lrl is from 0 to 1, with 0 indicating no difference between groups
 MMSE: Mini Mental State Examination, MMSE-E: Mini Mental State Examination education, Katz ADL: Katz Activity of Daily Living scale, Lawton Brody EADL: Lawton Brody Enstrumental Daily Living Assessment scale, MNT: Mini Nutritional Assessment test, DM: Diabetes mellitus

The fact that the average age of the patients in that study was 77.88, which is younger than our study, may have caused this difference.

In our research, male patients scored higher than female patients on the Katz ADL assessment ($p=0.017$). In a study evaluating the relationship between old age and falls, female patients also had lower total scores on the Katz scale than male patients (20). We believe that this may be because the studies were conducted among people who needed medical assistance and elderly women are more fragile.

When Katz ADL scores were compared according to the presence of chronic diseases, those without hypertension were found to perform better than those with HT ($p=0.021$). Although not statistically significant, the performance of those without CAD was higher than that of those with CAD ($p=0.331$); the performance of those without diabetes was higher than that of those with diabetes ($p=0.212$). Interestingly, however, patients with osteoporosis had higher Katz ADL scores than those without ($p=0.746$). In a study published in Sri Lanka, the Katz ADL was evaluated according to chronic diseases (17). Accordingly, patients with DM, HT, malignancy, musculoskeletal diseases and/or osteoarthritis have higher averages than those without (17). In another study comparing the scores of patients with and without diabetes on the Katz ADL, patients with DM were found to have lower Katz scores (21). Chronic diseases often negatively affect the daily living activities of the elderly, and our data in this study and the literature support this result.

As the education level of our patients increased, the scores obtained from the daily living activity and instrumental daily living activity scales generally increased. A similar relationship

between education and daily living activity scales was also found in a study conducted with elderly patients in Kayseri (22). Our data is consistent with the literature.

Of the items on the Lawton Brody EADL, patients indicated that they were able to travel the most (98.64%), while they indicated that they were able to shop the least (73.87%). In a study conducted in Indonesia with 55 patients aged 60-90, the item in which the patients were most successful was shopping, and the item in which they were least successful was traveling (23). The reason for this difference may be the differences in the number of patients in the studies and the regions where they were conducted.

In the research, patients' existing chronic diseases and the Lawton Brody EADL were compared, and no statistically significant difference was found. However, in a study comparing patients with osteoarthritis and a control group, it was found that instrumental daily living activities were lower in people with osteoarthritis (24). In another study, it was found that instrumental daily living activities were lower in patients with COPD (25). The reason for this discrepancy may be that the diseases we included were CAD, HT, osteoporosis, and DM, and these other diseases were not evaluated.

The nutritional status of our patients was assessed using the MNT. The study concluded that patients' education levels increased, leading to more accurate nutrition ($p=0.048$). No statistically significant relationship was found between gender and nutrition in our study ($p=0.507$). In a study evaluating nutrition in the elderly, it was stated that MNT scores were lower in the older age group, in women, in elderly people with low education levels, and in elderly people who were financially dependent (26). The results are similar to the

data of our study. In general, we can say that the factors that increase frailty also negatively affect the nutritional level. Patients with HT scored higher on the nutrition tests (mean 12.15) than those without HT (mean 11.34) ($p=0.023$). Similarly, patients with CAD (mean 12.23) scored higher than those without (mean 11.81), and patients with osteoporosis (mean 12.00) scored higher than those without (mean 11.98). However, the results were not statistically significant. When we compared DM and the nutritional assessment test, the results were different from the relationship between other chronic diseases and nutrition. Patients with DM (mean 11.80) scored lower than those without (mean 12.05). According to the results of a study published in Finland, the presence of chronic diseases that increase frailty in the elderly generally negatively affects nutrition (27). In our study, some disease groups of elderly individuals had higher nutrition scores, which was inconsistent with the literature. In all three diseases we evaluated (DM, CAD, osteoporosis), lifestyle changes and regular nutrition are recommended as primary treatment. Therefore, patients may have received nutrition education after receiving their diagnosis. This may be the reason for the contradiction with the literature.

Study Limitation

The research is retrospective in nature and the data is limited to archival records. This is the first limitation of the research. Other limitations of the research include its single-center nature and the number of participants. Therefore, the results cannot be generalized to the population. It may be beneficial to conduct multi-centered and large-scale researches on the subject.

CONCLUSION

In our research evaluating individuals aged eighty and over, patients' basic-instrumental daily living activities, cognitive status, and nutritional status were assessed. Patients scored an average of 5.58 out of 6 on the Katz ADL, 6.90 out of 8 on the Lawton-Brody Instrumental Activities of Daily Living scale, 25.73 out of 30 on the MMSE, and 11.99 out of 14 on the MNT. In short, patients did not achieve 100% success in any of these four sub-categories. Participant success was positively or negatively affected by many parameters such as age, gender, education level, and existing chronic diseases. In the clinical evaluation of patients aged 80 and over, the possibility of increased levels of dependence and decreased abilities in daily living activities, cognitive function, and nutrition should be considered. Therefore, using assessment scales with known validity and reliability in geriatric assessments can help achieve a more objective result.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Scientific Research Ethics Committee of University of Health Sciences Türkiye, Adana Training and Research Hospital (decision number: 818, date: 23.10. 2025).

Informed Consent: This study is a retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.A.D., Z.A., Concept: M.A.D., Z.A., Design: M.A.D., Z.A., Data Collection or Processing: M.A.D., Z.A., Analysis or Interpretation: M.A.D., Z.A., Literature Search: M.A.D., Z.A., Writing: M.A.D., Z.A.

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Evaluation of the Relationship between Health Literacy and Rational Drug Use in Patients Admitting to a Family Health Center

Aile Sağlığı Merkezine Başvuran Hastalarda Sağlık Okuryazarlığı ve Akılcı İlaç Kullanımının İlişkisinin Değerlendirilmesi

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ABSTRACT

Objective: This study aimed to demonstrate that problems encountered in protecting individuals' health status, accessing healthcare services, participating in the treatment process, and using the correct medicine in the right amount and at the right time may be related to the level of health literacy.

Material and Methods: This cross-sectional study was conducted with 300 volunteers who applied to Yenibey no. 2 Family Health Center in Seyhan district, Adana province, between June 1, 2023 and July 31, 2023, after obtaining ethical approval. The first part of the data collection form consisted of 31 questions, the first 6 of which covered sociodemographic data. The remaining questions were designed to measure medication use habits related to rational drug use and the effects of health literacy. The second part contained the 32-item Türkiye Health Literacy Survey.

Results: Among the 300 participants who applied to Yenibey No. 2 Family Health Center in Seyhan, Adana, the mean general health literacy score was 28.5±7.7 points, with approximately 64% having inadequate or problematic/limited health literacy levels. Low health literacy was strongly and statistically significantly associated ($p=0.001-0.013$) with irrational drug use behaviors, including self-medication without consulting a physician (25% frequently, 68% occasionally), using medicines based on suggestions from relatives/friends/neighbors, frequently keeping a continuous medicine stock at home (34%), and frequently requesting specific medicines to be prescribed during doctor visits. Higher education level, higher income, and having SGK or private insurance were significantly associated with better health literacy, whereas female gender, presence of chronic diseases, irregular follow-up, and more than 14 outpatient visits per year were linked to lower health literacy scores.

Conclusion: In conclusion, targeted educational and awareness-raising interventions aimed at improving health literacy particularly focusing on low-education and low-income groups, women, and individuals with chronic diseases can enhance rational drug use practices and reduce the burden on the healthcare system. This study once again underscores the critical importance of primary care physicians' roles in patient education and guidance in regions such as Adana.

Keywords: Health literacy, family medicine, rational drug use

ÖZ

Giriş: Bu çalışma, bireylerin sağlık durumlarını koruma, sağlık hizmetlerine erişim, tedavi sürecine katılım ve doğru ilacı doğru miktarda ve doğru zamanda kullanma konularında karşılaştıkları sorunların sağlık okuryazarlığı düzeyiyle ilişkili olabileceğini göstermeyi amaçlamıştır. Gereç ve Yöntemler Bu kesitsel çalışma, etik kurul onayı alındıktan sonra, 1 Haziran 2023 ile 31 Temmuz 2023 tarihleri arasında Adana ili Seyhan ilçesi Yenibey 2 no'lu Aile Sağlığı Merkezi'ne başvuran 300 gönüllü ile gerçekleştirilmiştir. Veri toplama formunun ilk bölümü 31 sorudan oluşmakta olup, bunlardan ilk 6'sı sosyodemografik verileri kapsamaktadır. Kalan sorular, akılcı ilaç kullanımıyla ilgili ilaç kullanım alışkanlıklarını ve sağlık okuryazarlığının etkilerini ölçmek üzere tasarlanmıştır. İkinci bölüm ise 32 maddelik Türkiye Sağlık Okuryazarlığı Anketi'ni içermektedir.

Bulgular: Adana Seyhan Yenibey no. 2 Aile Sağlığı Merkezi'ne başvuran 300 katılımcının genel sağlık okuryazarlığı ortalaması 28,5±7,7 puan olup, yaklaşık %64'ü yetersiz veya sorunlu/sınırlı düzeydedir. Düşük sağlık okuryazarlığı düzeyi, doktora danışmadan kendi başına ilaç kullanma (%25 sık, %68 ara sıra), çevreden öneriyle ilaç alma, evde sürekli ilaç stoğu bulundurma (%34 sık), doktordan kendi isteğiyle ilaç

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yazdırma talebinde bulunma gibi irrasyonel ilaç kullanım davranışlarıyla güçlü ve istatistiksel olarak anlamlı ilişki göstermektedir ($p=0.001-0.013$). Daha yüksek eğitim, gelir düzeyi ve SGK/özel sigorta varlığı sağlık okuryazarlığını artırırken; kadın cinsiyet, kronik hastalık, düzensiz takip ve yılda 14'ten fazla poliklinik ziyareti düşük sağlık okuryazarlığı ile ilişkilidir.

Sonuç: Sonuç olarak, özellikle düşük eğitimli ve düşük gelirli gruplara, kadınlara ve kronik hastalıkları olan bireylere odaklanan, sağlık okuryazarlığını geliştirmeyi amaçlayan hedefli eğitim ve farkındalık artırma müdahaleleri, akılcı ilaç kullanım uygulamalarını artırabilir ve sağlık sistemine olan yükü azaltabilir. Bu çalışma, Adana gibi bölgelerde birinci basamak hekimlerinin hasta eğitimi ve rehberliğindeki rollerinin kritik önemini bir kez daha vurgulamaktadır.

Anahtar Kelimeler: Sağlık okur yazarlığı, aile hekimi, akılcı ilaç kullanımı

INTRODUCTION

In our country, the Ministry of Health defines health literacy as the cognitive and social skills that determine individuals' ability and motivation to access, understand, and use information in a way that promotes and maintains good health (1).

The World Health Organization broadly defines health literacy as the ability of individuals to gain access to, understand, and use information in ways that promote and maintain good health for themselves, their families, and their communities (2).

Undoubtedly, individuals' health literacy depends on the education system of the society they live in, the healthcare system, the healthcare environment they are in, their families, jobs, local social and cultural factors, and their own social skills (3). Low levels of health literacy reduce adherence to treatment and lead to insufficient knowledge about the disease. This can negatively affect disease management (3,4). Lack of knowledge and low awareness about preventive health services cause delayed presentations (5). In patients with chronic diseases, it leads to disruptions in follow-up and treatment, thereby threatening public health (6).

Medicines are extremely important for the prevention and treatment of diseases in both individuals and society. In recent years, treatments for many previously untreatable diseases have been developed, along with newer and more reliable medicines. These advancements and easier access to healthcare services have led to an increase in demand for and consumption of medicines. Additionally, negative factors such as stress, smoking, alcohol, environmental pollution, and consumption of unhealthy foods impair public health, leading to the emergence of new diseases and an increase in healthcare expenditures. Because of the rise in resource use and the negative impact on human health, rational use of these medicines is essential (7,8).

In our country, approximately 35% of total healthcare expenditures consist of medicine costs. Furthermore, it is estimated worldwide that more than half of medicines are prescribed or used unnecessarily (7,9,10).

In rational medicine use, in addition to the responsibilities of the patient and physician, pharmacies, relatives of the patient, medicine manufacturers, responsible authorities, and the media also bear responsibility. There are many

factors influencing irrational medicine use. Lack of education, sociocultural characteristics, individuals' misconceptions, and certain administrative problems are the main factors affecting this situation (11).

Health is an important part of every individual's life, and it is vital for everyone to make informed decisions regarding their health. Health literacy helps individuals manage their own health, prevent diseases, achieve early diagnosis, and receive treatment, while also having a significant impact on the sustainability and cost of healthcare systems (12).

Health literacy improves individuals' quality of life and enables them to remain healthy for longer periods. It eliminates health inequalities among individuals and facilitates easier communication and understanding with healthcare workers. This, in turn, involves the individual in the diagnosis and treatment process, leading to more accurate decisions (13).

This study aimed to demonstrate that problems encountered in protecting individuals' health status, accessing healthcare services, participating in the treatment process, and using the correct medicine in the right amount and at the right time may be related to the level of health literacy.

MATERIAL and METHODS

This cross-sectional study was conducted with 300 volunteers who applied to Yenibey No. 2 Family Health Center in Seyhan district, Adana province, between June 1, 2023 and July 31, 2023, after obtaining ethical approval. Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Adana Training and Research Hospital, University of Health Sciences, with decision number: 2597 date: 25.05.2023). The study was conducted in accordance with the Declaration of Helsinki.

The study population consisted of 10,000 individuals registered at the family health center. The sample size was calculated as 263 using the Epi Info statistical program, based on 90% power and a 0.05 alpha confidence level/margin of error.

The first part of the data collection form consisted of 31 questions, the first 6 of which covered sociodemographic data. The remaining questions were designed to measure medication use habits related to rational drug use and the effects of health literacy. The second part contained the 32-item Türkiye Health Literacy Survey (TSOY-32). TSOY-32 is a 32-item Likert-type scale developed by Okyay and

Abacıgil (14) in 2016, based on the principles and conceptual framework of the European Health Literacy Survey. It is a valid and reliable instrument that enables the assessment of health literacy levels. The scale is scored using the following formula, yielding scores between 0 and 50: $\text{index} = (\text{arithmetic mean} - 1) \times (50/3)$

Using the above formula, overall health literacy and subscale scores were calculated. The values obtained from the formula calculation, ranging between 0 and 50, were evaluated in four separate levels. This classification is as follows:

- 0-25 points: Inadequate health literacy
- 26-33 points: Problematic/limited health literacy
- 34-42 points: Sufficient health literacy
- 43-50 points: Excellent health literacy

Statistical Analysis

When evaluating the findings obtained in the study, IBM SPSS Statistics 22 software was used for statistical analyses. Continuous parameters obtained in the study were presented as mean and standard deviation, while categorical variables were expressed as numbers and percentages. The conformity of the parameters to normal distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. In the evaluation of the study data, in addition to descriptive statistical methods (mean, standard deviation, frequency), the Kruskal-Wallis test was used for intergroup comparisons of quantitative data that did not show normal distribution. For comparisons between two groups of parameters that did not follow a normal distribution, the Mann-Whitney U test was applied. For comparisons of qualitative data, the chi-square test, Fisher's exact chi-square test, and Monte Carlo Exact chi-square test correction were used. Statistical significance was evaluated at the $p < 0.05$ level.

RESULTS

The mean age of the participants was 42.09 ± 13.63 years (minimum 18, maximum 74). Among the volunteers who participated in the study, 67.3% (n=202) were female and 32.7% (n=98) were male. The sociodemographic characteristics of the participants are summarized in Table 1.

Participants were asked which healthcare facility they first consulted when they became ill. 217 participants (72.3%) reported that they first preferred the family health center. The mean number of outpatient visits in the last year was 14.8 ± 8.7 (median 13, min-max: 1-46). 163 participants (54.3%) had 14 or fewer healthcare visits in the last year (Table 2).

The mean \pm SD, median, and min-max values of the subscale scores obtained from the TSOY-32 questionnaire are presented in Table 3. The overall health literacy score mean was determined to be 28.5.

A significant relationship was found between participants' use of medicines based on recommendations from relatives,

friends, or neighbors and their health literacy levels. Those who never used medicines based on environmental suggestions had significantly higher health literacy scores ($p=0.013$) (Table 4). However, no statistically significant difference was found between advising medicines to others and health literacy scores ($p=0.456$) (Table 4).

A statistically significant difference was detected between keeping a medicine stock at home and health literacy levels. Participants who frequently kept a continuous stock at home had significantly lower health literacy levels compared to others ($p=0.001$) (Table 4).

When participants who requested medicines on their own initiative during doctor visits were compared, significant results were obtained. Those who frequently demanded medicines had significantly lower health literacy scores compared to others ($p=0.003$) (Table 4).

DISCUSSION

Of the participants, 25% reported frequent and 68.3% occasional self-medication without consulting a physician. The most commonly used drug groups were analgesics (89%), cold remedies (58.3%), antipyretics (46.7%), and antibiotics (23.3%). Literature reports self-medication rates ranging from 42.9% to 75.6% (15-19). These variations may stem from regional socioeconomic and cultural differences. Over-the-

Table 1. Sociodemographic data

Parameter	All participants (n=300) n (%)
Gender	
Female	202 (67.3)
Male	98 (32.7)
Marital status	
Married	235 (78.3)
Single	65 (21.7)
Education level	
Literate	15 (5.0)
Primary school	82 (27.3)
Middle school	46 (15.3)
High school	67 (22.3)
University and above	90 (30.0)
Social security	
SGK	226 (75.3)
Green card	53 (17.7)
Private insurance	7 (2.3)
None	14 (4.7)
Income level	
Minimum wage or below	140 (46.7)
Between 1-2 minimum wages	91 (30.3)
Two minimum wages or above	69 (23.0)

counter availability, leftover medications at home, and prior illness experiences are key facilitators of this behavior.

Higher education levels were significantly associated with reduced self-medication without physician consultation, consistent with findings by İşler (19) and Akici et al. (20). Higher education appears to promote greater adherence to rational drug use principles.

The rate of using medications based on suggestions from relatives, friends, or neighbors was 22.7% [İşler 24.3% (19), Özkan 25.6% (21), Pınar 8% (16), Karataş 14.8% (22)]. This practice contradicts rational drug use principles, and its relationship with education level shows mixed results in the literature (negative correlation in İşler (19), reduction in Özkan et al. (21), no association in Pınar et al. (16)).

Early discontinuation of prescribed treatment was reported by 37% (frequent) and 42.7% (occasional), with main reasons including perceived improvement, fear of excess medication, and forgetfulness (17,19,21). This behavior was more common among females, younger individuals, and those with lower education. These findings may be explained by women's limited social awareness and younger individuals' poorer adherence despite knowledge. Such irrational patterns can contribute to severe outcomes, as evidenced by a retrospective single-center analysis in an intensive care unit setting where acute drug intoxications (primarily analgesics and antidepressants) and drug misuse led to prolonged stays, mechanical ventilation needs, and notably higher mortality (11.5% in drug use cases vs. 0.6% in intoxications), underscoring the public health risks of improper drug handling (23).

Prospectus reading was frequent in 57.7% of participants; this habit was significantly higher among those under 40.5 years and university graduates (İşler 86.1% (19), (Pınar 72%) (16)). Education and younger age appear to enhance information-seeking behavior.

Home stockpiling of medications was frequent in 34.3% and occasional in 57.7%, while approximately 65% reported requesting medications on their own initiative during doctor visits (16,19,22). Stockpiling was more common among women, whereas self-requested prescriptions were significantly lower among university graduates. The more flexible patient-physician interaction in family health centers may contribute to these higher rates.

Antibiotic use for non-specific viral symptoms was frequent in 19.3% and occasional in 27%, with significantly higher rates among those with lower education (22). This pattern aligns with regional observations of irrational antibiotic prescribing

Table 2. Data on first consultation place and number of visits

Parameter	All participants (n=300) n (%)
First healthcare facility consulted when ill	
Family health center	217 (72.3)
Hospital	83 (27.7)
Number of visits in the last year	
14 visits or fewer	163 (54.3)
More than 14 visits	137 (45.7)
Number of visits in the last year	
Mean ± standard deviation	14.8±8.7
Median	13
Minimum-maximum	1-46

Table 3. Health literacy subscale scores

Parameter	Mean ± SD	Median	Min-max
Overall health literacy score	28.5±7.7	28.7	10.9-44.3
Treatment and services			
Accessing information	30.7±9.5	33.3	4.2-50
Understanding information	34.1±8.7	33.3	8.3-50
Appraising information	21.4±9.3	20.8	4.2-45.8
Applying information	38.1±8.7	37.5	4.2-50
Disease prevention and health promotion			
Accessing information	27.9±10.5	33.3	4.2-50
Understanding information	27.6±11.1	29.2	4.2-50
Appraising information	22.8±9.9	20.8	0-45.8
Applying information	25.2±8.0	25.0	4.2-45.8
Health-related information			
Accessing information	29.3±9.1	31.3	6.3-47.9
Understanding information	30.9±9.2	31.3	10.4-47.9
Appraising information	22.1±8.7	22.9	2.1-41.7
Applying information	31.6±7.1	31.3	8.3-47.9

SD: Standard deviation

Table 4. Comparison of health literacy scores according to medication use behaviors		
Parameter	Health literacy score (Mean ± SD)	p
Using medicines without consulting a doctor		
Yes, frequently	24.8±8.1	0.001
Yes, rarely	29.7±7.3	
No, never	29.6±6.3	
Using medicines based on suggestions from surroundings		
Yes, frequently	24.0±7.3	0.013
Yes, rarely	26.8±8.7	
No, never	29.2±7.4	
Advising medicines to others		
Yes, frequently	27.0±7.7	0.456
Yes, rarely	28.4±8.0	
No, never	28.8±7.6	
Would you like medicines to be sold outside pharmacies?		
No	28.2±7.7	0.255
No opinion	28.5±9.3	
Yes	30.5±7.4	
Do you think it is correct that antibiotics are not sold without prescription?		
No	28.5±9.1	0.041
No opinion	23.7±6.8	
Yes	28.8±7.4	
Do you buy medicines to keep at home?		
Yes, frequently	25.4±7.9	0.001
Yes, rarely	30.1±7.1	
No, never	29.7±7.7	
Do you request medicines to be prescribed at your own request when visiting a doctor?		
Never	30.7±6.9	0.003
Sometimes	29.1±7.6	
Frequently	26.4±8.0	
SD: Standard deviation		

and patient demands in dental and surgical settings, where education and awareness interventions are emphasized to curb resistance (24). This reflects broader gaps in public health knowledge.

Study Limitation

The overall mean TSOY-32 score was 28.5±7.7, with 31.3% inadequate, 33% problematic/limited, 31.3% sufficient, and 4.3% excellent health literacy (HL) levels. These results align with other Turkish studies using the same scale, inadequate + limited often 60-70% (14,25,26). The lowest subscale score was in “appraising information,” indicating greater difficulty in critically evaluating information compared to accessing, understanding, or applying it (14,25,26). This challenge is further compounded by poor readability of Turkish online health resources; for instance, an evaluation of 50 Turkish migraine websites found that none were “easy” to read, with ~75% classified as “difficult” or “very difficult,” often requiring

high-school or college-level skills highlighting systemic barriers to effective patient information access and HL in Türkiye (27).

Associations between HL and sociodemographic variables showed: younger age (<40.5 years) was linked to higher HL scores (16,19). Females had significantly lower HL scores than males but aligning with some Turkish studies by Mut (26) and İşler (19).

University-level or higher education, higher income, and SGK/private insurance coverage were associated with significantly higher HL Özkan et al. (21), Mut (26). Similarly, in a local Adana-based study on Type 2 diabetes patients at an Akkapı Family Health Center, higher education and income levels were significantly linked to better glycemic control (lower HbA1c), underscoring the role of socioeconomic factors in chronic disease management and potentially in HL-related behaviors (28).

Participants with chronic diseases, multiple chronic conditions, or irregular follow-up had significantly lower HL (21). Low HL is known to increase chronic disease prevalence and complications.

Those preferring family health centers as their first consultation point and those with more than 14 outpatient visits in the past year had significantly lower HL (21). This pattern is consistent with local Adana-based retrospective analyses of family medicine clinic records, where high patient volumes, chronic disease burden, and socioeconomic factors were prominent in primary care settings, potentially contributing to lower HL and increased healthcare utilization (29).

Irrational behaviors including self-medication without consultation, using medications based on others' advice, home stockpiling, self-requested prescriptions, not reading prospectuses, and early treatment discontinuation were all significantly associated with lower HL scores. Local evidence from Çukurova-region studies further supports the link between low awareness, patient demands, and irrational antibiotic/drug use patterns (24). These findings confirm that higher HL promotes rational drug use and support the limited existing literature on this relationship.

CONCLUSION

In conclusion, this study highlights the critical role of HL in rational drug use and underscores the need for targeted interventions to improve HL levels, particularly among individuals with lower education, lower income, and women. Regional data from Adana-based institutions reinforce the urgency of patient education and rational prescribing practices to address these issues locally (24).

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Adana Training and Research Hospital, University of Health Sciences, with decision number: 2597 date: 25.05.2023).

Informed Consent: This study is a retrospective study.

Footnotes

This article was prepared based on the thesis study titled "Evaluation of the Relationship between Health Literacy and Rational Drug Use in Patients Admitting to a Family Health Center" with thesis number 842298.

Authorship Contributions

Surgical and Medical Practices: F.Ö., Concept: F.Ö., M.T., Design: F.Ö., M.T., Data Collection or Processing: F.Ö., Analysis or Interpretation: F.Ö., M.T., Literature Search: F.Ö., M.T., Writing: F.Ö., M.T.

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