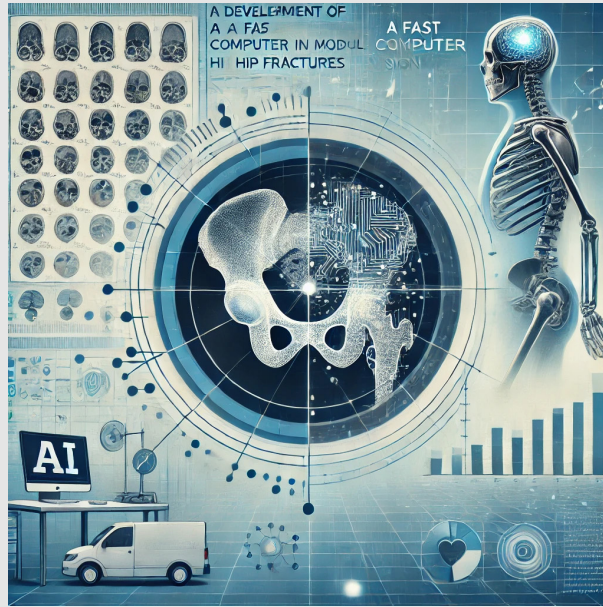


# European Archives of Medical Research

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# Evaluation of Attitudes Toward Nutritional Assessment, Knowledge of Nutrition Care, and Perceived Quality of Care Among Intensive Care Nurses

✉ Cansu Polat Dünya<sup>1</sup>, ✉ Melike Çelik<sup>2</sup>, ✉ Fatma Nur Ceylan<sup>3</sup>

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## Abstract

**Objective:** Malnutrition in intensive care unit patients significantly affects recovery and increases morbidity and mortality. Adequate nutritional support is essential, but nutritional care is often overlooked, and intensive care nurses play a key role in nutritional management. This study aimed to assess the knowledge levels, attitudes, and perceived quality of nutritional care among intensive care nurses to identify gaps in clinical practice.

**Methods:** This cross-sectional study was conducted with 147 intensive care nurses working at Isparta City Hospital. Data were collected using an information form and a validated scale evaluating the importance of nutritional assessment, knowledge of nutritional care, and perceived quality of care. Descriptive statistics, t-tests, ANOVA, Pearson's correlation, and multiple linear regression analyses were used to analyze the data.

**Results:** The mean score for the importance of nutritional assessment was  $23.39 \pm 2.92$ , knowledge level was  $25.24 \pm 5.38$ , and perceived quality of care was  $37.53 \pm 4.82$ . A significant relationship was found between positive attitudes toward nutritional care and perceived quality of care ( $p < 0.001$ ). Attitude toward nutritional care significantly predicted perceived quality of care (Adj.  $R^2 = 0.216$ ,  $p < 0.001$ ). Nurses with higher levels of knowledge also perceived better quality of care.

**Conclusion:** Intensive care nurses generally have positive attitudes toward nutritional care, but knowledge gaps and perceived quality of care need improvement. Further studies should explore the effectiveness of different educational strategies in improving nutritional management in intensive care units.

**Keywords:** Nutritional assessment, intensive care units, nurses, attitude, quality of care

## INTRODUCTION

Patients in intensive care units are frequently exposed to severe catabolic stress, acute illnesses, and muscle loss, which contribute to functional impairment and increase the risk of malnutrition (1). Malnutrition not only slows the recovery process but also increases the risk of complications, leading to serious clinical issues such as infections, delayed wound healing, and pressure ulcers. Therefore, ensuring adequate nutritional

support for intensive care patients is a critical intervention with significant potential to improve clinical outcomes and reduce morbidity (2,3). Guidelines published by the American society for parenteral and enteral nutrition and the European society for clinical nutrition and metabolism establish standards for the nutritional management of intensive care patients (4). However, global studies have indicated that the prevalence of malnutrition in intensive care patients ranges from 15% to 68%,



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and this condition is closely associated with increased morbidity and mortality (5).

Despite numerous studies highlighting the adverse clinical outcomes of malnutrition, assessment of the nutritional status of hospitalized patients and provision of appropriate nutritional support are still widely overlooked (2,6,7). A key challenge in effectively addressing malnutrition lies in the failure to timely identify patients at risk and the limited engagement of professional nutritional support teams in the nutritional care process (6,7). Given their direct and continuous involvement in patient care, intensive care nurses, who provide round-the-clock care to critically ill patients, play a key role in nutritional management. Nurses are expected to identify patients at risk of malnutrition, monitor their nutritional processes, and implement appropriate nursing care to address potential complications that may arise during this process (8,9).

Doménech Briz et al. (9), in a recent systematic review, highlighted that nurses lack sufficient knowledge regarding nutritional care and that their awareness of their roles in this area is not at the desired level. This lack of knowledge and awareness underscores the need for targeted educational interventions aimed at empowering nurses to play a more proactive role in nutritional management (9,10). In our country, few studies have addressed the knowledge levels, attitudes, and practices of intensive care nurses regarding nutritional assessment and care (11-15). This study aimed to describe the knowledge levels, attitudes, and practices of intensive care nurses regarding nutritional care, thereby providing an overview of the current situation. The findings from this research are crucial for identifying gaps in current clinical practice and are expected to contribute to the development of educational programs aimed at enhancing nurses' knowledge and awareness of nutritional management, as well as guiding the improvement of clinical practices in this area.

## METHODS

### Study Design and Setting

This cross-sectional study was conducted in May and December of 2023.

### Population and Samples of the Study

The study population consisted of intensive care nurses working in the adult intensive care units of Isparta City Hospital in May 2023 (n=218). Based on the known population sampling calculation, at least 140 intensive care nurses were included in the sample, with a 95% confidence interval and a 5% margin

of error. The study was completed with the participation of 147 intensive care nurses. Nurses working in intensive care for at least 1 year were included in the study. Nurses who were on leave or had a medical report during the study period and those who did not agree to participate were excluded. This study was reported according to the strengthening the reporting of observational studies in epidemiology guidelines.

### Data Collection

The data collection process involved using the information form and the scale for evaluating the importance of nutritional assessment, knowledge level on nutritional care, and perceived quality of nutritional care in nurses. The intensive care nurses completed the forms through a self-report mechanism. The data collection took approximately 15-20 minutes.

**Information Form:** The researchers prepared this form in accordance with the literature (9-15). The form included the socio-demographic characteristics of the nurses (age, gender, education level, etc.) and their professional experiences (type of intensive care unit, nutritional care training status, etc.).

### The Scale For Evaluating the importance of Nutritional Assessment, Knowledge Level on Nutritional Care, and Perceived Quality of Nutritional Care in Nurses:

The scale used to measure the importance of nutritional assessment, knowledge level regarding nutritional care, and perceived quality of nutritional care among nurses was developed by Theilla et al. (16), and its Turkish validity and reliability study was conducted by Gürlek Kısacık et al. (17). This scale consists of three sections: The first section includes seven items that evaluate nurses' attitudes toward the clinical importance of nutritional assessment and their perception of nutritional assessment as a fundamental component of nursing care. The total score ranged from 7 to 28, with higher scores indicating a more positive attitude toward the importance of assessing the nutritional status of patients. In the study by Gürlek Kısacık et al. (17), Cronbach's alpha values for the scale sections were found to be 0.82 for the attitude dimension, 0.63 for the knowledge level dimension, and 0.85 for the perceived quality of care dimension. The second section contains 10 reverse-scored items that assess nurses' knowledge levels regarding nutritional care. The total score ranged from 10 to 40, with higher scores reflecting greater knowledge in nutritional care. The third section consists of nine items that evaluate nurses' perceptions of the quality of nutritional care provided in their clinical settings. The total score ranged from 9 to 45, with higher scores indicating that nurses positively evaluate the quality of nutritional care in their units. Each section was scored and evaluated independently. In this study, Cronbach's alpha values were found to be 0.83 for the

attitude dimension, 0.82 for the knowledge level dimension, and 0.88 for the perceived quality of care dimension.

**Ethical Considerations**

Ethics committee approval was obtained from the Istanbul University Social and Humanities Research Ethics Committee (case number: 2023/110, decision date: 03.04.2023). Institutional permission was obtained from Isparta City Hospital. The study also gathered informed consent from the nurses by informing them about the study. Furthermore, the authors have granted permission for the scale to be used. This study conformed to the principles of the Declaration of Helsinki.

**Statistical Analysis**

The IBM Statistical Package for the Social Sciences (version 26.0) software was used for data analysis. Frequency and percentage distributions were used to evaluate categorical variables, whereas mean and standard deviation were used for continuous variables. Independent Samples t-test and One-Way ANOVA were applied to compare quantitative continuous data between independent groups. For significant differences identified in one-way variance analysis, the Bonferroni post-hoc test was used to determine the groups responsible for the difference. The relationships between the scales were examined using Pearson’s correlation analysis. Multiple linear regression analysis was performed to determine whether there was an association between variables that were significantly correlated. A p-value of less than 0.05 was considered statistically significant.

**RESULTS**

It was determined that the average age of intensive care nurses was 35.16±8.17 years, with 59.9% (n=88) of nurses being female and 83% (n=122) holding a bachelor’s degree. The nurses had an average of 12.88±8.34 years of experience, and 52.4% (n=77) had received training in nutritional practices. The self-assessed adequacy of nurses in providing nutritional care was observed to be 5.51±2.26 (Minimum-Maximum: 0-10) (Table 1).

It was found that the mean score of intensive care nurses regarding the Importance of Nutritional Assessment was 23.39±2.92, the mean score for Knowledge Level on Nutritional Care was 25.24±5.38, and the mean total score for Perceived Quality of Nutritional Care was 37.53±4.82 (Table 2).

A statistically significant difference was also detected in the Knowledge Level dimension based on the type of intensive care unit where the nurses worked (p<0.001) (Table 3).

A positive and significant relationship was found between the perceived quality of nutritional care among intensive care

nurses and their attitudes toward nutritional care (p<0.001), as well as their self-assessed adequacy in providing nutritional care (p<0.05) (Table 4).

According to the results of the regression analysis, a significant relationship was identified between attitude and perceived quality of care (R=0.476). It was found that the variables of attitude and self-assessed adequacy in nutritional care explained 21.6% of the total variance in perceived quality of care

**Table 1. Socio-demographic and professional characteristics of intensive care nurses**

Variable	Group	n	%
Age	21-29	50	34.0
	30-39	43	29.3
	40-53	54	36.7
	Mean±SD/Min.-Max.	35.16±8.17	21-53
Gender	Female	88	59.9
	Male	59	40.1
Education level	High school graduate	10	6.8
	Bachelor’s degree	122	83.0
	Master’s degree	15	10.2
Intensive care	Anesthesia and reanimation	91	61.9
	Cardiovascular surgery	11	7.5
	General	45	30.6
Years of Experience in intensive care unit	1-5	36	24.5
	6-15	58	39.5
	16-25	43	29.3
	26-35	10	6.8
	Mean±SD/Min.-Max.	12.88±8.34	1-35
Status of receiving nutrition practice training	Yes	77	52.4
	No	70	47.6
Perceived competence level in nutritional care (0-10: None-highest level)	Mean±SD/Min.-Max.	5.51±2.26	1-10

SD: Standard deviation, Min.-Max.: Minimum-maximum, n: Number

**Table 2. Mean Scores of the importance of nutritional assessment, knowledge, and perceived quality of care**

Scale dimensions	Mean±SD	Min.-Max.
Importance of nutritional assessment	23.39±2.92	13-28
Nutrition care knowledge	25.24±5.38	12-39
Quality of nutrition care	37.53±4.82	20-45

SD: Standard deviation, Min.-Max.: Minimum-maximum



(Adj. R<sup>2</sup>=0.216). Attitude toward nutritional care had a significant impact on the model ( $\beta=0.448$ ), with each 1-unit standard deviation change in this variable leading to a 0.448-unit change in perceived quality of care ( $t=6.08$ ,  $p<0.001$ ). However, self-assessed adequacy in nutritional care did not have a significant effect on perceived quality of care ( $t=1.66$ ,  $p>0.05$ ) (Table 5).

## DISCUSSION

Given the high prevalence of malnutrition in intensive care patients and its negative impact on patient outcomes (3,5), this study contributes significantly to the literature by evaluating nurses' knowledge levels, attitudes, and perceived quality of

nutritional care. Although various studies have been conducted on the importance of nutritional care in the literature (8,9,10,15), particularly in our country, few have focused on the role of intensive care nurses in this process (11-15). This gap highlights the originality and importance of our study, as our findings are expected to contribute to both local and international clinical practice. Our findings revealed that although nurses generally have a positive attitude toward nutritional care, deficiencies exist in their knowledge levels and perceived quality of care, indicating that these gaps need to be addressed through educational interventions. The recognition of nutritional assessment as an integral part of nursing care and the positive

**Table 3. Comparison of intensive care nurses' socio-demographic and professional characteristics with the importance of nutritional assessment, knowledge, and perceived quality of care**

Variable	Group	n	Importance of nutritional assessment		Nutrition care knowledge		Quality of nutrition care	
			Mean±SD	t-F/p	Mean±SD	t-F/p	Mean±SD	t-F/p
Gender	Female	88	23.60±2.62	1.09*	24.88±5.23	-0.10*	37.25±4.84	-0.86*
	Male	59	23.07±3.32	0.278	25.78±5.59	0.319	37.95±4.81	0.391
Education level	High school graduate	10	23.30±3.37	0.02** 0.980	27.60±5.19	1.17** 0.315	37.10±4.48	0.29** 0.745
	Bachelor's degree	122	23.41±2.50		25.15±5.39		37.46±4.90	
	Master's degree	15	23.27±5.26		24.40±5.33		38.40±4.53	
Intensive care unit worked in	Anesthesia and reanimation	91	23.68±2.58	1.45** 0.237	23.71±4.53	<b>12.53**</b> <b>0.000</b> <b>2.3&gt;1***</b>	37.53±4.82	0.24** 0.790
	Cardiovascular surgery	11	23.45±2.46		30.00±5.85		36.64±2.06	
	General	45	22.78±3.57		27.16±5.66		37.76±5.32	
Status of receiving nutrition practices training	Yes	77	23.90±2.73	2.24* 0.026	25.39±5.72	0.36* 0.722	38.18±4.47	1.73* 0.086
	No	70	22.83±3.04		25.07±5.01		36.81±5.11	

\*Independent Samples t-test, \*\*One-way analysis of variance (ANOVA), \*\*\*Bonferroni test, values indicated with  $p<0.05$  are statistically significant

**Table 4. The correlation between the importance of nutritional assessment, knowledge of nutritional care, and quality of nutritional care**

		Importance of nutritional assessment	Nutrition care knowledge	Quality of nutrition care	Perceived competence level in nutritional care
Importance of nutritional assessment	r	1.0			
	p	-			
Nutrition care knowledge	r	0.018	1.0		
	p	0.832	-		
Perceived quality of nutritional care	r	<b>0.460</b>	0.086	1.0	
	p	<b>0.000</b>	0.298	-	
Perceived competence level in nutritional care	r	0.102	0.063	<b>0.168</b>	1.0
	p	0.221	0.447	<b>0.042</b>	-

r: Pearson correlation coefficient, Values indicated with  $p<0.05$  are statistically significant

Model Summary	R	R <sup>2</sup>	Adj. R <sup>2</sup>	Standard error of estimate	F=21.10	P=0.000*	DW=1.75
	0.476	0.227	0.216	4.270			
Variables	Unstandardized coefficients		Standardized coefficients		T	P	VIF
	$\beta$	Standard error	Beta				
Constant		18.805	2.909	-	6.47	0.000	-
Independent variables	Importance of nutritional assessment	0.739	0.122	0.448	6.08	0.000	1.01
	Perceived competence level in nutritional care	0.261	0.157	0.122	1.66	0.099	1.01
Dependent variables	Quality of nutritional care					Cook: 0.09	
*One-Way analysis of variance results, Adj. R <sup>2</sup> : Adjusted R <sup>2</sup> , Cook: Cook distance, DW: Durbin-watson, VIF: Variance inflation factor							

attitudes of intensive care nurses toward this issue are crucial for improving clinical outcomes (6,8,9). In our study, we determined that nurses exhibit a positive attitude toward the importance of nutritional assessment. Similarly, the literature emphasizes that intensive care nurses hold positive attitudes regarding the importance of nutritional assessment (11,12,14,16). Additionally, our study found that 52.4% of nurses had received nutritional support training, and those who had received this training were more likely to recognize the importance of nutritional assessment than those who had not. This indicates that education has a positive effect on nurses' attitudes. It was also found that nurses considered themselves moderately competent in providing nutritional care, a finding consistent with that of Kurt and Gürdoğan (12). In this study, 58.7% of the nurses had received in-service training, and 72.9% stated that they felt moderately competent in providing nutritional care. Although education has been shown to have a positive impact on nurses' attitudes, further research is needed to determine which educational programs are most effective and assess their long-term impact. Future studies should investigate the effectiveness of different types of training, such as in-service education, certification programs, and workshops, by examining their effects on both patient knowledge levels and patient outcomes. Additionally, factors such as the frequency and duration of these programs should be considered to enhance their effectiveness. In our country, legal regulations aimed at increasing nurses' responsibilities in providing nutritional care have led healthcare institutions to initiate improvement efforts in this area. Steps such as certification of nutritional support nurses and educational activities have strengthened the role of nurses in nutritional care (18). It is well known that educational interventions improve nurses' competencies in nutritional

care, positively impacting patient outcomes and enhancing the overall quality of care (19). Therefore, healthcare institutions must prioritize such educational programs. Our findings also indicate that nurses working in cardiovascular surgery intensive care units have higher knowledge levels than those working in general intensive care and anesthesia and reanimation units. This difference may be attributed to the patient profile, complexity of care, and level of multidisciplinary collaboration in cardiovascular units. These findings suggest that educational programs should be tailored to the specific needs of each unit. Future research should explore how higher levels of knowledge in cardiovascular units impact patient outcomes, providing clearer insights into the link between educational interventions and clinical improvement.

It is widely recognized that intensive care nurses' knowledge level in nutritional care is crucial for adhering to clinical guidelines and ensuring safe care. In our study, nurses perceived the quality of nutritional care they provided as inadequate. Additionally, nurses who considered their knowledge of nutritional care to be sufficient had higher scores for perceived quality of care. These findings suggest that positive attitudes directly influence perceived quality of care, which is of significant importance for improving patient care. The study revealed that nurses' positive attitudes toward nutritional care were a significant predictor of perceived quality of care.

### Study Limitations

This study has several limitations. Conducting the research in a single center limits the generalizability of the results. Additionally, given that the study is descriptive, the impact of interventions aimed at improving nurses' knowledge of nutritional care could not be evaluated. Reliance on self-reported data may also

introduce bias. Future studies should collect data from multiple centers and conduct intervention studies to evaluate the long-term effects of educational programs.

## CONCLUSION

In conclusion, this study found that intensive care nurses have a positive attitude toward the importance of nutritional assessment, but there are deficiencies in their knowledge levels and perceived quality of care. To address these gaps, targeted educational programs should be implemented. Furthermore, nutrition management protocols should be revised with a multidisciplinary approach, and nurses should take a more active role in this process.

## Ethics

**Ethics Committee Approval:** Ethics committee approval was obtained from the Istanbul University Social and Humanities Research Ethics Committee (case number: 2023/110, decision date: 03.04.2023). Institutional permission was obtained from Isparta City Hospital.

**Informed Consent:** The study also gathered informed consent from the nurses by informing them about the study.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: C.P.D., M.Ç., Concept: C.P.D., M.Ç., Design: C.P.D., M.Ç., F.N.C., Data Collection or Processing: C.P.D., F.N.C., Analysis or Interpretation: C.P.D., M.Ç., Literature Search: C.P.D., F.N.C., Writing: C.P.D., M.Ç., F.N.C.

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

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## REFERENCES

- Chen W, Song J, Gong S. Advances in nutritional metabolic therapy to impede the progression of critical illness. *Front Nutr.* 2024;11:1416910.
- Hill A, Elke G, Weimann A. Nutrition in the intensive care unit-a narrative review. *Nutrients.* 2021;13:2851.
- Pardo E, Lescot T, Preiser JC, Massanet P, Pons A, Jaber S, et al. Association between early nutrition support and 28-day mortality in critically ill patients: the FRANS prospective nutrition cohort study. *Crit Care.* 2023;27:7.
- Cattani A, Teixeira PP, Silva FM. A systematic review on the agreement between clinical practice guidelines regarding the steps of the nutrition care process of adult patients who are critically ill. *JPEN J Parenter Enteral Nutr.* 2022;46:1769-86.
- Díaz G, T D Correia MI, Gonzalez MC, Reyes M. The global leadership initiative on malnutrition criteria for the diagnosis of malnutrition in patients admitted to the intensive care unit: A systematic review and meta-analysis. *Clin Nutr.* 2023;42:182-9.
- Hoffmann M, Schwarz CM, Fürst S, Starchl C, Lobmeyr E, Sendlhofer G, et al. Risks In management of enteral nutrition in intensive care units: a literature review and narrative synthesis. *Nutrients.* 2020;13:82.
- Mohialdeen Gubari MI, Hosseinzadeh-Attar MJ, Hosseini M, Mohialdeen FA, Othman H, Hama-Ghareeb KA, et al. Nutritional status in intensive care unit: a meta-analysis and systematic review. *Galen Med J.* 2020;9:e1678.
- Boeykens K. Nutritional support in the intensive care unit: implications for nursing care from evidence-based guidelines and supporting literature. *dimens crit care nurs.* 2021;40:14-20.
- Doménech Briz V, Gea-Caballero V, Chover-Sierra E, Czaplá M, Fehler P, Rodríguez-Calvo A, et al. Knowledge level of ICU nurses regarding nutritional assessment of critically ill patients: a systematic review. *nurs rep.* 2024;14:586-602.
- Lyons GCE, Summers MJ, Marshall AP, Chapple LS. Systematic review of clinicians' knowledge, attitudes, and beliefs about nutrition in intensive care. *Nutr Clin Pract.* 2022;37:825-42.
- Kıymaz D, Kılıç Ü, Yücesan S, Öztürk R, Toraman M. The knowledge levels of intensive care nurses on nutritional care. *Kırşehir Ahi Evran University Journal of Health Sciences.* 2023;7:172-84.
- Kurt D, Gürdoğan EP. awareness in intensive care nurses. *IGUSABDER.* 2023;19:240-54.
- Çoşgun T, Kısacık ÖG. Determination the attitude toward the nutritional assessment, the level of knowledge of nutritional care and the perceived quality of care among nurses. *Manisa Celal Bayar University Journal of Institute of Health Science.* 2021;8:204-17.
- Gezer N, Arslan E. Nurses' Knowledge and attitudes regarding nutrition support: A descriptive study. *MAUNSagBil Derg.* 2023;3:1-12.
- Turan M, Cengiz Z, Olmaz D. evidence-based investigation of nurses' nutrition interventions in intensive care patients regarding enteral nutrition. *dimens crit care nurs.* 2024;43:123-9.
- Theilla M, Cohen J, Singer P, Liebman C, Kagan I. The assessment, knowledge and perceived quality of nutrition care amongst nurses. *J Nutr Med Diet Care.* 2016;2:1-5.
- Gürlek Kısacık Ö, Çoşgun T, Taştekin A. The psychometric properties of the turkish version of the assessment questionnaire of the importance of nutritional assessment, the level of knowledge and perceived quality of nutritional care for nurses. *Ege Üniv Hemş Fak Derg.* 2019;35:123-35.
- Karaca Sivrikaya S, Eryılmaz A. Nutritional supplement in the team nursing. *Journal of Samsun Health Sciences.* 2018;3:33-7.
- Mancin S, Pipitone V, Testori A, Ferrante S, Soekeland F, Sguanci M, et al. Clinical nurse specialists in nutrition: a systematic review of roles and clinical experiences. *Int Nurs Rev.* 2024;71:521-30.

# Determination of Risk Factors for Endometrial Polyp Formation in Patients Who Had

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## Abstract

**Objective:** We aimed to evaluate the risk factors of patients who underwent endometrial sampling due to abnormal uterine bleeding (AUB) and were found to have endometrial polyps.

**Methods:** Patients who applied to İstanbul Bahçelievler State Hospital Gynecology and Obstetrics Clinic with complaints of abAUB between September 2022 and December 2023 were retrospectively investigated. Patients were grouped as endometrial polyp and other pathologies according to the pathology results. Both groups were compared in terms of age, gravida, parity, type of birth, height, weight, body mass index, comorbidities, presence of accompanying cervical polyps, age at menarche, age at menopause, and hemoglobin values.

**Results:** The mean age of menarche of the endometrial polyp group was lower than that in the other pathologies group ( $p=0.0001$ ). The mean BMI was significantly higher in the polyp group than in the other pathologies group ( $p=0.0001$ ). In addition, hypertension was found to be significantly higher in the polyp group ( $p=0.009$ ).

**Conclusion:** In our study, we found that early age at menarche, high body mass index, and hypertension were important risk factors for the development of endometrial polyps. Therefore, we recommend detailed anamnesis in clinically compatible patients, question these risk factors in their medical history, and warn them of the development of endometrial polyps if present.

**Keywords:** Endometrial polyp, hypertension, body mass index

## INTRODUCTION

Normal menstrual bleeding is defined as regular bleeding between 5 and 80 mL, occurring every 24-38 days and lasting 4-8 days. It has been shown in previous studies that it is seen in one-third of women, especially in reproductive age (1). According to the International Federation of Gynecology and Obstetrics (FIGO), abnormal uterine bleeding (AUB) can be acute or chronic. Bleeding that occurs for most of the last 6 months and is abnormal in terms of amount, regularity and timing is defined as chronic AUB (2). Bleeding that requires immediate intervention by a physician is referred to as acute AUB.

FIGO Systems 1 and 2 are used to evaluate patients with AUB. This system was developed to allow physicians to define normal and abnormal menstrual bleeding in a common terminology. FIGO System 1 is an anamnesis-based evaluation based on the frequency, duration, pattern, and flow volume of menstrual bleeding, and the presence or absence of intermenstrual bleeding. In this way, it is aimed to reach a preliminary diagnosis regarding the disorder that causes AUB with the history taken from the patient.

The FIGO System 2, which was first defined in 2011 and revised in 2018, categorizes possible causes of AUB. This classification defines polyps, adenomyosis, leiomyoma, malignancy, and



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hyperplasia (PALM), which can be detected by imaging methods or histopathological evaluation, as structural causes. Coagulopathy, ovulatory dysfunction, endometrial and iatrogenic causes (COEI) constitute non-structural causes. In addition, potential contributors (N) that cannot be classified in any other way are also categorized (3).

Endometrial polyp is the excessive proliferation of endometrial stroma and glands extending into the uterine cavity (4). Their size, location, structure, and number may vary, and these differences cause changes in symptoms. While they may be asymptomatic, they may experience intermenstrual bleeding, postmenstrual spotting, or AUB that may cause significant blood loss. The pathogenesis and natural course of endometrial polyps are not clearly known. Some risk factors for breast cancer, such as advanced age, estrogen exposure, and tamoxifen use for breast cancer (5). Although it is frequently observed in the reproductive period, it can also occur in the postmenopausal period. Polyps are mostly benign. However, malignancy risk factors such as increasing age (>60), postmenopausal status, AUB over the age of 40 years, tamoxifen use, additional diseases (such as diabetes, hypertension, obesity) and hereditary cancer syndromes have been identified (6). Studies on the malignancy probability of endometrial polyps have shown different results, ranging from 0.5% to 5% (7).

Endometrial sampling should be recommended for patients over the age of 45 who complain of AUB and for patients under the age of 45 who have unopposed estrogen exposure, do not respond to treatment, and have malignancy risk factors, such as obesity and polycystic ovary syndrome.

In this study, we aimed to investigate the risk factors of patients who applied to our hospital with complaints of AUB. Endometrial sampling was performed, and endometrial polyps were detected as a result of pathology.

## METHODS

The study was initiated with the approval of the Non-Interventional Clinical Research Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital (approval number: 48670771-514.99-233702584, date: 09/01/2024). All procedures were performed adhered to the ethical principles of the Helsinki Declaration. Informed consent was obtained from all patients.

In this study, we retrospectively investigated patients who applied to İstanbul Bahçelievler State Hospital Gynecology and Obstetrics Clinic with complaints of AUB, including

postmenopausal bleeding, between September 2022 and December 2023 were retrospectively investigated. Anamnesis information, pelvic examination and ultrasonography findings, laboratory parameters, and pathology results of patients who underwent endometrial sampling were recorded.

Patients were grouped as endometrial polyp and other pathologies according to pathology results. Risk factors in patients with endometrial polyps were evaluated by comparing the age, gravida, parity, mode of delivery, height, weight, body mass index, comorbidities, presence of accompanying cervical polyps, age at menarche, age at menopause, and hemoglobin values.

## Statistical Analysis

In this study, statistical analyses were performed using the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program. In the evaluation of the data, in addition to descriptive statistical methods (mean, standard deviation, median, interquartile range), the distribution of the variables was examined using the Shapiro-Wilk normality test. The independent t-test was used to compare pairwise groups of variables with normal distribution, and the Mann-Whitney U test was used to compare pairwise groups of variables that did not show normal distribution. The chi-square test was used for comparisons of qualitative data. Logistic regression analysis was performed to identify factors affecting endometrial polyps. The results were evaluated at the significance level of  $p < 0.05$ .

## RESULTS

A total of 161 patients were included in the study. The pathology causing AUB in 59 of the patients (36%) was endometrial polyp, and 53 of these patients (30.5%) were in the postmenopausal period. The mean age of patients with endometrial polyps was 49.36 years, and that of patients with non-polyp pathology was 48.83 years. Although the mean age at menarche was lower in the endometrial polyp group than in the other pathologies groups, the mean gravida and parity were significantly higher. In addition, normal birth rates were found to be higher in the polyp group than in the other pathologies group (Table 1).

The mean BMI of the endometrial polyp group was significantly higher than that of the other pathologies group (Figure 1). In addition, 32.2% of the patients in the endometrial polyp group had a known diagnosis of hypertension, whereas this rate was 14.7% in patients with other pathologies ( $p = 0.009$ ). There were no significant differences between the two groups with respect to diabetes mellitus (Table 2).

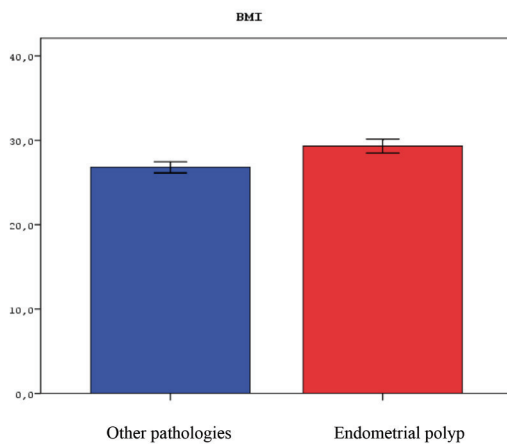
The mean hemoglobin values at the first admission in the endometrial polyp group were calculated as 11.05±1.47 g/dL, and in the other pathologies group, 12.54±1.42 g/dL. The difference between the two groups was statistically significant (Figure 2).

Cervical polyps were also present in 32.2% of patients in the endometrial polyp group and in 40.2% of patients in the other pathologies group (Table 3). Logistic regression analysis was performed to determine the factors affecting the development of endometrial polyps. Results showed that the risk of polyp development increased with decreasing age of menopause (Table 4).

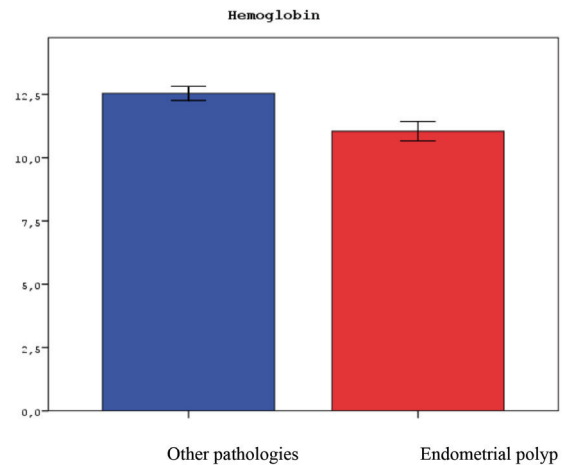
**Table 1. Evaluation of patients in terms of age, age at menarche and gravida parity and mode of delivery**

		Other pathologies n=102		Endometrial polyp n=59		p
Age	Mean±SD	48.83±8.27		49.36±8.77		0.706*
Age at menarche	Mean±SD	12.49±0.85		11.9±0.76		<b>0.0001*</b>
Gravida	Mean±SD	2.85±1,66		3.32±1.38		<b>0.001†</b>
	Median (IQR)	2 (2-3)		2 (2-4)		
Parity	Mean±SD	2.61±1.52		2.90±1.21		<b>0.009†</b>
	Median (IQR)	2 (2-3)		2 (2-4)		
Mode of delivery	VB	45	44.12%	44	74.58%	<b>0.001+</b>
	C/S	41	40.20%	13	22.03%	
	VB+C/S	16	15.69%	2	3.39%	

\*Independent t-test, †Mann-Whitney U test, +Chi-square test  
 VB: Vaginal birth, C/S: Cesarean Section, IQR: Interquartile range, SD: Standard deviation



**Figure 1.** Mean BMI values of both groups  
 BMI: Body mass index



**Figure 2.** Mean hemoglobin values of both groups

**Table 2. Association of endometrial polyp with BMI, DM, and HT**

		Other pathologies n=102		Endometrial polyp n=59		p
BMI	Mean±SD	26.8±3.37		29.32±3.15		<b>0.0001*</b>
DM	No	86	84.31%	49	83.05%	0.834+
	Yes	16	15.69%	10	16.95%	
HT	No	87	85.29%	40	67.80%	<b>0.009+</b>
	Yes	15	14.71%	19	32.20%	

\*Independent t-test, +Chi-square test  
 BMI: Body mass index, DM: Diabetes mellitus, HT: Hipertension, SD: Standard deviation

**Table 3. Patients with cervical polyps in both groups**

		Other pathologies n=102		Endometrial polyp n=59		p
Cervical polyp	No	61	59.80%	40	67.80%	0.312+
	Yes	41	40.20%	19	32.20%	

+Chi-square test

**Table 4. Logistic regression analysis**

	OR (%95 CI)	p
Gravida	2.13 (0.27-3.82)	0.475
Parity	0.39 (0.05-3.33)	0.392
Age at menarche	0.43 (0.13-1.42)	0.166
Age at menopause	0.61 (0.4-0.92)	<b>0.014</b>
BMI	1 (0.78-1.27)	0.974
HT	1.8 (0.64-2.31)	0.128

BMI: Body mass index, HT: Hypertension OR: Odds ratio, CI: Confidence interval

## DISCUSSION

Endometrial polyps are benign pathologies that can be detected in the reproductive age and postmenopausal period. They usually cause AUB and infertility. Dreisler et al. (8) in their study on Danish women between the ages of 20 and 74, found endometrial polyps in 7.8% of women with AUB. Anastasiadis et al. (9) in their study investigating the prevalence and malignancy potential of endometrial polyps in patients with AUB, detected the prevalence of endometrial polyps to be 8.9%. Günakan et al. (10) investigated endometrial histopathological results and endometrial cancer risk in a geriatric population and found that the most common histopathological finding was endometrial polyp with 26.6%. In our study, endometrial polyps were detected in 36% of women presenting with AUB, and we observed that it was more common than studies in the literature.

In our study, 18 (30.5%) patients with polyps were in the postmenopausal period. We also found that the mean age at menarche in patients with polyps was lower than that in the other pathologies groups. We believe that these differences are related to estrogen exposure.

In the patients who participated in our study, the mean BMI of the endometrial polyp group was significantly higher than that of the other pathologies. Serhat et al. (11) investigated the relationship between diabetes, hypertension, and obesity and endometrial polyp development. They found that the average BMI of the patients in whom they detected polyps was higher than the control group. Wong et al. (12) stated that in endometrial polyps for which they performed hysteroscopic resection, premalignant lesions were more common in older

and obese patients. Nappi et al. (13) stated in their study that age, menopause, HT, and obesity were associated with the presence of endometrial polyps in one-way logistic analysis, but there was no similar relationship in multi-way logistic analysis. In another study, Onalan et al. (14) reported that obesity was associated with endometrial polyp development, polyp size, and number of polyps in patients undergoing in vitro fertilization. It is known that estrogen exposure increases with BMI. Based on these results, our study supports the theory of estrogen exposure and polyp development.

In our study, a significant relationship was found between the presence of endometrial polyps and HT, while a similar relationship was not found with DM. Bueloni-dias et al. (15) found that DM, HT, and dyslipidemia were significantly more common in postmenopausal women with endometrial polyps. Hassa et al. (16) similar to our study, stated that hypertension is a risk factor for endometrial polyp, but they did not detect a relationship between DM and endometrial polyp. Baiocchi et al. (17) in their study in which they presented their 12-year experience regarding the risk of malignancy in endometrial polyps, stated that there was a positive correlation between postmenopausal patients, patients over 60 years of age, and the presence of hypertension and the development of malignancy in the polyp.

### Study Limitations

Our study was conducted with a large patient group; however, multicenter prospective studies are needed to better evaluate the prognosis.

## CONCLUSION

Although endometrial polyps are pathologies with low malignant potential, they need to be treated because they can cause problems such as AUB and infertility. Our study found that early age at menarche, high BMI, and hypertension were important risk factors for the development of endometrial polyps. Therefore, we recommend detailed anamnesis in clinically compatible patients, question these risk factors in their medical history, and warn them of the development of endometrial polyps if present.

## Ethics

**Ethics Committee Approval:** The study was initiated with the approval of the Non-Interventional Clinical Research Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital (approval number: 48670771-514.99-233702584, date: 09/01/2024).

**Informed Consent:** Retrospective study.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: Y.Ö., S.G., V.M., Concept: Y.Ö., S.G., V.M., Design: Y.Ö., S.G., V.M., Data Collection or Processing: Y.Ö., S.G., V.M., Analysis or Interpretation: Y.Ö., S.G., V.M., Literature Search: Y.Ö., S.G., V.M., Writing: Y.Ö., S.G., V.M.

**Conflict of Interest:** Veli Mihmanlı, MD, is a Section Editor in the European Archives of Medical Research. He had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Other authors have nothing to disclose.

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

## REFERENCES

- Jain V, Chodankar RR, Maybin JA, Critchley HOD. Uterine bleeding: how understanding endometrial physiology underpins menstrual health. *Nat Rev Endocrinol.* 2022;18:290-308.
- Munro MG, Critchley HO, Broder MS, Fraser IS; FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet.* 2011;113:3-13.
- Munro MG, Critchley HOD, Fraser IS; FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet.* 2018;143:393-408.
- Clark TJ, Stevenson H. Endometrial polyps and abnormal uterine bleeding (AUB-P): What is the relationship, how are they diagnosed and how are they treated? *Best Pract Res Clin Obstet Gynaecol.* 2017;40:89-104.
- Berceanu C, Cernea N, Căpitănescu RG, Comănescu AC, Paitici Ş, Rotar IC, et al. Endometrial polyps. *Rom J Morphol Embryol.* 2022;63:323-34.
- Vitale SG, Haimovich S, Laganà AS, Alonso L, Di Spiezio Sardo A, Carugno J, et al. Endometrial polyps. an evidence-based diagnosis and management guide. *Eur J Obstet Gynecol Reprod Biol.* 2021;260:70-7.
- Savelli L, De Iaco P, Santini D, Rosati F, Ghi T, Pignotti E, et al. Histopathologic features and risk factors for benignity, hyperplasia, and cancer in endometrial polyps. *Am J Obstet Gynecol.* 2003;188:927-31.
- Dreisler E, Stampe Sorensen S, Ibsen PH, Lose G. Prevalence of endometrial polyps and abnormal uterine bleeding in a Danish population aged 20-74 years. *Ultrasound Obstet Gynecol.* 2009;33:102-8.
- Anastasiadis PG, Koutlaki NG, Skaphida PG, Galazios GC, Tsikouras PN, Liberis VA. Endometrial polyps: prevalence, detection, and malignant potential in women with abnormal uterine bleeding. *Eur J Gynaecol Oncol.* 2000;21:180-3.
- Günakan E, Atak Z, Albayrak M, Kurban Y, Şimşek GG. Endometrial histopathology results and evaluation of endometrial cancer risk in geriatric women. *Prz Menopauzalny.* 2018;17:18-21.
- Serhat E, Cogendez E, Selcuk S, Asoglu MR, Arioglu PF, Eren S. Is there a relationship between endometrial polyps and obesity, diabetes mellitus, hypertension? *Arch Gynecol Obstet.* 2014;290:937-41.
- Wong CLH, So PL. Prevalence and risk factors for malignancy in hysteroscopy-resected endometrial polyps. *Int J Gynaecol Obstet.* 2021;155:433-41.
- Nappi L, Indraccolo U, Di Spiezio Sardo A, Gentile G, Palombino K, Castaldi MA, et al. Are diabetes, hypertension, and obesity independent risk factors for endometrial polyps? *J Minim Invasive Gynecol.* 2009;16:157-62.
- Onalan R, Onalan G, Tonguc E, Ozdener T, Dogan M, Mollamahmutoglu L. Body mass index is an independent risk factor for the development of endometrial polyps in patients undergoing in vitro fertilization. *Fertil Steril.* 2009;91:1056-60.
- Bueloni-Dias FN, Spadoto-Dias D, Delmanto LR, Nahas-Neto J, Nahas EA. Metabolic syndrome as a predictor of endometrial polyps in postmenopausal women. *Menopause.* 2016;23:759-64.
- Hassa H, Korkmazer E, Tokgöz VY, Öge T. Independent risk factors for endometrial polyps: diabetes, hypertension, and obesity. *Asian Pacific Journal of Reproduction.* 2012;1:312-4.
- Baiocchi G, Mancini N, Pazzaglia M, Giannone L, Burnelli L, Giannone E, et al. Malignancy in endometrial polyps: a 12-year experience. *Am J Obstet Gynecol.* 2009;201:462.



# Comparison of Survival and Recurrence After Liver Transplantation in Hepatocellular Carcinoma Patients with and Without Diabetes

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## Abstract

**Objective:** Epidemiological evidence suggests that many types of cancer, including breast, pancreas, lung, colorectal and kidney cancers in patients with type 2 diabetes mellitus (T2DM), hepatocellular carcinoma (HCC) accounts for up to 90% of all primary liver malignancies. Liver transplantation (LT) is the only treatment modality for improved outcomes in patients with end-stage liver disease and HCC. We aimed to investigate the importance of DM on survival and recurrence and the relationship between DM and other prognostic factors in HCC patients undergoing LT.

**Methods:** This study included a retrospective analysis 200 patients with histologically confirmed HCC. patients were divided into two groups as DM and non-DM the primary end points in the present study were oncologic outcomes such as the recurrence rate, disease-free survival and overall survival of the HCC patients with or without DM.

**Results:** The diabetic and non-diabetic groups were not significantly different for, locoregional therapy, tumor recurrences, tumor differentiation, microvascular invasion (MVI), follow-up period, Child-Pugh score, alpha fetoprotein value, number of HCC lesions, body mass index value, and death rate ratio. However, model for end stage liver disease score was significantly higher in the diabetic group than in the non-diabetic group. There was no significant difference in the predicted disease-free survival and overall survival between the non-diabetic and the diabetic groups.

**Conclusion:** Our study demonstrated that there is no difference in HCC recurrence and survival between transplanted patients with and without DM. We revealed that characteristic features such as MVI, pathological grade of the tumor, number and size of the tumor have prognostic importance. LT can be chosen as a DM patients with HCC without changing long-term recurrence and survival results.

**Keywords:** Diabetes mellitus, hepatocellular carcinoma, liver transplantation, recurrence, survival

## INTRODUCTION

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and the third leading cause of cancer-related mortality (1). It accounts for up to 90% of all primary liver malignancies (2). In recent years, non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) have emerged as new risk factors for HCC (3). In this context, the etiologies with the highest prevalence in cirrhosis were reported as NAFLD (56%), cryptogenic

liver disease (51%), HCV infection (32%), diabetes (31%) and alcoholic liver disease (27%) (4). Type 2 diabetes mellitus (T2DM), which seriously affects public health worldwide, is characterized by hyperglycemia, hyperinsulinemia and peripheral insulin resistance. Epidemiological evidence suggests that many types of cancer, including breast, pancreatic, lung, colorectal, and kidney cancers, increase in patients with DM (5,6). Persistent hyperinsulinemia increases the bioavailability of insulin-



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like growth factor (IGF)-1 produced by the liver by promoting the production of IGF binding protein. This pathway activates the phosphoinositide-3-kinase/AKT/mammalian target of rapamycin signal, which is a key pathway in fatty liver associated with cancer (7,8). Diabetes shares the common pathophysiology of inducing fatty liver along with obesity. In the context of a growing number of individuals with obesity and an increasing prevalence of metabolic syndrome, both diseases have increased incidence rates worldwide in recent decades. In many diabetic patients, there are other metabolic factors, such as obesity and dyslipidemia. Fat accumulation in the liver induces chronic inflammation. With the combination of all these direct and indirect mechanisms, the production of inflammatory cytokines, such as tumor necrosis factor- $\alpha$ , interleukin-6 (IL-6), and nuclear factor- $\kappa$ B, which are involved in hepatocarcinogenesis, increases. It is postulated that the combination of these direct and indirect factors in diabetes, cirrhosis, and other metabolic disorders supports hepatocarcinogenesis (9). Regardless of the presence of underlying liver disease or cirrhosis, patients with DM were reported to have a 2- to 3-fold higher risk of developing HCC than those without DM (10). In parallel with the rapid increase in both HCC and DM, the risk of HCC can be reduced with appropriate management of DM, and the relationship between the two diseases must be strongly identified. Although advances in medical and surgical treatments have improved outcomes in patients with advanced and operable HCC, liver transplantation (LT) has been the only treatment modality for improved outcomes in patients with end-stage liver disease and HCC (11). In addition to the cause and effect relationship between DM and HCC, one unanswered question is how strongly DM affects survival and recurrence after ablative treatment, surgical resection, or LT. The present study aimed to investigate the importance of DM on survival and recurrence and the relationship between DM and other prognostic factors in patients with HCC undergoing LT from a clinical and pathophysiological perspective.

## METHODS

This study included a retrospective analysis of 1,360 consecutive liver transplant recipients who underwent the procedure for any reason at two centers between 2012 and 2023. The exclusion criteria were mixed HCC and cholangiocarcinoma on explant histological examination, non-HCC neoplasia, and death of any cause within the first 30 days after LT. After excluding four patients due to early mortality, 200 patients had histologically confirmed HCC. The study included patients who underwent LT due to HCC, cirrhosis for any reason, and patients who were histologically confirmed to have only HCC in the explant liver.

In the study, patients were divided into two groups: DM and non-DM. Of all patients with HCC who underwent LT, 40 had DM and 160 did not. All patients with an expected waiting list time longer than three months were treated with transarterial chemoembolization (TACE) and ablation as pre-transplant bridging therapy. Downscaling therapies before transplantation included TACE and ablation. The decision to treat and the type of treatment were discussed in a multidisciplinary meeting. Explant livers were examined for tumor size, number, differentiation, and microvascular invasion by specialist pathologists. The primary end points in the present study were oncologic outcomes, such as the recurrence rate, disease-free survival (DFS), and overall survival (OS) of patients with HCC with or without DM. In addition, it was important to examine the prognostic significance of DM in patients with HCC and LT. The secondary end points were to investigate whether long-term post-LT DM is a risk factor for HCC development and the relationship between DM and other risk factors for HCC. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee. The study was conducted in accordance with the Declaration of Helsinki. The ethics committee of Acibadem University approved this retrospective study (approval number: 2024-5/216, date: 28.03.2024). Written informed consent was waived because of the retrospective nature of the study.

## Statistical Analysis

Mean, standard deviation, median, minimum, maximum values, frequency, and percentage were used for descriptive statistics. The distributions of variables were checked with Kolmogorov-Smirnov test. Mann-Whitney U test was used for the comparison of quantitative data. The chi-square test was used for the comparison of qualitative data. Kaplan-Meier test was used in the survival analysis. SPSS 28.0 was used for statistical analyses.

## RESULTS

The parameters examined were the model for end stage liver disease score, tumor recurrence, tumor differentiation, microvascular invasion (MVI), follow-up period, Child-Pugh score, alpha fetoprotein (AFP) level, HCC lesion number, body mass index (BMI), and locoregional therapy (LRT). There were no significant differences in age and gender distribution of the patients between the diabetic and non-diabetic groups. The diabetic and non-diabetic groups did not differ significantly in terms of LRT, tumor recurrences, tumor differentiation, MVI, follow-up period, Child-Pugh score, AFP level, number of HCC

lesions, BMI level, and death rate ratio. However, the MELD score was significantly higher in the diabetic group than in the non-diabetic group (Table 1). There was no significant difference in the predicted disease-free survival time between the non-diabetic (113.1 months) and diabetic (97.5 months) groups (Figure 1).

There was no significant difference in the predicted survival time between the DM (102.4 months) and non-DM (105.3 months) groups (Figure 2). There was no significant difference in mortality between the DM and non-DM groups. Although there was no difference in long-term overall survival rates between the two groups, this finding was similar to that of other studies on patients with HCC who underwent LT (Table 2). In general, factors affecting the prognosis of post-LT HCC, such as MVI, degree of tumor differentiation, AFP level, and number of tumor lesions, did not differ between the two groups. However, in general, poor tumor differentiation, tumor number, and size were found to be important for prognosis (Table 3).

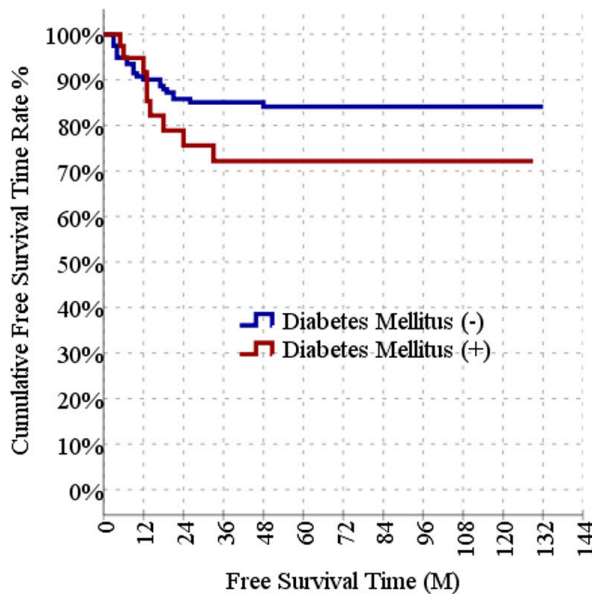
## DISCUSSION

The prevalence of NAFLD and NASH in patients with DM was 55.5 and 37.3%, respectively (12). Given that NASH is an earlier cause of HCC development than NAFLD, the presence of NASH in almost one-third of patients with DM raises questions about its relationship with HCC. Although DM has been implicated in the development of HCC in NAFLD, obesity and DM are both associated with the severity of liver fibrosis in patients with NASH. In fact, it is difficult to identify a cause-and-effect relationship between the co-existence of NAFLD and DM and the prognosis of HCC. DM is globally endemic. Only observational studies have supported the idea that DM is a risk factor for HCC. Observational studies are informative, but their limitations for robust causality inference should be considered (13). In parallel with the high prevalence of DM, the prevalence of cirrhosis and HCC due to NASH, which have increased in recent years, may not be related. These results can be affected by bias or misclassification. Insulin resistance independently affects the progression of liver fibrosis,

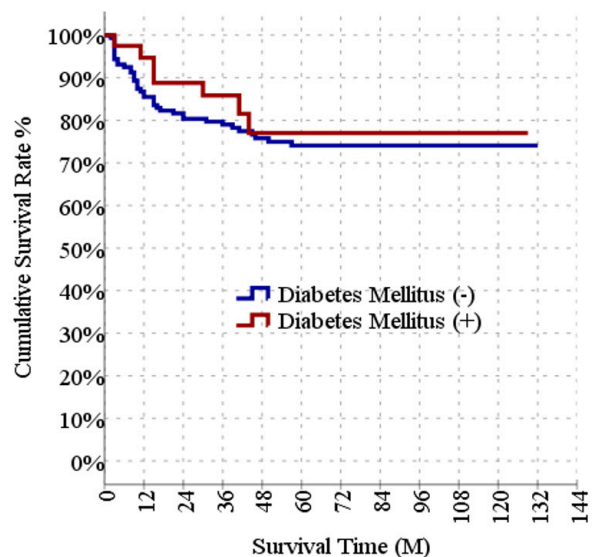
	Mean ± SD/n-%	Diabetes mellitus (No)		Diabetes mellitus (Yes)		P	
		Median	Mean ± SD/n-%	Median	Mean ± SD/n-%		
Age		64.5±8.6	66.9	64.7±8.4	65.3	0.998	m
Gender	Female	25	15.6%	9	22.5%	0.301	χ <sup>2</sup>
	Male	135	84.4%	31	77.5%		
BMI		26.4±3.8	26.0	26.8±3.7	27.0	0.638	m
Child-Pugh score	A	78	48.8%	16	40.0%	0.597	χ <sup>2</sup>
	B	73	45.6%	21	52.5%		
	C	9	5.6%	3	7.5%		
Meld score		13.0±6.6	11.0	15.5±6.6	14.0	0.019	m
AFP		90.6±296.3	8.9	84.8±249.0	7.3	0.585	m
Nuber of HCC lesions		2.6±2.8	2.0	3.1±3.0	2.0	0.158	m
Locoregional treatment	(No)	109	68.1%	26	65.0%	0.706	χ <sup>2</sup>
	(Yes)	51	31.9%	14	35.0%		
Tumor recurrens	(No)	137	85.6%	31	77.5%	0.210	χ <sup>2</sup>
	(Yes)	23	14.4%	9	22.5%		
Tumor differansiasion	Advnced	30	18.8%	5	12.5%	0.599	χ <sup>2</sup>
	Early	53	33.1%	13	32.5%		
	Intermediate	77	48.1%	22	55.0%		
Microvascular invasion	(No)	100	62.5%	25	62.5%	1.000	χ <sup>2</sup>
	(Yes)	60	37.5%	15	37.5%		
Follow-up time		57.3±35.1	62.5	48.5±32.7	40.0	0.151	m
Live/Died	Live	121	75.6%	33	82.5%	0.355	χ <sup>2</sup>
	Died	39	24.4%	7	17.5%		

<sup>m</sup>Mann-Whitney u test, <sup>χ<sup>2</sup></sup>Chi-square test, BMI: Body mass index, HCC: Hepatocellular carcinoma, AFP: Alpha fetoprotein

a risk factor for HCC. Obesity itself is associated with a two-fold increase in HCC risk and HCC-related mortality, regardless of BMI. Type 2 DM is associated with central obesity. This, in turn, stimulates carcinogenesis via the release of proinflammatory cytokines from the visceral adipose tissue. Han et al. did not report an increased risk of HCC in patients with type 2 DM and HBV-associated cirrhosis, whereas DM was not found to be a risk factor for HCC in a separate study comparing patients with non-HCC cirrhosis with HCC to HBV-infected patients with HCC (14).



**Figure 1.** Disease-free survival curve in patients with and without diabetes who underwent liver transplantation for hepatocellular carcinoma



**Figure 2.** Overall survival curve in patients with and without diabetes who underwent liver transplantation for hepatocellular carcinoma

The risk of cirrhosis caused by viral hepatitis and concomitant increased risk of HCC should not be ignored. Contrary to the findings suggesting a synergistic interaction between DM and other risk factors for HCC in hepatocarcinogenesis, alcohol and viral etiologies were also ruled out postoperatively, with the elimination of the diseased liver after liver transplantation. Unlike studies reporting that DM was an important risk factor for cirrhosis and HCC, in our study, chronic liver disease and cirrhosis, which are the most important risk factors for HCC in post-LT patients regardless of etiology, disappeared. After long-term (5-10 years) follow-up of these patients, DM was not found to be a risk factor for recurrence, which is the most important cause of HCC-related death.

Most studies showed that independent risk factors for increased risk of recurrence after LT were poor tumor differentiation and vascular invasion (15). In the present study, there was no difference between the two groups in terms of the risk factors. The lack of significant difference in OS and recurrence rates supported this view.

DM is a risk factor for HCC in alcoholic cirrhosis and is one of the most common risk factors for HCC in the Western countries (16). In our study, no subgroup analysis was performed in terms of DM etiology, survival, and recurrence. However, alcoholic liver disease and NAFLD have similar histopathological findings. DM, a risk factor for NAFLD, can exacerbate alcoholic liver disease and lead to the development of alcohol-related cirrhosis and HCC.

In a study using personal participation data analysis, Rao et al. (17) showed that the risk of HCC mortality was twice higher in those with diabetes than in those without diabetes. The risk of mortality in diabetic HCC patients was higher than in other cancers. In addition, DM is an independent risk factor associated with decreased overall OS and DFS in patients with HCC (18). Nakamura et al. (19) reported that between 2001 and 2010,

**Table 2. Comparison of long-term survival among patients with and without diabetes who underwent liver transplantation for hepatocellular carcinoma**

	Cumulative survival rate		
	Total	Diabetes mellitus (-)	Diabetes mellitus (+)
1 <sup>st</sup> year	88.3%	86.8%	94.6%
2 <sup>nd</sup> year	83.0%	81.6%	88.7%
3 <sup>rd</sup> year	80.9%	79.7%	85.8%
4 <sup>th</sup> year	76.2%	75.8%	76.9%
5 <sup>th</sup> year	74.7%	74.1%	76.9%
10 <sup>th</sup> year	74.7%	74.1%	76.9%

cancer was the most common cause of death among patients with diabetes in Japan (38%). In this study, liver cancer (6%) occurred after lung cancer (7%). Therefore, HCC was identified as a cause of both important comorbidity and mortality in patients with diabetes. Most studies regarding the effect of DM on the prognosis of HCC have stated that DM worsens the prognosis of HCC. In a large prospective study conducted in China, Wang et al. (20) showed that the presence of diabetes was associated with increased liver cancer-related mortality. A separate meta-analysis revealed poor overall survival in HCC patients with diabetes even in patients who underwent non-surgical treatment, such as radiofrequency ablation, or curative treatment, including hepatic resection (21). Among these patients, there were no HCC patients who underwent transplantation. LT has the potential to cure tumors and underlying liver disease, which is an important risk factor for new lesion development. Because there is no difference in HCC recurrence and survival between transplanted patients with and without DM, we are in favor of eliminating HCC as the direct cause of death in patients with DM. However, some studies have argued that the effect of diabetes on the prognosis of HCC varies depending on the clinical setting. A meta-analysis examining patients with diabetes who developed HCC after curative treatment demonstrated that diabetes worsened overall survival in patients with HCC  $\leq 5$  cm. However, this effect was not observed in HCCs  $>5$  cm (22). In a prospective study by Ho et al. (23) the presence of diabetes was not an independent prognostic factor of HCC within the Milan criteria, but was associated with decreased survival. These data suggest that, at least in patients with early and treatable HCC, diabetes worsens long-term prognosis. This is probably a result of decreased residual liver function due to diabetes. We did not perform a subgroup analysis among early or advanced

stage HCC patients in our study. Characteristic features of tumors are associated with better prognosis in advanced liver cancer. As a matter of fact, our study revealed that characteristic features such as MVI, pathological grade of the tumor, and number and size of the tumor have prognostic importance. Non-viral HCC is more likely to be diagnosed at an advanced stage. The poor prognosis of DM-associated HCC in this population may be attributable to a lower chance of curative treatment at an advanced stage. To date, only epidemiological and preclinical evidence has supported the association between DM and chronic liver disease, including HCC. Advanced liver disease may also induce the onset of diabetes, and a synergistic and bidirectional relationship existing for the two clinical entities. Additionally, the identification of diabetes as a risk factor for the progression and development of HCC and liver disease has led to confusion. The relationship between the two diseases is complex.

Those who identified DM as the reason for the increased risk of HCC pointed to the parallelism in the increase of HCC, DM, and NAFLD in recent years (24). However, the tumor microenvironment plays a key role in tumorigenesis. In particular, the tumor immune microenvironment affects tumor progression and prognosis. Components of the HCC immune structure were found to be associated with clinical outcomes (25,26). Although medical control of DM did not affect the prognosis and development of HCC in the treatment of HCC, immune surveillance was restored by targeting programmed cell death-1 receptor (PD1) or the PD1 ligand (PD-L1) in CD8+ T cells with immune checkpoint inhibitors (27,28). In fact, we know very little about the effect of DM on treatment outcomes after liver transplantation in patients with HCC. In many patients with HCC, there are very few curative treatment options other than liver transplantation due to impaired liver function, usually due to

**Table 3. Univariate and multivariate analysis for factors affecting prognosis for hepatocellular carcinoma after liver transplantation**

	Univariate				Multivariate			
	p	HR	95% CI for HR		p	HR	95% CI for HR	
			Lower	Upper			Lower	Upper
Alpha feto protein (ng/mL)	0.769	1.000	0.999	1.001	0.642	1.000	0.998	1.001
Tumor size (mm)	0.002	1.016	1.006	1.027	0.181	1.009	0.996	1.021
Number of tumor lesions	0.002	1.117	1.041	1.199	0.113	1.074	0.983	1.174
Locol-regional treatment	0.728	1.114	0.607	2.043	0.719	0.881	0.442	1.756
Tumor recurrence	<0.001	6.706	3.744	12.011	<0.001	6.262	3.056	12.833
Tumor differentiation (Ref: intermediate)	0.437				0.725			
Advence	0.421	1.343	0.655	2.756	0.626	1.224	0.542	2.765
Early	0.497	0.785	0.391	1.578	0.610	0.811	0.363	1.813
Microvascular invasion	0.024	1.954	1.094	3.491	0.714	0.862	0.389	1.910

CI: Confidence interval, HR: Heart rate

cirrhosis. However, because of the comorbidities associated with DM and metabolic syndrome and the frequency of advanced-stage tumors, oncological treatment options are also limited.

Studies comparing long-term outcomes after LT for NAFLD-HCC patients with DM or other metabolic syndromes and HCC with other etiologies are inconsistent. The 5-year OS was comparable for NASH, HCV, and alcohol-induced HCC in the United Network for Organ Sharing analysis.(29) and in the study by Reddy et al. (30), Wong et al. (31) showed reduced OS in their study comparing post-LT OS in non-NASH-HCC patients and patients with NAFLD-HCC.

In advanced-stage patients with limited curative treatment options, the criteria for LT have been expanded with a low risk of recurrence, especially with downscaling and bridging treatments. LT particularly prevents the overuse of ineffective treatment methods and eliminates unnecessary costs and side effects. The risk of NASH-HCC, which is mostly caused by DM, is a growing health concern globally. Although it has a relatively low incidence so far, many questions about its management and especially its treatment remain unanswered. They undergo hepatic resection more often and undergo fewer liver transplants. However, the etiology of HCC is not considered in the treatment algorithm, especially for LT. Studies on OS, rate of force development, and recurrence outcomes after LT in patients with HCC and DM are rare. NAFLD is most commonly associated with cardiovascular disease, DM, obesity, and dyslipidemia. This makes LT management more challenging.

Approximately 40% of all deaths in the first 30 days of post-transplantation in NAFLD-NASH-HCC patients, including DM and obesity, are due to cardiovascular complications. The operation may be technically challenging in these patients. This reflects high operational revision rates with prolonged operation time, major transfusion requirements, hepatic arterial damage and malposition, inferior vena cava injury, and uncontrollable major hemorrhages. Likewise, there are increased complication rates in the first 30 days after transplantation in patients with DM and obesity. These conditions include wound infection, sepsis, renal failure, and prolonged mechanical ventilation and hospital stay (32). However, post-LT complications were not examined as subgroups.

As long-term complications, DM, dyslipidemia, renal impairment, and NASH LT post-LT are risk factors for the development of CV events. The prevalence of DM in patients with NAFLD before LT is between 33% and 66% (33). DM can significantly affect the prognosis of patients with LT by leading to a higher 10-year mortality rate associated with increased CV events and high infection rates (34,35). Despite the development of many

antidiabetic treatment modalities, the increasing prevalence of HCC is noteworthy. This suggests the need for investigation of metabolic and pro-oncogenic factors other than diabetes itself and the development of hepatoprotective methods related to this.

### Study Limitations

Our study had some limitations, such as its retrospective nature, lack of subgroup analysis, and small number of patients with DM. Further randomized prospective studies are needed to elucidate the exact relationship between the risk of increased HCC and the duration and severity of DM.

## CONCLUSION

Most studies regarding the effect of diabetes on the prognosis of HCC patients stated that DM worsens the prognosis of HCC. Our study demonstrated that there was no difference in HCC recurrence and survival between transplanted patients with and without DM. We revealed that characteristic features, such as MVI, pathological grade of the tumor, and the number and size of the tumor, have prognostic importance. LT can prevent the overuse of ineffective treatment methods and eliminate unnecessary costs and side effects. Therefore, it can be used for DM patients with HCC without changing long-term recurrence and survival results.

### Ethics

**Ethics Committee Approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee. The study was conducted in accordance with the Declaration of Helsinki. The ethics committee of Acbadem University approved this retrospective study (approval number: 2024-5/216, date: 28.03.2024).

**Informed Consent:** Written informed consent was waived because of the retrospective nature of the study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: U.T., İ.B.B., Concept: U.T., İ.B.B., Design: U.T., Data Collection or Processing: U.T., İ.B.B., Analysis or Interpretation: U.T., Literature Search: U.T., İ.B.B., Writing: U.T.

**Conflict of Interest:** No conflicts of interest were declared by the authors.

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## REFERENCES

1. Konyon P, Ahmed A, Kim D. Current epidemiology in hepatocellular carcinoma. *Expert Rev Gastroenterol Hepatol*. 2021;15:1295-307.
2. Liu Y, Wang Y, Guo X, He Y, Zhou J, Lv Q, et al. Comparative effectiveness of adjuvant treatment for resected hepatocellular carcinoma: a systematic review and network meta-analysis. *front oncol*. 2021;11:709278.
3. Foerster F, Gairing SJ, Müller L, Galle PR. NAFLD-driven HCC: Safety and efficacy of current and emerging treatment options. *J Hepatol*. 2022;76:446-57.
4. Lee WG, Wells CI, McCall JL, Murphy R, Plank LD. Prevalence of diabetes in liver cirrhosis: A systematic review and meta-analysis. *Diabetes Metab Res Rev*. 2019;35:e3157.
5. Shikata K, Ninomiya T, Kiyohara Y. Diabetes mellitus and cancer risk: review of the epidemiological evidence. *Cancer Sci*. 2013;104:9-14.
6. Walker JJ, Johnson JA, Wild SH. Diabetes treatments and cancer risk: the importance of considering aspects of drug exposure. *Lancet Diabetes Endocrinol*. 2013;1:132-9.
7. Kudo Y, Tanaka Y, Tateishi K, Yamamoto K, Yamamoto S, Mohri D, et al. Altered composition of fatty acids exacerbates hepatotumorigenesis during activation of the phosphatidylinositol 3-kinase pathway. *J Hepatol*. 2011;55:1400-8.
8. Nakatsuka T, Tateishi K, Kudo Y, Yamamoto K, Nakagawa H, Fujiwara H, et al. Impact of histone demethylase KDM3A-dependent AP-1 transactivity on hepatotumorigenesis induced by PI3K activation. *Oncogene*. 2017;36:6262-71.
9. Kasuga M, Ueki K, Tajima N, Noda M, Ohashi K, Noto H, et al. Report of the Japan Diabetes Society/Japanese Cancer Association Joint Committee on diabetes and cancer. *Cancer Sci*. 2013;104:965-76.
10. Mantovani A, Targher G. Type 2 diabetes mellitus and risk of hepatocellular carcinoma: spotlight on nonalcoholic fatty liver disease. *Ann Transl Med*. 2017;5:270.
11. Villanueva A. Hepatocellular Carcinoma. *N Engl J Med*. 2019;380:1450-62.
12. Harrison SA. Liver disease in patients with diabetes mellitus. *J Clin Gastroenterol*. 2006;40:68-76.
13. Younossi ZM, Golabi P, de Avila L, Paik JM, Srishord M, Fukui N, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. *J Hepatol*. 2019;71:793-801.
14. Han H, Deng H, Han T, Zhao H, Hou F, Qi X. Association between hepatocellular carcinoma and type 2 diabetes mellitus in Chinese hepatitis b virus cirrhosis patients: a case-control study. *Med Sci Monit*. 2017;23:3324-34.
15. Chan SC. Section 2. Small-for-size liver graft and hepatocellular carcinoma recurrence. *Transplantation*. 2014;97 Suppl 8:S7-S10.
16. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, et al. Obesity and the risk of primary liver cancer: A systematic review and meta-analysis. *Clin Mol Hepatol*. 2021;27:157-74.
17. Rao Kondapally Seshasai S, Kaptoge S, Thompson A, Di Angelantonio E, Gao P, Sarwar N, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. *N Engl J Med*. 2011;364:829-41.
18. Raff EJ, Kakati D, Bloomer JR, Shoreibah M, Rasheed K, Singal AK. Diabetes mellitus predicts occurrence of cirrhosis and hepatocellular cancer in alcoholic liver and non-alcoholic fatty liver diseases. *J Clin Transl Hepatol*. 2015;3:9-16.
19. Nakamura J, Kamiya H, Haneda M, Inagaki N, Tanizawa Y, Araki E, Ueki K, Nakayama T. Causes of death in Japanese patients with diabetes based on the results of a survey of 45,708 cases during 2001-2010: report of the committee on causes of death in diabetes mellitus. *J Diabetes Investig*. 2017;8:397-410.
20. Wang YG, Wang P, Wang B, Fu ZJ, Zhao WJ, Yan SL. Diabetes mellitus and poorer prognosis in hepatocellular carcinoma: a systematic review and meta-analysis. *PLoS One*. 2014;9:e95485.
21. Liu G, Xia F, Fan G, Yu J, Bao L, Zhang C, et al. Type 2 diabetes mellitus worsens the prognosis of intermediate-stage hepatocellular carcinoma after transarterial chemoembolization. *Diabetes Res Clin Pract*. 2020;169:108375.
22. Wang WM, Xu Y, Yang XR, Wang YH, Sun HX, Fan J. Prognostic role of diabetes mellitus in hepatocellular carcinoma patients after curative treatments: a meta-analysis. *Hepatobiliary Pancreat Dis Int*. 2011;10:346-55.
23. Ho SY, Yuan MH, Chen CC, Liu PH, Hsu CY, Huang YH, et al. Differential survival impact of diabetes mellitus on hepatocellular carcinoma: role of staging determinants. *Dig Dis Sci*. 2020;65:3389-402.
24. Hardy T, Oakley F, Anstee QM, Day CP. Nonalcoholic fatty liver disease: pathogenesis and disease spectrum. *Annu Rev Pathol*. 2016;11:451-96.
25. Shimada S, Mogushi K, Akiyama Y, Furuyama T, Watanabe S, Ogura T, et al. Comprehensive molecular and immunological characterization of hepatocellular carcinoma. *EBioMedicine*. 2019;40:457-70.
26. Heinrich B, Gertz EM, Schäffer AA, Craig A, Ruf B, Subramanyam V, et al. The tumour microenvironment shapes innate lymphoid cells in patients with hepatocellular carcinoma. *Gut*. 2022;71:1161-75.
27. Zhu AX, Finn RS, Edeline J, Cattani S, Ogasawara S, Palmer D, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. *Lancet Oncol*. 2018;19:940-52.
28. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *N Engl J Med*. 2020;382:1894-905.
29. Wong RJ, Chou C, Bonham CA, Concepcion W, Esquivel CO, Ahmed A. Improved survival outcomes in patients with non-alcoholic steatohepatitis and alcoholic liver disease following liver transplantation: an analysis of 2002-2012 United Network for Organ Sharing data. *Clin Transplant*. 2014;28:713-21.
30. Reddy SK, Steel JL, Chen HW, DeMateo DJ, Cardinal J, Behari J, et al. Outcomes of curative treatment for hepatocellular cancer in nonalcoholic steatohepatitis versus hepatitis C and alcoholic liver disease. *Hepatology*. 2012;55:1809-19.
31. Wong CR, Njei B, Nguyen MH, Nguyen A, Lim JK. Survival after treatment with curative intent for hepatocellular carcinoma among patients with vs without non-alcoholic fatty liver disease. *Aliment Pharmacol Ther*. 2017;46:1061-9.
32. Dare AJ, Plank LD, Phillips AR, Gane EJ, Harrison B, Orr D, et al. Additive effect of pretransplant obesity, diabetes, and cardiovascular risk factors on outcomes after liver transplantation. *Liver Transpl*. 2014;20:281-90.
33. John PR, Thuluvath PJ. Outcome of patients with new-onset diabetes mellitus after liver transplantation compared with those without diabetes mellitus. *Liver Transpl*. 2002;8:708-13.
34. Bhat V, Tazari M, Watt KD, Bhat M. New-onset diabetes and preexisting diabetes are associated with comparable reduction in long-term survival after liver transplant: a machine learning approach. *Mayo Clin Proc*. 2018;93:1794-802.
35. Peláez-Jaramillo MJ, Cárdenas-Mojica AA, Gaete PV, Mendivil CO. Post-liver transplantation diabetes mellitus: a review of relevance and approach to treatment. *Diabetes Ther*. 2018;9:521-43.

# The Role of 3D Simulation in Surgery Decision Making in Rhinoplasty Patients: A Survey-Based Study

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## Abstract

**Objective:** Three-dimensional (3D) and computerized imaging technologies are increasingly popular in the field of rhinoplasty and other esthetic surgical procedures. In this study, we evaluated the role of 3D simulated preoperative rhinoplasty images in patient decision-making.

**Methods:** We conducted this retrospective study included patients who underwent rhinoplasty between January 1, 2022 and January 1, 2023. Our clinic uses VECTRA® (H2 Handheld 3D Face, Breast, and Body Imaging System, Canfield Canfield Scientific, Parsippany, NJ, USA) imaging technology for 3D simulation. A total of 146 patients (female, 108; male, 38) participated in the study. The mean age was 30.94 years; the age range was 18-64 years. Survey: Did the results obtained using the 3D imaging program before your surgery influence your decision to undergo surgery?

**Results:** The data was collected through an online survey platform to provide ease of access and convenience for respondents. The responses were then compiled and analyzed using statistical software to identify trends and key findings. 88.4% of the patients reported that 3D imaging affected their decision to undergo surgery.

**Conclusion:** Our study suggests that 3D simulation systems will become increasingly important in surgical practice and that clinics using these systems will become more active in the future.

**Keywords:** Rhinoplasty, 3D simulation, aesthetics

## INTRODUCTION

Three-dimensional (3D) and computerized imaging technologies are increasingly popular in the field of rhinoplasty and other esthetic surgical procedures. These technologies allow for improved visualization and detailed preoperative planning, providing both surgeons and patients with a clearer understanding of potential surgical outcomes (1,2). In particular, 3D facial contouring programs provide a platform for simulating postoperative outcomes from various perspectives (1-3). In this study, we evaluated the role of 3D simulated preoperative rhinoplasty images in patient decision-making for surgery.

## METHODS

### Study Design

This retrospective study included patients who presented for rhinoplasty between January 1, 2022 and January 1, 2023. Our clinic uses VECTRA® (H2 Handheld 3D Face, Breast, and Body Imaging System, Canfield Canfield Scientific, Parsippany, NJ, USA) imaging technology for 3D simulation (Figure 1a,1c).

We applied imaging technology (Canfield Scientific, Parsippany, NJ, USA) for 3D simulation. The aim of this study was to evaluate the impact of 3D imaging simulations on the decision to undergo surgery. We surveyed the patients 1 year after surgery. We asked the patients, "Did 3D imaging affect your decision to undergo



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**Figure 1.** (a) VECTRA® imaging technology is applied for 3D simulation pre-operation simulation, (b) postoperative result after one year, (c) VECTRA® (H2 Handheld 3D Face, Breast, and Body Imaging System; Canfield)

3D: Three-dimensional

surgery?" We performed power statistical analysis. Statistical analyses were performed based on the survey responses. The study was approved by the Ondokuz Mayıs University Clinical Research Ethics Committee (approval number: 2024-475, date: 30.10.2024).

### Features and Capabilities

**High-Resolution Imaging:** The 3D system uses multiple high-resolution cameras to capture detailed images from different angles, which are then combined to create a coherent 3D model.

**Simulation Software:** This software allows surgeons to manipulate a 3D model by simulating various surgical procedures and outcomes. This step helps visualize potential changes and set realistic expectations for the patient.

**Measurement Tools:** This system includes precise measurement tools that allow surgeons to evaluate anatomical structures and plan surgery with high accuracy.

**Patient Communication:** The 3D system provides a visual representation of potential outcomes, improving communication

between the surgeon and patient, and allowing for a clear understanding of the surgical plan and expected results.

**Pre-Postoperative Comparison:** The system allows for side-by-side comparisons of preoperative simulations with actual postoperative results, thereby helping to assess surgical success and patient satisfaction.

### Participants

**Findings:** A total of 146 patients (female, 108, male, 38) participated in the study. The mean age was 30.94 years; the age range was 18-64 years.

The educational background of the patients was as follows: 66.4% university graduates, 17.8% high school graduates, 8.9% master's degree, 6% doctorate, and 1.4% primary school graduates. Participants were selected from a pool of patients who underwent rhinoplasty within the past 12 months. The inclusion criteria were: Age: Patients between 18-64 years, Gender: Male and female patients,

Health: Patients without significant comorbidities that may affect recovery or outcomes, Consent: Patients who gave informed consent to participate in the study.

**Survey Design**

The questionnaire consisted of the following sections:

**Demographic Data:**

- Gender: Male, female, do not want to specify
- Age: Numeric input
- Education status: Primary school graduate, high school graduate, university graduate, diploma, doctorate, other

**The Effect of 3D Imaging on the Decision of Surgery:**

- Did the results obtained using the 3D imaging program before your surgery affect your decision to undergo surgery?
- Yes
- No
- Other (Please specify)

**Statistical Analysis**

The data were collected through an online survey platform to provide ease of access and convenience to the respondents. The responses were then compiled and analyzed using statistical software to identify trends and key findings. 88.4% of patients reported that 3D imaging affected their decision to undergo surgery (Figure 2).

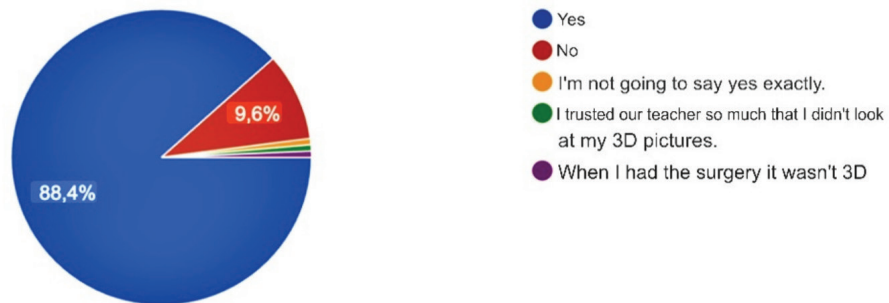
**DISCUSSION**

**Impact of 3D Imaging on Surgical Decision-Making**

The survey results indicate that 3D imaging plays an important role in the decision-making process for patients considering rhinoplasty. The vast majority of patients reported that preoperative 3D images influenced their decision to undergo surgery. These findings suggest that visualization of potential outcomes may provide reassurance and confidence, leading to patients being more likely to proceed with surgery (4,5).

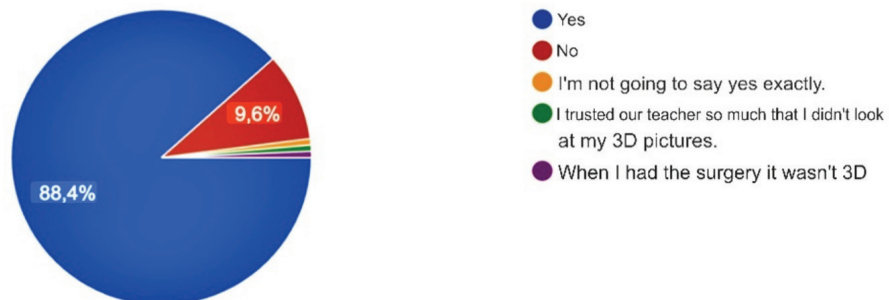
Did the results you saw with the 3D imaging program before your surgery affect your decision to have the surgery?

146 replies



Did the results you saw with the 3D imaging program before your surgery affect your decision to have the surgery?

146 replies



**Figure 2.** Did the result you saw with the 3D imaging program before your surgery affect your decision to have surgery?

3D: Three-dimensional

Our study demonstrated the significant impact of 3D imaging technologies on patient satisfaction and decision-making in rhinoplasty. 3D imaging is a reliable tool for setting realistic expectations and achieving high levels of patient satisfaction (5-7). We recommend further research with larger, more diverse populations and longer follow-up periods to confirm these findings and further enhance the integration of 3D imaging into aesthetic surgery.

Overall, the high level of satisfaction among patients who reported similar or better-than-expected results suggests that 3D imaging is a valuable tool for improving patient satisfaction (8). By providing a realistic preview of potential outcomes, patients may enter the surgery with a clearer understanding of what to expect, which may reduce anxiety and increase overall satisfaction with the results (8-10).

While the study provides valuable information, it has some limitations that should be addressed in future research. The sample size, while adequate, could be expanded to include a more diverse patient population. In addition, follow-up beyond 1 year may provide more information about the stability of results and long-term patient satisfaction.

## CONCLUSION

Our study suggests that 3D simulation systems will become increasingly important in surgical practice and that clinics using these systems will become more active in the future.

### Ethics

**Ethics Committee Approval:** The study was approved by the Ondokuz Mayıs University Clinical Research Ethics Committee (approval number: 2024-475, date: 30.10.2024).

**Informed Consent:** Patients who gave informed consent to participate in the study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: E.S., M.B.G., A.D., Concept: B.G., Design: E.S., M.B.G., A.D., Data Collection or Processing:

E.S., M.B.G., A.D., Analysis or Interpretation: E.S., M.B.G., A.D., Literature Search: B.G., Writing: E.S., M.B.G., A.D.

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

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## REFERENCES

1. Mottini M, Seyed Jafari SM, Shafiqi M, Schaller B. New approach for virtual surgical planning and mandibular reconstruction using a fibula free flap. *Oral Oncol.* 2016;59:e6-9.
2. Herrero Antón de Vez H, Herrero Jover J, Silva-Vergara C. Personalized 3D printed surgical tool for guiding the chisel during hump reduction in rhinoplasty. *Plast Reconstr Surg Glob Open.* 2018;6:e1668.
3. Mühlbauer W, Holm C. Computer imaging and surgical reality in aesthetic rhinoplasty. *Plast Reconstr Surg.* 2005;115:2098-104.
4. Mehta U, Mazhar K, Frankel AS. Accuracy of preoperative computer imaging in rhinoplasty. *Arch Facial Plast Surg.* 2010;12:394-8.
5. Moscatiello F, Herrero Jover J, González Ballester MA, Carreño Hernández E, Piombino P, Califano L. Preoperative digital three-dimensional planning for rhinoplasty. *Aesthetic Plast Surg.* 2010;34:232-8.
6. Lekakis G, Claes P, Hamilton GS 3rd, Hellings PW. Evolution of Preoperative Rhinoplasty Consult by Computer Imaging. *Facial Plast Surg.* 2016;32:80-7.
7. Singh P, Pearlman S. Use of computer imaging in rhinoplasty: A survey of the practices of facial plastic surgeons. *Aesthetic Plast Surg.* 2017;41:898-904.
8. Toriumi DM, Dixon TK. Assessment of rhinoplasty techniques by overlay of before-and-after 3D images. *Facial Plast Surg Clin North Am.* 2011;19:711-23.
9. Suszynski TM, Serra JM, Weissler JM, Amirlak B. Three-dimensional printing in rhinoplasty. *Plast Reconstr Surg.* 2018;141:1383-5.
10. Pavri S, Zhu VZ, Steinbacher DM. Postoperative edema resolution following rhinoplasty: A three-dimensional morphometric assessment. *Plast Reconstr Surg.* 2016;138:973e-9e.

# The Monitorization of the Return of Spontaneous Circulation Using Peripheral Oxygen Saturation with Near Infrared Spectroscopy in Out-of-Hospital Cardiac Arrest

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## Abstract

**Objective:** Near-infrared spectroscopy (NIRS) is frequently used to predict the return of spontaneous circulation (ROSC) and evaluate the oxygenation of organs. The aim of this study was to predict ROSC by assessing extremity oxygenation during cardiopulmonary resuscitation (CPR).

**Methods:** This prospective observational study was conducted between March 2019 and March 2020 at the emergency department (ED). The extremity and brain oxygen saturation data of patients with out-of-hospital cardiac arrest (OHCA) were collected from 66 patients aged >18 years who were transported to the ED by ambulance or by relatives due to non-traumatic OHCA. After excluding 40 patients, analysis was performed for the data of 26 patients who met the study inclusion criteria.

**Results:** The 26 patients included in the study comprised 11 males and 15 females with an average age of  $65.27 \pm 12.44$  years. ROSC was achieved in 15 patients. No statistically significant difference was found between the initial and final NIRS scores of patients without ROSC ( $p > 0.05$ ). A statistically significant difference was found between the initial and final NIRS scores at all measurement points in patients with ROSC ( $p < 0.05$ ). The initial and final NIRS values at all measurement points were significantly higher in patients with ROSC than in those without ROSC ( $p < 0.05$ ).

**Conclusion:** The return rate of spontaneous circulation was higher in patients with better extremity oxygenation and increased extremity oxygenation during CPR. Evaluating extremity oxygenation with NIRS during resuscitation can help predict ROSC in patients with OHCA.

**Keywords:** Near-infrared spectroscopy, cardiopulmonary resuscitation, return of spontaneous circulation

## INTRODUCTION

Although new guidelines on resuscitation techniques are published every 5 years and techniques are continuously improved, the survival rates of cases of out-of-hospital cardiac arrest (OHCA) are still low (1). The success of resuscitation is not only related to the return of spontaneous circulation but also to proper oxygenation of vital organs. In recent guidelines, the importance of this issue has been emphasized (2,3). Oxygenation of extremities is as important as vital organs in patients with

arrest. Recently, the use of near-infrared spectroscopy (NIRS) to evaluate the oxygenation of the brain and other organs has increased. NIRS is frequently used both for the prediction of the return of spontaneous circulation and for the evaluation of organ oxygenation (4-7). NIRS, previously used for oxygenation monitoring in cardiovascular surgery, is now used to evaluate organ oxygenation in many diseases (8-10). NIRS measures the total oxygen saturation in a specific tissue volume by approximately evaluating the hemoglobin oxygen saturation in



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the terminal vascular network of the tissues (11). This technology, which can be used to evaluate extremity oxygenation during cardiopulmonary resuscitation (CPR) and after CPR, can provide important therapeutic information by evaluating extremity perfusion or continuous monitoring. Extremities that remain hypoxic for a long time might be evidence that peripheral oxygenation is insufficient. Good oxygenation of peripheral tissues is evidence of efficient cardiopulmonary resuscitation and return of spontaneous circulation. By evaluating extremity oxygenation during CPR, the necessary precautions can be taken both during and after CPR.

The aim of this study was to predict return of spontaneous circulation (ROSC) by assessing extremity oxygenation using NIRS during CPR.

#### **Oximeters and INVOS-5100c (INVOS 5100c Covidien, Boulder, CO, USA):**

The INVOS-5100c used in this study uses continuous wave application and evaluates the scattering components of light attenuation using a light source and two detectors that are spaced close to each other. Thus, measuring the oxy and deoxy hemoglobin values can provide an absolute assessment of the ratio of total hemoglobin expressed as a percentage of tissue oxygen saturation (12-16).

The regional oxygen saturation (rSO<sub>2</sub>) value gives the percentage of oxygen saturation defined as the total oxygenation index by INVOS 5100 (Somanetics / Covidien, Mansfield, USA). NIRS monitoring also allows for the evaluation of fractional tissue oxygen extraction, which gives a measure of the amount of oxygen removed by tissue and predicts the balance between local oxygen delivery and consumption (17,18). This value represents saturation and is expressed as a percentage. In addition to personal differences, in some studies, tissue oxygenation decreases by 25% from baseline measurements are known as hypoxia indicators (19). In the current study, NIRS measurements were continuously recorded during CPR, and these measurements were evaluated in patients who did or did not obtain ROSC.

## **METHODS**

### **Study Design and Setting**

In this prospective observational study, data on extremity and brain oxygen saturation were collected from patients with OHCA. Brain and extremity oxygenation data were collected by emergency medicine specialists and were not used in any treatment protocols or therapeutic decisions. The study was conducted in University of Health Sciences Turkey, Prof. Dr.

Cemil Taşcıoğlu City Hospital Emergency Medicine Department between March 2019 and March 2020. Approval for the study was granted by the local ethics committee before the start of the study (approval number: 48670771-514.10, date: 02.04.2019). Written consent was obtained from the legal representative of each patient included in the study. All CA cases were managed according to the 2015 American Heart Association advanced life support (ALS) guidelines.

### **Participants**

The study included patients aged >18 years who were transported to the emergency department (ED) by ambulance due to non-traumatic OHCA were included in the study. Patients were excluded from the study if they had a history of vascular disease (aortic aneurysm rupture, peripheral artery disease) or received an emergency diagnosis that could affect peripheral circulation, had a lesion occupying space in the brain (tumor, hemorrhage etc.), had a cerebrovascular event, a traumatic CA, if they had a pulse on first presentation, hyperthermia or hypothermia, or if they were pregnant.

CPR was started or continued immediately after patient arrival at the ED. ALS was provided to all patients by a CPR team consisting of 4 nurses and 1 emergency medicine resident led by an emergency medicine specialist. The CPR of all patients was managed by the same emergency medicine specialist. CPR was performed on the patients until ROSC or termination of resuscitation. Patients with no return of spontaneous circulation after thirty minutes were accepted as exitus. No type of mechanical compression devices were used in any of the patients in this study. The time from the estimated arrest until reaching the hospital was recorded. Patients with an estimated arrest duration of <10 minutes were coded as 1, and those with >10 minutes were coded as 2.

### **NIRS Measurements**

Immediately after starting CPR in the ED, NIRS monitoring was started using the INVOS 5100C device. Thirty seconds is sufficient to establish NIRS measurements at all points. Resuscitation was not interrupted during monitoring. NIRS measurements were continued until ROSC or termination of CPR. Brain oxygenation was measured by selecting the frontal region, upper extremity right and left forearm flexor region radial and ulnar artery trace, and for the lower extremity, by selecting the dorsal side of both feet dorsalis pedis artery trace. Brain and extremity oxygenation was performed using the first INVOS 5100C device, and the extremity oxygenation was performed with a second device. One probe was attached to each area after proper field cleaning and continuous measurements were performed. The obtained data were recorded.

## Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn.18.00 software (SPSS, Chicago, IL, USA). Descriptive statistics were presented as frequency, percentage, mean  $\pm$  standard deviation (SD) and median, minimum, and maximum values. The Mann-Whitney U test was used to analyze differences between the measurement values of the two groups. Receiver operating characteristic (ROC) analysis was performed to calculate the sensitivity, specificity, and area under curve (AUC) values of specific variables in discriminating between ROSC and non-ROSC patients. NIRS value differences between the start and end of the CPR were calculated with this formula; [(final value - initial value)/initial value]. NIRS measurements are independent variables, and ANCOVA analysis was applied to determine factors influencing the NIRS measurements. Effect sizes were calculated using partial eta squared ( $\eta^2$ ) (0.01: small, 0.10: medium, 0.25: large) (20). A value of  $p < 0.05$  was regarded as statistically significant (20).

## RESULTS

A total of 66 patients were initially included in the study, and 40 were excluded for various reasons: 23 had hypothermia or hyperthermia, 8 were diagnosed with a cerebrovascular event, 4 were detected to have aortic dissection, and 5 were found to have metastatic brain tumor. Thus, an evaluation was made of 26 patients with OHCA, including 11 males and 15 females, with a mean age of  $65.27 \pm 12.44$  years. Diabetes mellitus, hypertension, and ischemic heart disease were detected in 9 patients. The initial rhythms on admission to ED were determined as asystole in 14 (53.8%), Pulseless electrical activity in 4 (15.4%), and ventricular fibrillation in 8 (30.8%) patients. ROSC was achieved in 15 patients (Table 1).

Pre-hospital arrest duration was statistically significantly shorter, and the pH levels were significantly higher in patients with ROSC than in those without ROSC. No statistically significant differences were detected between patients with and without ROSC in terms of age, CPR duration, and laboratory values, such as glucose, urea, creatinine, sodium, potassium, ALT, AST,  $PO_2$ ,  $PCO_2$ , lactate, and hemoglobin values (Table 2).

In patients without ROSC, no significant difference was observed between the initial and final NIRS scores at all measurement points ( $p > 0.05$ ) (Table 3). In patients without ROSC, the mean  $rSO_2$  value in the right brain at the beginning of CPR was  $17.18 \pm 5.34\%$  (Q1-Q3 = 15-15) and  $18.82 \pm 8.68\%$  (Q1-Q3 = 18.82-8.68) at the end. There was no statistical relationship between these values. The mean initial  $rSO_2$  value in the left brain was  $16.55 \pm 4.5\%$  (Q1-Q3

= 15-15) and the final value was  $18.09 \pm 6.93\%$  (Q1-Q3 = 18.09-6.93) ( $p > 0.05$ ). The  $rSO_2$  values at the beginning of the right upper extremity was  $18.82 \pm 8.61\%$  and  $21.36 \pm 10.41\%$  at the end, and there was no statistically significant difference between the values ( $p > 0.05$ ). The  $rSO_2$  value at the beginning of the left upper extremity was  $18.18 \pm 7.83\%$  and at the end was  $20.36 \pm 9.46\%$ , and there was no statistically significant difference ( $p > 0.05$ ). The  $rSO_2$  values at the beginning of the right lower extremity was  $22.09 \pm 8.42\%$  and  $22.82 \pm 9.47\%$  at the end, and there was no statistically significant difference ( $p > 0.05$ ). The  $rSO_2$  values at the beginning of the left lower extremity was  $22.36 \pm 8.98\%$  and  $22.18 \pm 8.76\%$  at the end of the experiment, and there was no statistically significant difference ( $p > 0.05$ ).

In patients with ROSC, a statistically significant difference was found in the initial and final NIRS scores at all measurement points ( $p = 0.000$ ) (Table 4). In patients with ROSC, the  $rSO_2$  value in the right brain at the beginning of CPR was  $20.73 \pm 8.59\%$ , and the  $rSO_2$  value at the end was  $53.4 \pm 11.44\%$ . There was a statistically significant difference between these values. The left brain  $rSO_2$  value at the beginning was  $21 \pm 8.91\%$  and the final value was  $54.33 \pm 12.31\%$ . ( $p = 0.000$ ). The  $rSO_2$  values at the beginning of the right upper extremity was  $23.2 \pm 14.14\%$  and  $48.8 \pm 13.03\%$  at the end of the study period, and the difference was statistically significant ( $p = 0.000$ ). The  $rSO_2$  values at the beginning of the left upper extremity was  $22.4 \pm 13.98\%$  and  $46.2 \pm 11.12\%$  at the end, with a statistically significant difference ( $p = 0.000$ ). The  $rSO_2$  values at the beginning of the right lower extremity was  $23.6 \pm 13.53\%$  and  $45.87 \pm 12.05\%$  at the end of the study period, and the difference was statistically significant ( $p = 0.000$ ). The  $rSO_2$  values at the beginning of the left lower extremity was  $23.4 \pm 13.21\%$  and  $48.2 \pm 11.73\%$  at the end of the study period, and the difference was statistically significant ( $p = 0.000$ ).

Table 1. Patient characteristics		
	n	%
Age (Mean + SD)	65.27 $\pm$ 12.44	
Male gender	15/26	57.70
Initial rhythm		
Asystole	14/26	53.8
Pulseless electrical activity	4/26	15.4
Ventricular fibrillation	8/26	30.8
Diabetes mellitus	9/26	34.6
Hypertension	9/26	34.6
Coronary artery disease	9/26	34.6
Return of spontaneous circulation (+)	15/26	57.7
SD: Standard deviation		

**Table 2. Laboratory parameters and others**

Variables		All patients	ROSC		p
			(+)	(-)	
		Mean ± SD	Mean ± SD	Mean ± SD	
Glucose	mg/dL	272.04±151.85	237.27±151.06	319.45±146.32	0.178
Urea	mg/dL	72.46±45.07	65.67±40.63	81.73±51.03	0.483
Creatinine	mg/dL	1.71±1.48	1.77±1.87	1.63±0.74	0.378
Sodium	mmol/L	138.92±11.36	139.53±14.38	138.09±5.65	0.639
Potassium	mmol/L	5.60±1.42	5.53±1.46	5.69±1.43	0.783
Alanine aminotransferase	U/L	99.58±144.08	89.07±161.72	113.91±122.01	0.337
Aspartate aminotransferase	U/L	172.96±246.26	160.07±255.52	190.55±244.17	0.836
PO <sub>2</sub>	mmHg	80.82±81.81	105.14±95.47	47.65±43.30	0.092
PCO <sub>2</sub>	mmHg	49.32±18.86	45.96±16.01	53.91±22.14	0.364
pH		7.05±0.16	7.10±0.16	6.97±0.14	<b>0.043</b>
Lactate	mmol/L	9.47±3.61	9.32±3.26	9.69±4.19	0.803
Hemoglobin	g/L	10.77±3.47	10.77±3.88	10.76±3.01	0.659
Prehospital arrest duration	code	1.54±0.51	1.33±0.49	1.82±0.40	<b>0.016</b>
Age	year	65.27±13.40	63.53±14.23	67.64±12.44	0.452
CPR duration	min.	28.65±11.10	25.67±13.07	32.73±6.07	0.151

ROSC: Return of spontaneous circulation, PO<sub>2</sub>: Partial oxygen pressure, PCO<sub>2</sub>: Partial carbon dioxide pressure, CPR: Cardiopulmonary resuscitation, pH: Power of hydrogen, Min: Minutes, SD: Standard deviation

**Table 3. NIRS values in patients without ROSC**

	Patients without ROSC				
	Values at the start of CPR		Values at the end of CPR		p
	Mean ± SD	Median (Q1-Q3)	Mean ± SD	Median (Q1-Q3)	
Right brain (%)	17.18±5.34	15 (15-15)	18.82±8.68	15 (18.82-8.68)	0.317
Left brain (%)	16.55±4.5	15 (15-15)	18.09±6.93	15 (18.09-6.93)	0.18
Right upper extremity (%)	18.82±8.61	15 (15-16)	21.36±10.41	16 (21.36-10.41)	0.068
Left upper extremity (%)	18.18±7.83	15 (15-15)	20.36± 9.46	15 (20.36-9.46)	0.109
Right lower extremity (%)	22.09±8.42	15 (15-31)	22.82±9.47	31 (22.82-9.47)	0.2
Left lower extremity (%)	22.36±8.98	15 (15-30)	22.18±8.76	30 (22.18-8.76)	0.581

NIRS: Near-infrared spectroscopy, CPR: Cardiopulmonary resuscitation, ROSC: Return of spontaneous circulation, SD: Standard deviation

**Table 4. NIRS values in patients with ROSC**

	Patients with ROSC				
	Values at the start of CPR		Values at the end of CPR		p
	Mean ± SD	Median (Q1-Q3)	Mean ± SD	Median (Q1-Q3)	
Right brain (%)	20.73±8.59	15 (15-25)	53.4±11.44	53 (46-62)	<b>0.001</b>
Left brain (%)	21±8.91	15 (15-28)	54.33±12.31	53 (44-60)	<b>0.001</b>
Right upper extremity (%)	23.2±14.14	15 (15-24)	48.8±13.03	48 (40-59)	<b>0.001</b>
Left upper extremity (%)	22.4±13.98	15 (15-22)	46.2±11.12	47 (40-58)	<b>0.001</b>
Right lower extremity (%)	23.6±13.53	15 (15-31)	45.87±12.05	50 (37-54)	<b>0.001</b>
Left lower extremity (%)	23.4±13.21	15 (15-30)	48.2±11.73	51 (39-57)	<b>0.001</b>

CPR: Cardiopulmonary resuscitation, ROSC: Return of spontaneous circulation, SD: Standard deviation

In addition, the difference between the initial and final NIRS measurement values of patients with and without ROSC was determined at all measurement points. These differences were found to be statistically significantly higher in patients with ROSC than in those without ROSC ( $p=0.000$ ) (Table 5). The possibility of ROSC was found to be increased when an increase of more than 13.3% was achieved in the left-brain region measurement values. (specificity 90.91%, sensitivity 100%, AUC=0.988). When the same situation was evaluated for the right brain, a 32% increase was sufficient to determine the ROSC (specificity: 90.91%, sensitivity: 93.33%, AUC: 0.988). The specificity was 90.91%, sensitivity was 86.67%, and AUC was 0.931 in determining ROSC in individuals with an increase of 26.6% in the measurement values in the right upper extremity. The specificity was 81.82%, sensitivity was 100%, and AUC was 0.952 for determining ROSC in those with an increase of 6.66% in the measurement values in the left upper extremity. The specificity was 100%, sensitivity was 73.33%, and the AUC was 0.936 for determining ROSC in those with an increase of 37% in the measurement values in the right lower extremity. The specificity was 100%, sensitivity was 100%, and the AUC was 1.000 for determining ROSC in those with an increase of 6.6% in the measurement values in the left lower extremity (Figure 1).

When the main effects explaining the final value of the left brain NIRS result were evaluated, the main effects of duration of arrest ( $F(1,21)=0.56$ , ns,  $\eta^2=0.026$ ) and pH ( $F(1,21)=0.02$ , ns,  $\eta^2=0.001$ ) was not statistically significant. When corrected for baseline left brain measurement, the correction factor was significant ( $F(1,21)=9.20$ ,  $p=0.006$ ,  $\eta^2=0.305$ ) and the main effect of ROSC ( $F(1,21)=49.04$ ,  $p<0.001$ ,  $\eta^2=0.7$ ) was found to be significant in the model.

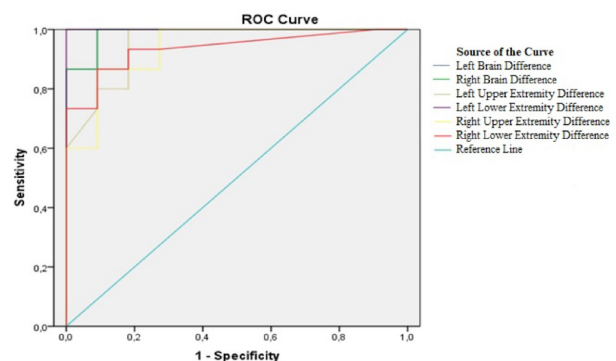
When the main effects explaining the final value of the right brain NIRS result were evaluated, the main effects of duration of arrest ( $F(1,21)=1.19$ , ns,  $\eta^2=0.054$ ) and pH ( $F(1,21)=0.24$ , ns,  $\eta^2=0.011$ ) was not statistically significant. When corrected for baseline right brain measurement, the correction factor was

significant ( $F(1,21)=9.20$ ,  $p=0.006$ ,  $\eta^2=0.305$ ) and the main effect of ROSC ( $F(1,21)=49.04$ ,  $p<0.001$ ,  $\eta^2=0.7$ ) was found to be significant in the model.

When the main effects explaining the final value of the left upper extremity NIRS result were evaluated, the main effects of duration of arrest ( $F(1,21)=1.49$ , ns,  $\eta^2=0.066$ ) and pH ( $F(1,21)=0.13$ , ns,  $\eta^2=0.006$ ) was not statistically significant. When corrected for baseline left upper extremity measurement, the correction factor was significant ( $F(1,21)=9.99$ ,  $p=0.005$ ,  $\eta^2=0.322$ ) and the main effect of ROSC ( $F(1,21)=23.67$ ,  $p<0.001$ ,  $\eta^2=0.530$ ) was found to be significant in the model.

When the main effects explaining the final value of the left lower extremity NIRS result were evaluated, the main effects of duration of arrest ( $F(1,21)=0.023$ , ns,  $\eta^2=0.001$ ) and pH ( $F(1,21)=0.02$ , ns,  $\eta^2=0.012$ ) was not statistically significant. When corrected for baseline left lower extremity measurement, the correction factor was significant ( $F(1,21)=9.19$ ,  $p=0.006$ ,  $\eta^2=0.304$ ) and the main effect of ROSC ( $F(1,21)=26.11$ ,  $p<0.001$ ,  $\eta^2=0.554$ ) was found to be significant in the model.

When the main effects explaining the final value of the right upper extremity NIRS result were evaluated, the main effects



**Figure 1.** ROC analysis of the differences in the measurements of all regions  
ROC: Receiver operating characteristic

Table 5. NIRS value differences in patients with and without ROSC					
NIRS value differences	Patients without ROSC		Patients with ROSC		p
	Mean ± SD	Median (Q1-Q3)	Mean ± SD	Median (Q1-Q3)	
Left brain	0.08±0.23	0 (0-0)	1.84±0.84	1.93 (1.16-2.53)	0.000
Right brain	0.07±0.25	0 (0-0)	1.82±0.85	1.83 (1.07-2.53)	0.000
Right upper extremity	0.14±0.32	0 (0-0.19)	1.54±1.14	1.38 (0.59-2.6)	0.000
Left upper extremity	0.12±0.26	0 (0-0.07)	1.47±0.99	1.67 (0.68-2.2)	0.000
Right lower extremity	0.02±0.05	0	1.32±1.03	1.47 (0.13-2.53)	0.000
Left lower extremity	-0.01±0.04	0 (0-0)	1.45±1.05	1.47 (0.6-2.53)	0.000

NIRS: Near-infrared spectroscopy, CPR: Cardiopulmonary resuscitation, ROSC: Return of spontaneous circulation, SD: Standard deviation



of duration of arrest ( $F(1,21)=2.273$ , ns,  $\eta^2=0.098$ ) and pH ( $F(1,21)=0.11$ , ns,  $\eta^2=0.005$ ) was not statistically significant. When corrected for baseline right upper extremity measurement, the correction factor was significant ( $F(1,21)=6.04$ ,  $p=0.023$ ,  $\eta^2=0.223$ ) and the main effect of ROSC ( $F(1,21)=17.26$ ,  $p<0.001$ ,  $\eta^2=0.451$ ) was found to be significant in the model.

When the main effects explaining the final value of the right lower extremity NIRS result were evaluated, the main effects of duration of arrest ( $F(1,21)=0.57$ , ns,  $\eta^2=0.026$ ) and pH ( $F(1,21)=0.01$ , ns,  $\eta^2=0.000$ ) was not statistically significant. When corrected for baseline right lower extremity measurement,

the correction factor was significant ( $F(1,21)=5.97$ ,  $p=0.024$ ,  $\eta^2=0.221$ ) and the main effect of ROSC ( $F(1,21)=15.57$ ,  $p<0.001$ ,  $\eta^2=0.426$ ) was found to be significant in the model (Table 6).

## DISCUSSION

The results of this study of patients with OHCA demonstrated that the ROSC rate was higher in patients with high extremity oxygenation than in patients with lower extremity oxygenation levels. Patients with lower extremity oxygenation cannot regain spontaneous circulation. A good correlation was also observed between extremity and cerebral saturation in patients with

**Table 6. ANOVA analyzes to identify factors affecting NIRS measurements**

		F	p	$\eta^2$	$\eta^2p$
Final value of left brain	ROSC	49.0398	<0.001	0.614	0.700
	Initial value of left brain	9.2035	697.78	0.115	0.305
	Arrest time	0.5647	42.81	0.007	0.026
	pH	0.0170	1.29	0.000	0.001
	Residuals		75.82		
Final value of right brain	ROSC	40.354	<0.001	0.587	0.658
	Initial value of right brain	5.946	0.024	0.087	0.221
	Arrest time	1.191	0.288	0.017	0.054
	pH	0.244	0.627	0.004	0.011
	Residuals				
Final value of left upper extremity	ROSC	23.673	<0.001	0.421	0.530
	Initial value of left upper extremity	9.992	0.005	0.178	0.322
	Arrest time	1.495	0.235	0.027	0.066
	pH	0.130	0.722	0.002	0.006
	Residuals				
Final value of left lower extremity	ROSC	26.1102	<0.001	0.461	0.554
	Initial value of left lower extremity	9.1892	0.006	0.162	0.304
	Arrest time	0.0231	0.881	0.000	0.001
	pH	0.2575	0.617	0.005	0.012
	Residuals				
Final value of right upper extremity	ROSC	17.259	<0.001	0.370	0.451
	Initial value of right upper extremity	6.038	0.023	0.129	0.223
	Arrest time	2.273	0.147	0.049	0.098
	pH	0.109	0.745	0.002	0.005
	Residuals				
Final value of right lower extremity	ROSC	15.5670	<0.001	0.361	0.462
	Initial value of right lower extremity	5.9670	0.024	0.138	0.221
	Arrest time	0.5674	0.460	0.013	0.026
	pH	0.0104	0.920	0.000	0.000
	Residuals				

NIRS: Near-infrared spectroscopy, ROSC: Return of spontaneous circulation

OHCA with and without ROSC. Based on these results, extremity saturation measurements can be an indication of ROSC. This is the first study to evaluate extremity oxygenation during CPR using a non-invasive technique. There are studies in the literature that have frequently evaluated brain oxygenation during CPR, and only one study has evaluated abdominal oxygenation (11,16,21-26). Although there are studies evaluating extremity oxygenation with NIRS in various diseases, no studies have evaluated this during CPR (27-29).

In a study conducted in the intensive care unit, the relationship between peripheral oxygenation and mortality was evaluated in patients with multiple organ failure. Shapiro et al. (30) evaluated 3 groups in their studies. The first group included patients with septic shock with systolic blood pressure <90 mmHg despite adequate fluid resuscitation, the second group included patients who only had sepsis, and the third group included patients without infections who were checked in through the emergency room. In all patients, measurements were made using NIRS from the thenar region. The measurements were evaluated before and after the venous occlusion created using a tourniquet. It has been reported that patients with septic shock who have poor peripheral circulation and whose oxygen saturation does not increase rapidly after removal of venous occlusion mostly develop organ failure. As a result of that study, it was stated that patients with rapid reperfusion after ischemia have better organ perfusion. Thus, it was concluded that in critical patients, extremity oxygenation would be a good method for evaluating the perfusion of other organs (30). The results of the current study support these findings. Patients with high peripheral oxygenation on admission, which continued to rise during CPR, were more likely to return to spontaneous circulation. This finding can be attributed to the fact that patients with peripheral circulation will also have good oxygenation in the brain and other vital organs.

A study by Payen et al. (31) also supported the results of the current study. In that study, Payen et al. (31) compared the peripheral circulation of patients with septic shock with that of healthy individuals. In patients who underwent the venous occlusion test at the brachial artery level, macrohemodynamic (systolic blood pressure, cardiac output, pulmonary artery catheterization) and microhemodynamic (lactate, pH, and base deficit) parameters and peripheral tissue oxygenations assessed by NIRS were compared in the assessment of tissue oxygenation at a cellular level. According to the results of that study, relationships were found between NIRS measurements and all of these parameters. Specifically, peripheral oxygenation

was detected to be lower in the NIRS group than in the healthy control group. The mortality of patients with poor reperfusion after the venous occlusion test was found to be higher. NIRS measurements were detected to be lower in patients with low blood pH and high lactate. It has been argued that using both micro and macrohemodynamic parameters with peripheral oxygen saturation monitoring would be beneficial for the prediction of patient mortality (31). In the current study, although no relationship was determined between macro and micro hemodynamic parameters and ROSC, a direct relationship with the arrest duration was found. ROSC rates were lower in patients who had more than 10 minutes of arrest duration. As the CA duration increases, there can be expected to be a variation in bioindicators such as serum pH and lactate, which are hypoxia indicators. Although this finding was not statistically significant, many of the current study patients who did not have ROSC had low blood pH and high blood lactate levels.

Many studies using NIRS to detect ROSC have focused on brain oxygenation. In a study previously conducted by the authors, abdominal oxygenation was also evaluated. These studies evaluated the oxygenation of vital organs. The results of these studies demonstrate that patients with increased brain and abdominal oxygen saturation have a better chance of ROSC. The current study considered that peripheral tissue oxygenation is at least as valuable as the oxygenation of the brain and abdominal organs. Similar to previous studies, the results illustrated that patients with increased peripheral tissue oxygenation achieved return of spontaneous circulation.

### Study Limitations

The most important limitation of this study was the limited number of patients. Further studies with a broader patient population will most likely support these results. In this study, extremity oxygenation was measured during CPR, and the lowest values on admission and the highest measurement values at the endpoint of CPR were obtained. Long-term measurements were not performed after ROSC. Long-term extremity oxygenation monitoring in patients who were hospitalized in intensive care may also provide different information. These measurements were not compared with healthy individuals or methods proven to predict ROSC. Long-term measurements may be useful in predicting both mortality and ischemia in other vital organs in patients admitted to the intensive care unit. The lack of a mechanical compression device was another limitation of the study. Although CPR standardization was achieved by our team, studies using compression devices are necessary.

## CONCLUSION

Evaluating extremity oxygenation with NIRS during resuscitation can help predict ROSC in patients with OHCA. The return rate of spontaneous circulation was higher in patients with initially better extremity oxygenation and an increase in extremity oxygenation during CPR.

### Ethics

**Ethics Committee Approval:** The study was conducted in University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital Emergency Medicine Department between March 2019 and March 2020. Approval for the study was granted by the local ethics committee before the start of the study (approval number: 48670771-514.10, date: 02.04.2019).

**Informed Consent:** Written consent was obtained from the legal representative of each patient included in the study.

### Footnotes

#### Authorship Contributions

Concept: H.K., A.K., Design: H.K., A.K., Data Collection or Processing: H.K., Ö.B., M.Ş., S.Ü., Analysis or Interpretation: H.A., Ş.E.A., Literature Search: H.K., A.K., B.M.A., A.D., Writing: H.K., A.K., Ö.B., S.Ü.

**Conflict of Interest:** Asım Kalkan, MD, is a Section Editor in the European Archives of Medical Research. He had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Other authors have nothing to disclose.

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## REFERENCES

- Myat A, Song KJ, Rea T. Out-of-hospital cardiac arrest: current concepts. *Lancet*. 2018;391:970-9.
- Hassager C, Nagao K, Hildick-Smith D. Out-of-hospital cardiac arrest: in-hospital intervention strategies. *Lancet*. 2018;391:989-98.
- Berg KM, Cheng A, Panchal AR, Topjian AA, Aziz K, Bhanji F, et al. Part 7: Systems of Care: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2020;142:S580-604.
- Takegawa R, Hayashida K, Rolston DM, Li T, Miyara SJ, Ohnishi M, et al. Near-infrared spectroscopy assessments of regional cerebral oxygen saturation for the prediction of clinical outcomes in patients with cardiac arrest: A review of clinical impact, evolution, and future directions. *Front Med (Lausanne)*. 2020;7:587930.
- Asim K, Gokhan E, Ozlem B, Ozcan Y, Deniz O, Kamil K, et al. Near infrared spectrophotometry (cerebral oximetry) in predicting the return of spontaneous circulation in out-of-hospital cardiac arrest. *Am J Emerg Med*. 2014;32:14-7.
- Sakaki K, Kitamura T, Kohira S, Torii S, Mishima T, Hanayama N, et al. Regional thigh tissue oxygen saturation during cardiopulmonary bypass predicts acute kidney injury after cardiac surgery. *J Artif Organs*. 2020;23:315-20.
- Asim K, Ozlem B, Gokhan E, Zihni Y, Deniz O, Mahmut T, et al. The use of cerebral oximetry in acute carbon monoxide intoxication: A preliminary study. *Keio J Med*. 2015;64:57-61.
- Westgarth-Taylor C, de Lijster L, van Bogaerijen G, Millar AJ, Karpelowsky J. A prospective assessment of renal oxygenation in children undergoing laparoscopy using near-infrared spectroscopy. *Surg Endosc*. 2013;33:609-12.
- Gillam-Krakauer M, Cochran CM, Slaughter JC, Polavarapu S, McElroy SJ, Hernanz-Schulman M, et al. Correlation of abdominal rSO<sub>2</sub> with superior mesenteric artery velocities in preterm infants. *J Perinatol*. 2013 Aug;33(8):609-12.
- Kaufman J, Almodovar MC, Zuk J, Friesen RH. Correlation of abdominal site near-infrared spectroscopy with gastric tonometry in infants following surgery for congenital heart disease. *Pediatr Crit Care Med*. 2008;9:62-8.
- Meex I, De Deyne C, Dens J, Scheyltjens S, Lathouwers K, Boer W, et al. Feasibility of absolute cerebral tissue oxygen saturation during cardiopulmonary resuscitation. *Crit Care*. 2013;17:R36.
- Torricelli A, Contini D, Dalla Mora A, Pifferi A, Re R, Zucchelli L, et al. Neurophotonics: non-invasive optical techniques for monitoring brain functions. *Funct Neurol*. 2014;29:223-30.
- Ferrari M, Quaresima V. A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application. *Neuroimage*. 2012;63:921-35.
- Meng L, Gelb AW, Alexander BS, Cerussi AE, Tromberg BJ, Yu Z, Mantulin WW. Impact of phenylephrine administration on cerebral tissue oxygen saturation and blood volume is modulated by carbon dioxide in anaesthetized patients. *Br J Anaesth*. 2012;108:815-22.
- Meng L, Cannesson M, Alexander BS, Yu Z, Kain ZN, Cerussi AE, et al. Effect of phenylephrine and ephedrine bolus treatment on cerebral oxygenation in anaesthetized patients. *Br J Anaesth*. 2011;107:209-17.
- Kalkan A, Bilir O, Ersunan G, Ozel D, Tas M, Memetoglu ME. Abdominal oxygen saturation for monitoring return of spontaneous circulation in out-of-hospital cardiac arrest using near infrared spectrophotometry. *Am J Emerg Med*. 2015;33:344-8.
- da Costa CS, Greisen G, Austin T. Is near-infrared spectroscopy clinically useful in the preterm infant? *Arch Dis Child Fetal Neonatal Ed*. 2015;100:F558-61.
- Naulaers G, Meyns B, Miserez M, Leunens V, Van Huffel S, Casaer P, et al. Use of tissue oxygenation index and fractional tissue oxygen extraction as non-invasive parameters for cerebral oxygenation. A validation study in piglets. *Neonatology*. 2007;92:120-6.
- Edmonds HL Jr, Ganzel BL, Austin EH 3rd. Cerebral oximetry for cardiac and vascular surgery. *Semin Cardiothorac Vasc Anesth*. 2004;8:147-66.
- Cohen J. *Statistical power analysis for the behavioral sciences*. 2nd ed. New York: Routledge; 2013.
- Fellahi JL, Butin G, Fischer MO, Zamparini G, Gérard JL, Hanouz JL. Dynamic evaluation of near-infrared peripheral oximetry in healthy volunteers: a comparison between INVOS and EQUANOX. *J Crit Care*. 2013;28:881.
- Genbrugge C, Dens J, Meex I, Boer W, Eertmans W, Sabbe M, et al. Regional cerebral oximetry during cardiopulmonary resuscitation: Useful or useless? *J Emerg Med*. 2016;50:198-207.

23. Frisch A, Suffoletto BP, Frank R, Martin-Gill C, Menegazzi JJ. Potential utility of near-infrared spectroscopy in out-of-hospital cardiac arrest: an illustrative case series. *Prehosp Emerg Care*. 2012;16:564-70.
24. Ahn A, Yang J, Inigo-Santiago L, Parnia S. A feasibility study of cerebral oximetry monitoring during the post-resuscitation period in comatose patients following cardiac arrest. *Resuscitation*. 2014;85:522-6.
25. Schewe JC, Thudium MO, Kappler J, Steinhagen F, Eichhorn L, Erdfelder F, et al. Monitoring of cerebral oxygen saturation during resuscitation in out-of-hospital cardiac arrest: a feasibility study in a physician staffed emergency medical system. *Scand J Trauma Resusc Emerg Med*. 2014;22:58.
26. Al-Subu AM, Hacker TA, Eickhoff JC, Ofori-Amanfo G, Eldridge MW. Two-site regional oxygen saturation and capnography monitoring during resuscitation after cardiac arrest in a swine pediatric ventricular fibrillatory arrest model. *J Clin Monit Comput*. 2020;34:63-70.
27. Scholkmann F, Scherer-Vrana A. Comparison of two NIRS tissue oximeters (Moxy and Nimo) for non-invasive assessment of muscle oxygenation and perfusion. *Adv Exp Med Biol*. 2020;1232:253-9.
28. Höller N, Urlesberger B, Mileder L, Baik N, Schwabegger B, Pichler G. Peripheral muscle near-infrared spectroscopy in neonates: Ready for clinical use? A systematic qualitative review of the literature. *Neonatology*. 2015;108:233-45.
29. Ding H, Wang G, Lei W, Wang R, Huang L, Xia Q, Wu J. Non-invasive quantitative assessment of oxidative metabolism in quadriceps muscles by near infrared spectroscopy. *Br J Sports Med*. 2001;35:441-4.
30. Shapiro NI, Arnold R, Sherwin R, O'Connor J, Najarro G, Singh S, et al. The association of near-infrared spectroscopy-derived tissue oxygenation measurements with sepsis syndromes, organ dysfunction and mortality in emergency department patients with sepsis. *Crit Care*. 2011;15:R223.
31. Payen D, Luengo C, Heyer L, Resche-Rigon M, Kerever S, Damoiseil C, et al. Is thenar tissue hemoglobin oxygen saturation in septic shock related to macrohemodynamic variables and outcome? *Crit Care*. 2009;13 Suppl 5:S6.

# Developing A Fast Computer Vision Model for Diagnosing and Classifying Hip Fractures

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## Abstract

**Objective:** The primary aim of this study was to refine the accuracy and efficiency of hip fracture detection using a new computer vision model based on the YOLOv8 algorithm, thereby addressing the current limitations in diagnostic methodologies and improving dataset constraints.

**Methods:** We conducted a retrospective study using anterior-posterior (AP) hip radiographs collected from adult patients at University of Health Sciences Turkey, Şişli Hamidiye Etfal and University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital between January 2021 and January 2023. A total of 676 radiographs were analyzed after applying classifications according to the AO/OTA system by orthopedic specialists. The dataset was divided into training, validation, and testing sets, and image augmentations were applied to enhance model training.

**Results:** The YOLOv8 model achieved a mean Average Precision at 0.5 IOU (mAP50) of 0.877 at the 99<sup>th</sup> epoch, demonstrating high diagnostic accuracy with a precision rate of 0.891 and recall of 0.797. These metrics indicate the model's effectiveness in accurately detecting and classifying hip fractures.

**Conclusion:** This study presents a significant enhancement in the use of artificial intelligence for medical imaging, particularly in detecting and classifying hip fractures, thereby demonstrating the potential of AI to augment clinical decision-making. Further studies are recommended to expand the application scope and improve the model's accuracy in various clinical environments.

**Keywords:** Hip fractures, artificial intelligence, image processing, computer-assisted, deep learning

## INTRODUCTION

In emergency services, diagnosis of fractures is important for guiding appropriate treatment to optimize patient outcomes. A missed diagnosis of either overuse or underuse of imaging techniques poses great risks. In addition to overuse, which wastes healthcare resources, these patients will be exposed to radiation for no necessary reason, whereas underuse may result in missed diagnosis. Misdiagnosis may result in delayed or inappropriate treatment, leading to negative impact on recovery time, increased healthcare costs, and, most importantly, potential harm to patients (1,2). These issues become all the more critical

in musculoskeletal injuries, where proper imaging forms the cornerstone for effective clinical decision-making. Some of the most significant disadvantages of traditional X-ray radiographs for diagnosis of fractures are image quality, angle, and clarity problems inherent in the emergency situation, which may render the situation indecipherable to human eyes regarding whether a fracture has occurred. Fracture classification is a necessary tool for clinicians because first, there is now a common language with which to describe the type, location, and severity of a fracture. This not only facilitates clinical communications, but also supports research by allowing consistent comparisons



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of treatment outcomes (3-5). Artificial intelligence (AI) is being inevitably deployed nearly every field of study, and medicine is not an exception. In the research area of diagnostic medicine, AI has held a huge promise, hence boosting accuracy, especially through computer vision techniques (6,7). However, models developed to this date achieve variable successes when applied to the field of fracture detection. Several studies have explored AI applications for automated medical image analysis, including fracture detection. However, most of these models have limiting factors: either they lack sufficient accuracy, especially for complex fractures, or large, high-quality public datasets that can be used for training more powerful models are not available. The present study aimed to address these gaps by developing a computer-vision-based model capable of diagnosing and classifying hip fractures from radiological images. The present research is based on previous studies, narrowing its focus to problems concerning hip fracture detection, a critical and complex area of orthopedic care. By creating a labeled dataset of radiological images and leveraging the YOLOv8 algorithm, a state-of-the-art object detection method, this study aims to improve both the accuracy and efficiency of fracture diagnosis in clinical settings. Our contributions will provide not only a practical tool for clinicians but also a dataset and methodology that can be further utilized by researchers in the field.

## METHODS

### Study Design

This retrospective study collected AP hip radiographs obtained from adult patients who presented to the University of Health Sciences Turkey, Şişli Hamidiye Etfal and University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital emergency department between January 2021 and January 2023. Ethical approval for the study was obtained from the University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Non-Interventional Research Ethics Committee (approval number: 252, date: 13.12.2023). Ethical approval for this study was obtained before data collection and was conducted

in adherence to institutional and national guidelines for the purpose of maintaining patient confidentiality and protection.

### Data Sets

The dataset consisted of 748 AP hip radiographs. During data pre-processing, 72 radiographs were excluded due to visual obstruction of the image, either by the presence of a patient's hand or any foreign object, such as keys or coins. A total of 676 hip radiographs were included in the study (Figure 1). Specific exclusions for "visible pollution" were developed in an attempt to make the exclusion process more standardized and include cases with visible extra-hip body parts, objects external to the patient, or where fracture visibility was unclear. The remaining images were then resized to 640x640 pixels using bilinear interpolation to retain the quality of the images during model training. Image quality after resizing was verified to ensure that the main diagnostic features, including bone structures and fracture lines, remained clear. Radiographs were then classified according to the AO/OTA classification system by two orthopedic specialists with 10 and 5 years of experience.

### Fracture Labeling

Regions of interest in anterior-posterior (AP) hip radiographs were manually annotated using image annotation software. Fractures were labeled using the AO/OTA classification system, with classes represented as,

1. Normal (no fracture),
2. 31-B (femoral neck fracture),
3. 31-A1 (femoral simple pertrochanteric fracture),
4. 31-A2 (femoral multifragmentary pertrochanteric fracture),
5. 31-A3 (femoral intertrochanteric fracture) (Figure 2).

The orthopedic surgeons who evaluated the images classified all images, and any disagreements were resolved by expert consensus meetings. Ultimately, the same results were obtained in all evaluations. The final number of radiographs analyzed in this dataset was 676 and was divided into 300 normal hips, 110



Figure 1. Distribution of graphs used in the study (Roboflow, Inc., <https://roboflow.com/>)

femoral neck fractures (31-B), 133 femoral simple pertrochanteric fracture (31-A1), 68 femoral multifragmentary pertrochanteric fracture (31-A2), and 65 femoral intertrochanteric fractures (31-A3). The dataset was divided into three sets: 70% training, 20% validation, and 10% testing.

### Augmented Images

Image augmentation increased the training set from 473 to 2365 images by applying transformations such as mirror horizontally (image flipped horizontally to simulate variation in patient positioning), rotation (images were rotated randomly between -15° and +15° to introduce minor variations in position for the radiographs), blur (this involved the use of up to 1.25 pixels of random blurring to simulate motion or low-quality differences in image capturing equipment), noise (random noise, up to 6% of the image, was added to simulate real variability in radiographs), exposure (the exposure values were randomly changed to vary between -16% and +16% to simulate different lighting conditions



**Figure 2.** Labelling of the graphs used in our study (Roboflow, Inc., <https://roboflow.com/>)

at the time of radiography). These augmentations were considered to reflect clinically relevant variations to improve the generalizability of the model to different clinical scenarios.

### Statistical Analysis

The YOLOv8 algorithm from Ultralytics was used to develop a computer vision model for hip fracture detection. The parameters used during training were Learning rate 0.001, Batch size auto, and epoch number 100 (Figure 3). YOLOv8 is known for its efficient real-time object detection and segmentation capabilities, which make it ideal for medical image analysis tasks. The use of YOLOv8 enabled the localization and classification of fractures. The performance of the model was measured in terms of accuracy, sensitivity, and specificity.

## RESULTS

The mean Average Precision at 0.5 IOU (mAP50), which measures model performance based on how well it identifies objects at a threshold of 0.5 IOUs, was 0.877 at the 99<sup>th</sup> epoch. This score indicates that most of the predicted bounding boxes overlapped with the actual annotations, demonstrating the high degree of accuracy obtained in locating fractures. Our model's precision was 0.891, indicating that most of the fractures identified were positive. We obtain a recall value of 0.797, which shows that the model has a strong true positive rate, which is an essential value in the clinical setting because missing a fracture may lead to severe harm to the patient. The results of the AI model (performance metrics and losses in training) over time are shown in Figure 4, which highlights the evolution of the model across subsequent steps. The first graph shows an increasing accuracy with slight variations in the values: a vague sign indicates that this model has been improving its object recognition and classifier skills over time. More specifically, validation metrics always increase from that point onward, which means that the model generalizes very well and can perform in unseen data. The box loss graph shows

### Configuration

Training arguments of your model

batch	-1
cache	ram
device	0
epochs	100
imgsz	640
patience	100

**Figure 3.** Training arguments of our model (Ultralytics LLC, <https://www.ultralytics.com/>).

the decrease after training in predicting correct boxes. The results demonstrate that the detection sensitivity has improved and allows for more accurate location of objects. A downward trend is also displayed in the “Class Loss” graph, which indicates better recognition and classification of object classes, as demonstrated by the ability of the proposed method to differentiate different object types more accurately. The final cut in the “Object Loss” graph shows that the model finally detected object presence in images with far fewer errors, leading to fewer false positives and false negatives.

## DISCUSSION

The most key finding of this study is the capability of the YOLOv8 model, which can achieve an mAP50 of 0.877, proving that it is highly precise in detecting and locating hip fractures. Considering that the proposed method achieved this level with a low dataset of only 676 images, it also demonstrates how efficiently the model can learn from fewer data without compromising

diagnostic accuracy. This is remarkable compared with findings from similar studies, such as those by Jiménez-Sánchez et al. (8) and Tanzi et al. (8,9) which made use of larger datasets but realized mPA values of 0.87 and 0.81, respectively. Efficiency in this matter from our model is a crucial aspect of a clinical setting where the need for speed and preciseness in diagnosis is paramount toward appropriate patient management. Jiménez-Sánchez et al. (8) used the ResNet-50 and AlexNet architectures to develop deep learning classification and localization models for 1347 images. These models were performed with an mPA value of 87. Tanzi et al. (9) developed a multi-stage architecture using 2453 images. This architecture consists of successive CNNs gradually. These models were performed with an mPA value of 0.81 (9). In another study conducted in 2022, Tanzi et al. (10) obtained an accuracy of 83% in fracture estimation using an architecture consisting of CNNs on 4207 images. This model predicted 29% better than 11 orthopedic surgeons. In this study, we created a model with 676 images using the YOLOv8 system in about 5 hours. This model had an mPA50 value of 0.877.

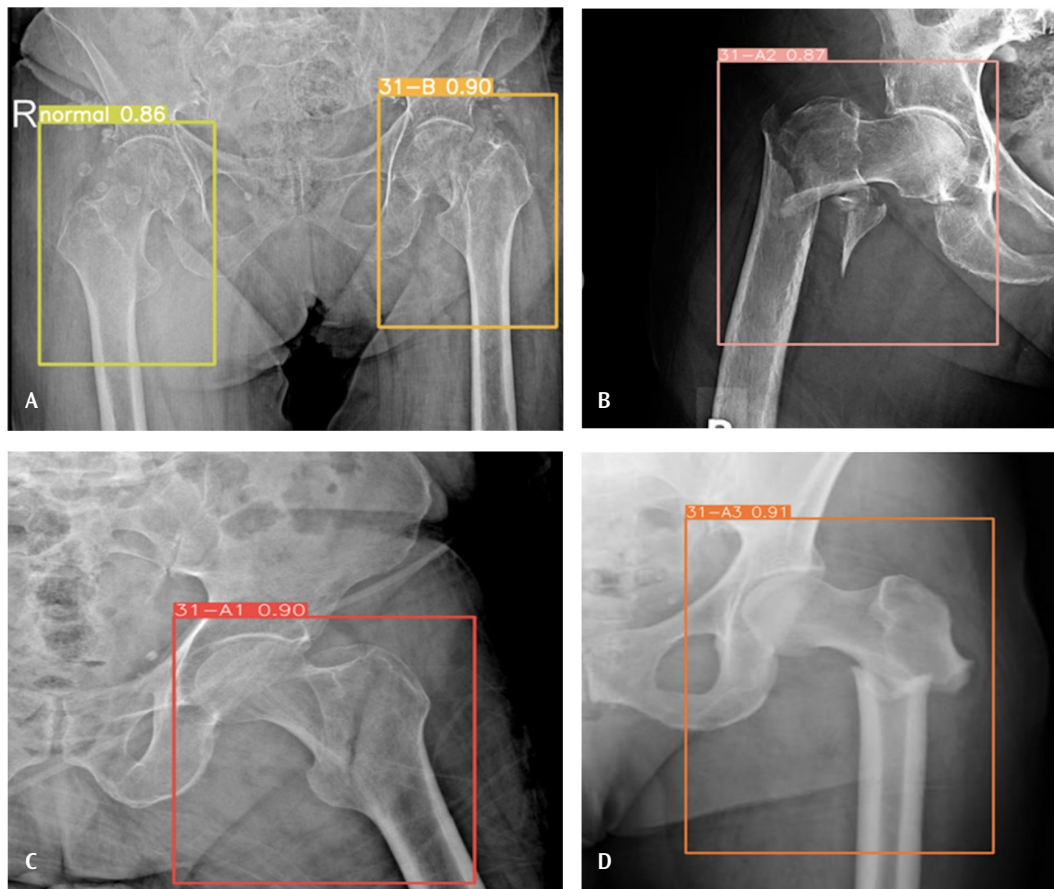


**Figure 4.** (A, B) Model accuracy measured on validation set, object loss, class loss, box loss graph during training of our model (Object loss measures the algorithm’s ability to correctly predict whether there are objects in an imagelabel. Class loss measures the algorithm’s ability to correctly guess which class objects in an image belong to. Box loss measures the algorithm’s ability to accurately predict the position and shape of objects in an image) (Ultralytics LLC, <https://www.ultralytics.com/>)



Despite using fewer images, our model produced outcomes comparable to those of other models in the literature. The training performance of the proposed model is shown in Figure 4. As can be seen, the proposed model follows the learning curve steadily. Figure 5 shows some of the test images that illustrate how our model detects and classifies proximal femur fractures. In solving AI problems, artificial neural networks model the connections between biological counterparts using weights between nodes. A positive weight reflects exciting relations, whereas inhibition links are represented by negative values. The sum of the products obtained from the weighted inputs determines the overall model output. Such common architectures are CNN and UNET (11). This research study employed Ultralytics YOLOv8, the most advanced form of the real-time object detection and image segmentation model. YOLOv8 is an engine behind a range of cutting-edge deep learning and computer vision advances that allow it to realize very fast speeds coupled with high accuracy. In this regard, our model was more efficiently developed with a higher predictive value. Ultralytics' YOLOv8 is the latest version of a well-known real-time object detection and image segmentation model.

Built on top of the latest developments in deep learning and computer vision, YOLOv8 performs incomparably with respect to the features of speed and accuracy. Whereas in some studies, a lot of data input is required for the classification and reporting of proximal femur fracture, in our study, from the results, it will be very obvious that the machine learned in a very short period of time with less data (12). For the model in our studies, we used 657 hip X-ray images, and we noticed that CNN training generally requires thousands of X-rays and some programming expertise. YOLOv8 has indeed eased our lives as medical professionals in terms of model building and has been an immense help in the spread of AI in medicine. This development underlines not only the efficiency of YOLOv8 for handling medical imaging tasks with limited datasets and demonstrates that AI technologies are becoming increasingly accessible and applicable in health care; thus, they could be a game-changer in diagnostic and therapeutic practices. Many researchers identify and classify fracture performance by comparing various computer vision models developed to those of doctors in recognizing and classifying fractures (13). These state-of-the-art studies present computer vision models with higher accuracy rates than those of



**Figure 5.** (A-D) Some images in which we tested our model's introduction of proximal femur fractures (Ultralytics LLC, <https://www.ultralytics.com/>)

physicians. In our work, there is no direct comparison between doctors and our model. No matter how good the identification and classification of a fracture are using computer vision models, the doctor always has the discretion on treatment planning. For this reason, computerized vision methods used in fracture diagnosis should be regarded as a means to speed up the diagnosis process for physicians and as a tool to contribute to the training of residents. Because we thought that differences in proximal femur radiographs could reduce the reliability of our model, we excluded such radiographs from our study. We have excluded some radiographs based on predefined strict criteria aimed at maintaining high image quality for effective model training. In this way, we attempted to prevent difficulties that may arise in the diagnosis and classification of fractures in radiographs that were not taken in the appropriate position. Our study only used hip radiographs from adult patients, so we were not able to evaluate the performance of our model in pediatric patients. In addition, since our model did not include radiographs of patients with additional pathologies, such as coxarthrosis, bone cysts, pelvis, and acetabular fractures, we could not test our ability to recognize and classify proximal femur fractures in such cases.

### Study Limitation

Epidemiological research indicates a progressive escalation in the incidence of PFFs (proximal femoral fractures) with advancing age, commencing at 40 years and accelerating markedly beyond the age of 75 (14). Consequently, this study exclusively utilized adult radiographic images. The model developed here has not been evaluated for application to pediatric populations. The quality and quantity of a dataset is very important for fracture detection and classification in computer vision. The fact that the images in the dataset are labeled correctly and are sufficiently clear increases the success of the model. Therefore, cleaner and high-quality images are required for each class to develop a better model. When we examine the studies in the literature, we find that the desired performance can be achieved using an appropriate artificial neural network architecture; however, the models and datasets used are not shared. This makes it difficult for academic publications to be verifiable and reproducible. In addition, the publication of the model used by the authors will contribute to scientific research. Therefore, in our study, we tried to overcome this problem by presenting both our model and the labeled data set in the appendix of our publication.

## CONCLUSION

This study demonstrated the power of the YOLOv8 model in the detection and classification of proximal femoral fractures, with an mAP50 of 0.877 with high precision of 0.891, and recall of 0.797. These findings indicate that AI diagnostics can be highly accurate and reliable and thus have great potential to improve clinical decision-making. The results also demonstrate the efficiency of the model on a smaller but well-annotated dataset, thus reducing computational demands with the intent of making advanced diagnostics more accessible to resource-constrained medical facilities. This is encouraging further studies to extend this model to a wide range of different patient demographics and fracture types, hence broadening the clinical utility of the tool to help further advances in medical imaging.

### Ethics

**Ethics Committee Approval:** Ethical approval for the study was obtained from the University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Non-Interventional Research Ethics Committee (approval number: 252, date: 13.12.2023).

**Informed Consent:** Retrospective study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: M.K., A.H.O., Y.S., G.A., B.G., R.A., Concept: M.K., A.H.O., Y.S., G.A., B.G., R.A., Design: M.K., A.H.O., Y.S., B.G., R.A., Data Collection or Processing: M.K., A.H.O., Y.S., G.A., B.G., R.A., Analysis or Interpretation: M.K., A.H.O., B.G., R.A., Literature Search: M.K., A.H.O., Y.S., G.A., B.G., R.A., Writing: M.K., A.H.O., Y.S., G.A., B.G., R.A.

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## REFERENCES

1. Ryan DJ, Yoshihara H, Yoneoka D, Egol KA, Zuckerman JD. Delay in hip fracture surgery: An analysis of patient-specific and hospital-specific risk factors. *J Orthop Trauma*. 2015;29:343-8.
2. French SD, Green S, Buchbinder R, Barnes H. Interventions for improving the appropriate use of imaging in people with musculoskeletal conditions. *Cochrane Database Syst Rev*. 2010;2010:CD006094.
3. Bachmann LM, Haberzeth S, Steurer J, ter Riet G. The accuracy of the Ottawa knee rule to rule out knee fractures: a systematic review. *Ann Intern Med*. 2004;140:121-4.

4. Beckenkamp PR, Lin CC, Macaskill P, Michaleff ZA, Maher CG, Moseley AM. Diagnostic accuracy of the Ottawa Ankle and Midfoot Rules: a systematic review with meta-analysis. *Br J Sports Med.* 2017;51:504-10.
5. Marsh JL, Slongro TF, Agel J, Broderick JS, Creevey W, DeCoster TA, et al. Fracture and dislocation classification compendium - 2007: Orthopaedic Trauma Association classification, database and outcomes committee. *J Orthop Trauma.* 2007;21:S1-133.
6. Singh A, Randive S, Breggia A, Ahmad B, Christman R, Amal S. Enhancing prostate cancer diagnosis with a novel artificial intelligence-based web application: Synergizing deep learning models, multimodal data, and insights from usability study with pathologists. *Cancers (Basel).* 2023;15:5659.
7. Agrawal D, Poonamallee L, Joshi S, Bahel V. Automated intracranial hemorrhage detection in traumatic brain injury using 3D CNN. *J Neurosci Rural Pract.* 2023;14:615-21.
8. Jiménez-Sánchez A, Kazi A, Albarqouni S, Kirchoff C, Biberthaler P, Navab N, et al. Precise proximal femur fracture classification for interactive training and surgical planning. *Int J Comput Assist Radiol Surg.* 2020;15:847-57.
9. Tanzi L, Vezzetti E, Moreno R, Aprato A, Audisio A, Massè A. Hierarchical fracture classification of proximal femur X-Ray images using a multistage Deep Learning approach. *Eur J Radiol.* 2020;133:109373.
10. Tanzi L, Audisio A, Cirrincione G, Aprato A, Vezzetti E. Vision transformer for femur fracture classification. *Injury.* 2022;53:2625-34
11. Xu F, Xiong Y, Ye G, Liang Y, Guo W, Deng Q, et al. Deep learning-based artificial intelligence model for classification of vertebral compression fractures: A multicenter diagnostic study. *Front Endocrinol (Lausanne).* 2023;14:1025749.
12. Paalvast O, Nauta M, Koelle M, Geerdink J, Vijlbrief O, Hegeman JH, et al. Radiology report generation for proximal femur fractures using deep classification and language generation models. *Artif Intell Med.* 2022;128:102281.
13. Zeren MT, Arslankaya S, Altuntaş Y, Cam N, Kirelli Y, Özdemir MH. Doctors versus YOLO: comparison between YOLO algorithm, orthopedic and traumatology resident doctors and general practitioners on detection of proximal femoral fractures on X-ray Images with multi methods. *International Journal on Artificial Intelligence Tools.* 2024;33:2350056.
14. Hashimoto K, Shinyashiki Y, Ohtani K, Kakinoki R, Akagi M. How proximal femur fracture patients aged 65 and older fare in survival and cause of death 5+ years after surgery: A long-term follow-up. *Medicine (Baltimore).* 2023;102:e33863.

# Increased Lower Urinary Tract Symptoms in Male Hyperthyroid Patients

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## Abstract

**Objective:** Hyperthyroidism is a condition characterized by excessive thyroid hormone production that affects multiple body systems, including the autonomic nervous system. The present study aimed to investigate the relationship between hyperthyroidism and lower urinary tract symptoms (LUTS) in male patients.

**Methods:** This prospective controlled study. Men newly diagnosed with hyperthyroidism were compared with a control group without any comorbidities. Patients with a history of urinary tract infections, neurogenic bladder diseases, and Benign prostatic hyperplasia /prostate cancer were excluded from the study. International Prostate Symptom Scores (IPSS) between the groups were compared, and the correlation between IPSS scores and free T4 levels was examined.

**Results:** Of the 58 patients, 20 were in the hyperthyroidism group and 38 were in the control group. The mean total IPSS and mean voiding scores were statistically higher in the hyperthyroidism group than in the control group. A positive correlation was found between IPSS scores and free T4 levels in the hyperthyroidism group.

**Conclusion:** In patients with hyperthyroidism, increased LUTS are observed. As serum free T4 levels increase, LUTS symptoms also increase.

**Keywords:** Hyperthyroidism, IPSS, lower urinary tract symptoms, storage, voiding

## INTRODUCTION

Thyroid hormones play an important role in maintaining homeostasis and regulating the sympathoadrenergic system (1). In iodine-sufficient countries, the global prevalence of hyperthyroidism is estimated to be 0.2-2.5% (2). Clinically, hyperthyroidism is primarily characterized by symptoms such as weight loss, sweating, tachycardia, and diarrhea. These symptoms are attributed to a malfunction in the automatic nervous system (1,3). Benign prostatic hyperplasia (BPH), urinary tract stones, and neurogenic bladder dysfunction are among the many potential causes of lower urinary tract symptoms (LUTS) in men. Additionally, normal urinary function, including both storage and voiding phases, requires coordinated activities of

the sympathetic, parasympathetic, and somatic nervous systems (4). Hyperthyroidism increases the effects of the sympathetic nervous system while reducing the effects of the parasympathetic nervous system. Through this pathway, hyperthyroidism may be a risk factor for LUTS. Although some studies have linked LUTS with hyperthyroidism, the association is not definitive (5,6). Therefore, we aimed to evaluate the effect of hyperthyroidism on LUTS in males.

## METHODS

This prospective controlled study was conducted after obtaining approval from the local ethics committee (approval number: 67, date: 22.02.2023). Male patients who presented to the internal



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medicine outpatient clinic between June 2023 and June 2024 were prospectively evaluated. Informed consent was obtained from all patients included in the study. The control group comprised male patients newly diagnosed with hyperthyroidism, whereas the control group comprised individuals without any known illnesses who underwent general health checkups. Patients with a history of conditions known to affect LUTS, such as urolithiasis, recurrent urinary tract infections, BPH treatment (alpha blockers), prostate cancer treatment, or bladder diseases, were excluded from the study. Hyperthyroidism was defined as low thyroid stimulating hormone (TSH) levels accompanied by elevated free T3 and free T4 levels based on normal reference ranges. The normal range of TSH levels was defined as 0.35-4.5 mU/L. The normal ranges of free T4 and free T3 levels were defined as 0.9-1.7 ng/dL and 2.0-4.4 pg/mL, respectively. The demographic data of the study population, including age, body mass index (BMI), and comorbidities, were recorded. Additionally, data such as prostate specific antigen (PSA) levels and prostate volume were analyzed in men for their potential association with LUTS. Finally, the International Prostate Symptom Scores (IPSS) were recorded to assess LUTS, including both the storage and voiding phases. All data were prospectively compared between the two groups prospectively established.

### Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 21.0 (SPSS Inc., Chicago, IL, USA). Data are presented as mean  $\pm$  standard deviation.

The Shapiro-Wilk test was used to assess the normality of the variables. The Mann-Whitney U test and independent samples t-test were used to compare the control and hyperthyroidism groups. We used The Pearson correlation test to measure the correlation between T4 levels and IPSS scores. A p-value of  $<0.05$  was considered statistically significant.

## RESULTS

A total of 58 male patients were included in the study. Among the patients, 20 were assigned to the hyperthyroidism group and 38 were included in the control group. The demographic and clinical data of the groups are presented in Table 1. The mean ages of the hyperthyroidism and control groups were  $53.6 \pm 10.3$  and  $58.6 \pm 13.5$  years, respectively ( $p=0.15$ ). The mean BMIs of the hyperthyroidism and control groups were respectively  $31.9 \pm 3.2$   $\text{kg/m}^2$  and  $30.3 \pm 4.4$   $\text{kg/m}^2$  ( $p=0.17$ ). In the hyperthyroidism group, 4 of 20 patients had diabetes mellitus, whereas in the control group, 6 of 38 patients had diabetes mellitus ( $p=0.724$ ). In the hyperthyroidism group, 3 of 20 patients had hypertension, whereas in the control group, 6 of 38 patients had hypertension ( $p=0.937$ ). The mean PSA levels in the control and hyperthyroidism groups were  $2.4 \pm 1.9$  ng/mL and  $2.5 \pm 1.5$  ng/mL, respectively ( $p=0.57$ ). The mean prostate volume was  $62.3 \pm 24.9$  cc in the hyperthyroidism group, compared to  $52.7 \pm 19.6$  cc in the control group ( $p=0.11$ ). The mean TSH levels were  $0.002 \pm 0.004$  mU/L in the hyperthyroidism group, compared to  $3.58 \pm 2.21$  mU/L in the control group ( $p<0.001$ ). The mean free T4 level was

**Table 1. Demographic and clinical data of the groups**

	Hyperthyroidism group n=20	Control group n=38	p
Age	$53.6 \pm 10.3$	$58.6 \pm 13.5$	0.15
BMI ( $\text{kg/m}^2$ )	$31.9 \pm 3.2$	$30.3 \pm 4.4$	0.17
Diabetes mellitus (Yes/No)	4/16	6/32	0.724
Hypertension (Yes/No)	3/17	6/32	0.937
PSA (ng/mL)	$2.5 \pm 1.5$	$2.4 \pm 1.9$	0.57
Prostate volume (cc)	$62.3 \pm 24.9$	$52.7 \pm 19.6$	0.11
TSH (mU/L)	$0.002 \pm 0.004$	$3.58 \pm 2.21$	<b>&lt;0.001</b>
Free T4 (ng/dL)	$6.87 \pm 2.7$	$1.25 \pm 0.2$	<b>&lt;0.001</b>
Free T3 (pg/mL)	$6.53 \pm 0.6$	$3.21 \pm 0.2$	<b>&lt;0.001</b>
IPSS, Total	$6.4 \pm 3.6$	$2.2 \pm 1.4$	<b>&lt;0.001</b>
IPSS, voiding	$4.5 \pm 2.7$	$0.9 \pm 0.7$	<b>&lt;0.001</b>
IPSS, storage	$1.6 \pm 0.8$	$1.3 \pm 0.8$	0.09

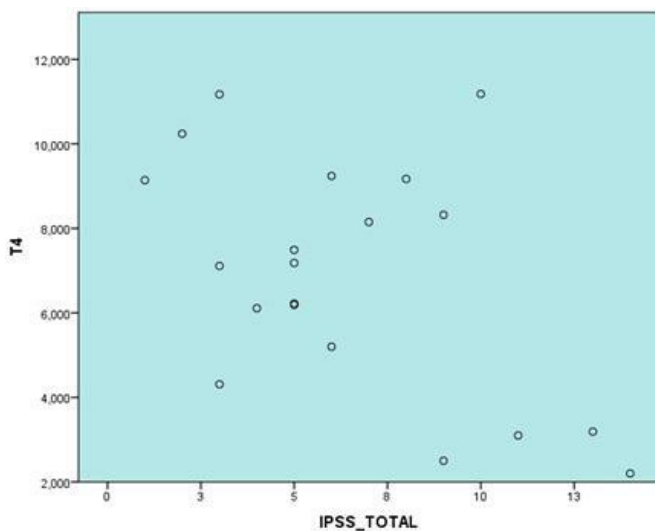
BMI: Body mass index, IPSS: International prostate symptom score, PSA: Prostate-specific antigen, TSH: Thyroid-stimulating hormone

6.87±2.7 ng/dL in the hyperthyroidism group and 1.25±0.2 ng/dL in the control group, respectively ( $p<0.001$ ). The mean free T3 level was found to be 6.53±0.6 pg/mL and 3.21±0.2 pg/mL in the hyperthyroidism and control groups, respectively ( $p<0.001$ ). As expected, a statistically significant difference in the thyroid values was observed between the groups. The mean total IPSS scores of the hyperthyroidism and control group were 6.4±3.6 and 2.2±1.4, respectively ( $p<0.001$ ). Additionally, the mean voiding scores were 4.5±2.7 for the hyperthyroidism group and 0.9±0.7 for the control group ( $p<0.001$ ). The mean storage scores were 1.6±0.8 for the hyperthyroidism group and 1.3±0.8 for the control group ( $p=0.09$ ). The total IPSS and voiding scores were significantly higher in the hyperthyroidism group than in the control group. The positive correlation between free T4 levels and total IPSS scores is presented in Figure 1. We found a significant correlation between free T4 levels and total IPSS scores ( $p=0.024$ ). In other words, in hyperthyroid patients, as the T4 level in the body increases, the IPSS scores also increase accordingly.

## DISCUSSION

Male LUTS is common, and its prevalence increases with age. LUTS can result from prostate-related conditions, urinary tract stones, or infections, as well as other systemic causes. Considering the wide range of symptoms associated with hyperthyroidism, it is plausible that it may be linked to LUTS through certain pathways. In this study, we demonstrated that hyperthyroid patients exhibit more urinary tract symptoms than normal patients, and these symptoms increase as serum T4 levels rise. Patients with hyperthyroidism often experience

increased thirst and fluid intake, which may contribute to frequent urination (7-9). Additionally, hyperthyroidism induces hyperdynamic circulation in the body, leading to increased cardiac output, elevated blood pressure, and reduced peripheral vascular resistance. Consequently, this may result in increased renal blood flow and urine output (10,11). Normal voiding occurs through the coordinated functions of the autonomic and somatic nervous systems. Parasympathetic activation induces detrusor muscle contraction, whereas alpha-adrenergic activity inhibition facilitates bladder neck opening. Simultaneously, relaxation of the external sphincter via somatic nerve input allows for voiding. In addition, increased beta-adrenergic activity can reduce detrusor contractility, potentially impairing voiding function (12-14). Andersen et al. (15) showed that patients with hyperthyroidism experienced increased urinary frequency and nocturia. The same study also showed that these symptoms improved in patients who achieved an euthyroid state after six months of treatment (15). In our study, which evaluated a larger cohort of hyperthyroid patients, an increase in LUTS was observed. However, unlike the study by Andersen et al. (15) we did not have post-treatment data for our patients. Instead, we demonstrated that LUTS was significantly worse in the hyperthyroidism group than in the control group. In another study, Goswami et al. (16) found that 40% of patients with Graves' disease had increased LUTS and urinary frequency. In urodynamic tests conducted on some patients, it was reported that peak and average urine flow rates were low and exhibited a flat plateau pattern during voiding. Furthermore, the symptoms of these patients improved after treatment. Although the main findings of our study are similar to those of Goswami et al. (16) a notable strength of their study is the inclusion of urodynamic tests in some patients to demonstrate LUTS, which is a limitation of our study. On the other hand, the lack of a control group and the failure to use a validated urinary symptom score questionnaire, such as IPSS, can be considered limitations in their study compared with our study. Ho et al. (5) found that female patients with hyperthyroidism had worse LUTS scores and lower urinary flow rates compared with the control group. Additionally, symptom improvement was observed after treatment. This study is similar to ours in terms of both the use of the IPSS questionnaire and the inclusion of a control group. In this study, the total IPSS and voiding and storage scores were calculated separately. The IPSS questionnaire was originally developed to evaluate BPH in men (17). However, it has since been shown that the IPSS questionnaire is not specific to gender or any particular disease (18,19). Therefore, we used the IPSS questionnaire to assess the LUTSs that we suspect are related to hyperthyroidism. There is



**Figure 1.** Correlation between T4 levels and total IPSSs  
IPSS: International prostate symptom score

a correlation between hyperthyroidism symptoms and serum thyroxine levels (20). Ho et al. (5) found no significant difference in thyroxine levels between female patients with hyperthyroidism and those with severe LUTS scores (5). In contrast, we found a statistically significant correlation between total IPSS scores and free T4 levels in male patients. The correlation between LUTS severity and thyroxine levels remains an open area for further research. Our study is not without limitations and has certain shortcomings. First, our study included a relatively small patient population. Second, if we had been able to evaluate symptomatic patients using post-void residual volume, uroflowmetry, or urodynamic studies, we could have gained more insight into the nature of LUTS.

## CONCLUSION

Hyperthyroidism causes LUTS in male patients, particularly during the voiding phase. Increased beta-adrenergic activity in hyperthyroid states may explain impaired voiding function. Future studies are needed that include validated questionnaires, control groups, and posttreatment symptoms of hyperthyroid patients.

## Ethics

**Ethics Committee Approval:** This prospective controlled study was conducted after obtaining approval from the local ethics committee (approval number: 67, date: 22.02.2023).

**Informed Consent:** Informed consent was obtained from all patients included in the study.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: B.C., Concept: B.C., O.C., Design: B.C., O.C., Data Collection or Processing: B.C., O.C., Analysis or Interpretation: B.C., O.C., Literature Search: B.C., O.C., Writing: B.C.

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## REFERENCES

- Silva JE, Bianco SD. Thyroid-adrenergic interactions: physiological and clinical implications. *Thyroid*. 2008;18:157-65.
- Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. *2018*;14:301-16.
- Burggraaf J, Tulen JH, Lalezari S, Schoemaker RC, De Meyer PH, Meinders AE, et al. Sympathovagal imbalance in hyperthyroidism. *Am J Physiol Endocrinol Metab*. 2001;281:190-5.
- De Groat WC. Integrative control of the lower urinary tract: Preclinical perspective. *Br J Pharmacol*. 2006;147(Suppl 2):25-40.
- Ho CH, Chang TC, Guo YJ, Chen SC, Yu HJ, Huang KH. Lower urinary tract symptoms and urinary flow rates in female patients with hyperthyroidism. *Urology*. 2011;77:50-4.
- Chung SD, Chen YK, Chen YH, Lin HC. Hyperthyroidism and female urinary incontinence: a population-based cohort study. *Clin Endocrinol (Oxf)*. 2011;75:704-8.
- Trivalle C, Doucet J, Chassagne P, Landrin I, Kadri N, Menard JF, et al. Differences in the signs and symptoms of hyperthyroidism in older and younger patients. *J Am Geriatr Soc*. 1996;44:50-3.
- Evered DC, Hayter CJ, Surveyor I. Primary polydipsia in thyrotoxicosis. *Metabolism*. 1972;21:393-404.
- Thoday KL, Mooney CT. Historical, clinical and laboratory features of 126 hyperthyroid cats. *Vet Rec*. 1992;131:257-64.
- Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med*. 2021;344:501-9.
- Vargas F, Atucha NM, Sabio JM, Quesada T, García-Estañ J. Pressure-diuresis-natriuresis response in hyperthyroid and hypothyroid rats. *Clin Sci (Lond)*. 1994;87:323-8.
- Anderson KE. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev*. 1993;45:253-308.
- Hudman D, Elliott RA, Whitaker P, Terry TR, Sandhu DP, Norman RI. Inhibition of the contractile responses of isolated human and rat bladders by clenbuterol. *J Urol*. 2001;166:1969-73.
- Levin RM, Ruggieri MR, Wein AJ. Identification of receptor subtypes in the rabbit and human urinary bladder by selective radio-ligand binding. *J Urol*. 1988;139:844-8.
- Andersen LF, Agner T, Walter S, Hansen JM. Micturition pattern in hyperthyroidism and hypothyroidism. *Urology*. 1987;29:223-4.
- Goswami R, Seth A, Goswami AK, Kochupillai N. Prevalence of enuresis and other bladder symptoms in patients with active Graves' disease. *Br J Urol*. 1997;80:563-6.
- Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol*. 1992;148:1549-64.
- Chancellor MB, Rivas DA. American Urological Association symptom index for women with voiding symptoms: lack of index specificity for benign prostate hyperplasia. *J Urol*. 1993;150:1708-9.
- Lepor H, Machi G. Comparison of aua symptom index in unselected males and females between fifty-five and seventy-nine years of age. *Urology*. 1993;42:36-40.
- Vos XG, Smit N, Endert E, Brosschot JF, Tijssen JG, Wiersinga WM. Age and stress as determinants of the severity of hyperthyroidism caused by Graves' disease in newly diagnosed patients. *Eur J Endocrinol*. 2009;160:193-9.

# PRP Application in the Treatment of Knee Osteoarthritis: A Comprehensive New Perspective in Light of Current Literature and Clinical Consensus Reports

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## Abstract

Knee osteoarthritis is a common chronic joint disease worldwide, representing a significant public health problem because of its impact on pain, functionality, and quality of life. Current treatment options, including pharmacological and physical therapies, aim to manage symptoms in the early and middle stages and delay surgical interventions. Platelet-rich plasma (PRP), an orthobiological treatment, has emerged as a promising treatment offering potential benefits, such as inflammation modulation, cartilage regeneration, and symptom relief. This review evaluates the role of PRP in the management of knee osteoarthritis by analyzing recent literature and consensus reports. The therapeutic effects of PRP are attributed to its bioactive components, including growth factors and cytokines, which promote tissue healing and regulate inflammatory processes. Clinical studies have demonstrated the efficacy of PRP for pain reduction and functional improvement, particularly in patients with mild-to-moderate knee osteoarthritis. However, variability in preparation protocols, dosage, and patient characteristic influence outcomes, highlighting the need for standardized protocols. Key factors such as centrifugation technique, activation method, and leukocyte concentration significantly affect the efficacy of PRP. Consensus reports have recommended PRP as an effective and safe option for the management of knee osteoarthritis, especially in the early and middle stages, and under certain conditions, has potential application in advanced cases. Although PRP shows promise as an innovative treatment, further high-quality, long-term studies are needed to optimize the protocol. This review highlights the efficacy of PRP among conservative treatments and its potential to improve outcomes in patients with knee osteoarthritis.

**Keywords:** Knee osteoarthritis, platelet rich plasma, PRP therapy, orthobiological treatments, cartilage regeneration, inflammation modulation

## INTRODUCTION

Knee osteoarthritis is the most common chronic joint disease worldwide. It is an important public health problem that causes pain and loss of function, which negatively affects the quality of life of individuals (1). It is estimated that between 7.2% and 16.7% of individuals over 45 years of age in the US experience symptomatic knee osteoarthritis (2). According to global studies, the prevalence of knee osteoarthritis was reported to be 22.9% in individuals aged 40 years and older, with an incidence of 203 per 10,000 person-years (3). As a result of these data, it can be seen

that the disease constitutes a significant and increasing burden worldwide.

Knee osteoarthritis is often managed in the late stages with knee arthroplasty, which requires a major surgical intervention and is associated with significant health costs (4). However, conventional treatment approaches, including pharmacological and physical therapies, are available to manage symptoms in the early and middle stages. These approaches also aim to delay surgical intervention. In this context, the need for innovative treatment approaches for knee osteoarthritis is increasing daily.



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In recent years, orthobiologic therapies, particularly platelet-rich plasma (PRP), have attracted attention for their potential to alleviate symptoms, promote tissue healing, and even reverse pathological processes by slowing disease progression. Moreover, orthobiologic therapies are undoubtedly becoming an important player in the treatment of osteoarthritis of the knee as an alternative or complementary option to surgical interventions, with the goals of modulating inflammation, promoting cartilage repair, and improving patients' quality of life.

In the field of orthobiological therapies, the heterogeneity of the evidence level in the existing literature and the lack of standardization of biological treatment protocols increase the importance of constantly updated information and consensus reports. This review examined the role of PRP in the management of knee osteoarthritis in the light of current literature and consensus reports, focusing on the popular use of PRP therapy, and evaluated the efficacy and outcomes of these approaches in clinical practice.

## Platelet-rich Plasma (PRP) in Knee Osteoarthritis

PRP is a plasma product derived from the patient's own blood with increased platelet concentration. It has emerged as a promising conservative treatment option for knee osteoarthritis aimed at alleviating symptoms and delaying surgical interventions. Thanks to the growth factors and cytokines it contains, it plays important roles in tissue regeneration, cellular renewal, and inflammation (5).

With PRP application, mainly by cell proliferation with growth factors [such as platelet-derived growth factor (PDGF), transforming growth- $\beta$ , vascular endothelial growth factor (VEGF), epidermal growth factor], by reducing the effect of catabolic mediators (such as interleukin-1 $\beta$  and metalloproteinases), by providing proliferation and differentiation of mesenchymal stem cells, mechanisms of action such as suppressing the release of inflammatory cytokines (such as interleukin-1 and tumor necrosis factor-alpha), increasing the level of anti-inflammatory cytokines (such as interleukin 10) and limiting matrix degradation while increasing collagen synthesis in the extracellular matrix have been reported in the literature. (6-12).

In preclinical in vitro and animal studies, PRP has been shown to have several heterogeneous mechanisms of action, including chondrocyte proliferation, inflammation modulation, and matrix production (13,14). The effects of these mechanisms have also been reported to increase with the frequency of administration and concentration in both in vitro and clinical studies (15-19). In numerous randomized controlled trials and

meta-analyses on the clinical efficacy of PRP, positive effects have been observed, particularly on pain control and functional improvement. According to the ESKKA-ORBIT consensus report, clinical evidence confirms the efficacy of PRP injections in the treatment of osteoarthritis of the knee, and there is consensus that there is sufficient pre-clinical and clinical evidence in the literature to support PRP injections as an appropriate treatment option in patients who do not respond to conservative therapies (20). However, several factors have been reported to influence the efficacy of PRP.

## 1. Preparation Techniques

PRP preparation methods are critical factors determining the efficacy and safety of the treatment. Although PRP is a plasma product in which platelets are concentrated, the protocols used in the preparation process may cause differences in the cellular and biochemical components of PRP. These differences may affect treatment outcomes.

### The open and closed methods

Although there are many methods for PRP preparation, all involve differential centrifugation. There are two main methods: open and closed techniques. Closed techniques are performed in a sterile environment with less risk of contamination, whereas open techniques require more manual intervention and may have a higher risk of contamination (21).

### The single and double centrifugation methods

The centrifugation protocol can affect the platelet concentration and the number of other ingredients and can be performed by single or double centrifugation. Double centrifugation provides a higher concentration of platelets and leukocytes than single centrifugation (22,23). It has also been reported to contain higher concentrations of growth factors, such as PDGF and VEGF, using the double centrifugation method (23,24).

### Centrifugation speed

The centrifugation speed and time have also been shown to have a significant effect on the homogeneity and concentration of the resulting cellular components (25). Centrifugation at lower speeds has been reported to provide more homogeneous extraction of cellular components (25,26). The available literature shows that PRP preparation protocols are highly variable and most studies do not provide adequate information. The protocol that is emphasized is to perform the first centrifugation at 100-300 g for 5-10 minutes and the second centrifugation at 400-700 g for 10-17 minutes (21).

### Activation methods

Activation methods are used to increase the effectiveness of PRP and trigger degranulation of platelets and release of growth factors, which are biologically active molecules in PRP, into surrounding tissues. The most common and well-known methods are performed using activators such as calcium chloride (CaCl<sub>2</sub>) and thrombin.

CaCl<sub>2</sub> mimics the natural activation of platelets, leading to gradual degranulation. Thrombin is a natural enzyme that initiates the coagulation cascade and exerts a short-term effect by rapidly degranulating platelets. In summary, thrombin has an intense and rapid effect, whereas CaCl<sub>2</sub> has a more prolonged and stable release (27,28).

### Leukocyte-Rich PRP (LR-PRP) and Leukocyte-Poor PRP (LP-PRP)

LR-PRP is a type of PRP in which leukocytes are concentrated along with platelets. The leukocytes in the PRP content have the capacity to secrete inflammatory mediators and proteases. LP-PRP is a form in which leukocytes are removed from the PRP content. This form aims to reduce the levels of inflammatory mediators. Both LR-PRP and LP-PRP improve pain and function in the treatment of knee osteoarthritis (29). However, no significant difference was observed between these improvements (30,31). However, LR-PRP has been reported to have local side effects, such as pain and swelling, with a higher rate of inflammation compared to LP-PRP (29-32). The higher inflammation in LR-PRP than in LP-PRP may cause increased pain in chronic inflammatory diseases.

According to a consensus report, it was reported that, according to the available literature, LR-PRP and LP-PRP are not preferable to either type, and that any type can be chosen in the management of knee osteoarthritis (20).

### PRP Injection Volume

It has been reported by the consensus group that the optimal volume (2-12 mL) for PRP injection may have an effect on treatment, but there is no evidence in the literature on this issue and no recommendation can be made at this point (20).

## 2. Patient Characteristics and Indications

The efficacy of PRP can vary greatly depending on the individual characteristics of the patient and the characteristics of the clinic. Therefore, there are important factors to be considered in patient selection to ensure the procedure is successful.

### Age

The effectiveness of PRP treatment varies according to patient age. PRP application protocols are an important factor affecting

treatment outcomes. With advancing age, platelet function may decrease, and the release capacity of growth factors may decrease (33,34). In a randomized double-blind study comparing patients with mild to moderate OA to a placebo control group, PRP therapy was most effective in patients aged 51-65 years and reported better results in knee osteoarthritis and in patients with low mechanical axis angle (19). In a study of patients with an average age of 56.1 years, PRP treatment was reported to be more effective than hyaluronic acid or placebo injections (35). In a patient group with an average age of 59.8 years, pain and functional improvement were observed after PRP treatment, and this improvement continued for up to 7 months (36). According to the consensus report, most studies covered a median age of 55 to 65 years, with the consensus that no specific age range can be recommended and that the response decreases with increasing age (20). The consensus group also stated that instead of focusing directly on chronological age, other factors should be considered (20).

### Body Mass Index (BMI)

BMI is another factor that may affect the success of PRP treatment. It is known that obesity accelerates the progression of osteoarthritis by increasing the mechanical load on the knee joints. However, there are limited references in the literature evaluating the efficacy of BMI and PRP, and in general, similar pain and functional scores improved at low and high BMI, and the results obtained were independent of BMI (37).

### Stage of Osteoarthritis

The efficacy of PRP may differ according to the stage of knee osteoarthritis. According to the Kellgren-Lawrence classification (KL), the stages in which PRP is most effective have been shown in the literature as early and intermediate stage OA (KL: I-III) (18,19,37-39). According to the consensus report, clinical evidence suggests that PRP is effective and indicated for mild to moderate knee OA (KL: I-III) (20). There is also a consensus that advanced stage (KL: IV) can be considered in selected cases (20).

### Concomitant Health Problems

Although the general health status of patients is believed to have an impact on the effectiveness of PRP treatment, there is limited information on the impact on comorbidities. In addition to recommendations and contraindications for knee injections, recommendations for additional diseases were reported in the consensus report specific to PRP treatment (20). In addition to contraindications due to local problems, such as infection and skin problems, recommendations have been made for systemic infection, malignancy, inflammatory diseases, and quantitative and qualitative platelet disorders in the blood.

- **Systemic Infection**

It was reported in a consensus report that in the presence of systemic infection, it should be kept in mind that PRP may have a negative effect on the functional status due to the immune and inflammatory processes at the systemic level (20).

- **Malignancy**

Although the risk of tumor proliferation with PRP content has not been reported in the literature, the theoretical risk-caused consensus group considered the presence of both benign and malignant tumors in the knee joint as a contraindication (20). Similarly, there is a consensus that even in the presence of distant malignancy outside the knee, the contraindication should apply until there is more evidence.

- **Inflammatory Diseases**

The presence of systemic inflammatory diseases (such as rheumatoid arthritis) and autoimmune diseases does not preclude PRP therapy for knee osteoarthritis, according to a consensus report (20).

- **Numerical and Qualitative Platelet Disorders in Blood**

It has been reported that the PRP formulation must have an absolute platelet count of 10 billion to have a long-lasting chondroprotective effect lasting up to 1 year in moderate knee osteoarthritis (38). However, there are no specific data on the safety and side effects of PRP therapy in patients with thrombocytopenia or platelet dysfunction. In the report of the consensus group; thrombocytopenia, thrombocytosis, or coagulopathy conditions are stated as relative contraindications because changes in platelet count and function may occur, and it is reported that the optimal platelet count range cannot be defined in PRP content (20).

### **Patellofemoral Osteoarthritis (PFOA)**

In the current literature, it has been reported that pain and functional improvement in patients in the treatment of PFOA with PRP continues for 6 and 12 months, but according to the consensus report, it can be considered an option for treatment (20,39-41).

## **3. Implementation Protocol**

### **Number of Doses in PRP Treatment**

Although there is no clear consensus in the literature, most studies suggest that multiple-dose PRP applications are more effective than single dose injections (42-45). It has been reported that although single-dose PRP applications provide pain and functional improvement in the short term, these

effects are not as sustainable as multiple-dose applications in the long term (42,43). However, in advanced knee osteoarthritis, although multiple injections do not provide any benefit, studies have reported that two doses are more effective than a single dose, and three doses are even more effective (18,44,45). The consensus group recommends administering injections at dose intervals of two to four (20).

### **Dose Range of PRP**

Although there is no clear result in the literature on the dose interval in treatment, according to the recommendation of the consensus group, it has been reported that since the activity of degranulate growth factors occurs in the first 3 weeks after injection, it may be appropriate to perform the application at intervals of 1 to 3 weeks (20).

### **Use of Non-steroidal Anti-inflammatory Drugs (NSAIDs) With PRP**

Regarding the use of NSAIDs after PRP injection, the effects of healing may be limited by reducing the release of growth factors (46,47). In addition, decreased platelet function was observed in PRP obtained from patients taking NSAIDs (47). Therefore, the consensus group recommends avoiding the use of NSAIDs up to 2 weeks before and 1 week after PRP application and the use of non-inflammatory drugs (such as paracetamol, dipyrone and tramadol) when necessary (20).

### **Use of Intra-articular Local Anesthetics With PRP**

Although there is no evidence in the literature to clarify the effects of local anesthetics on PRP treatment, in vitro studies have reported the negative effects of local anesthetics on platelet function (48). For these reasons, the consensus report does not recommend the use of PRP injection and local anesthesia, but it is stated that it can be applied subcutaneously without entering the capsule (20).

### **Corticosteroid Injection With PRP**

Specific studies on the combined use of PRP and corticosteroids are limited. However, given that both treatment modalities have their own advantages and disadvantages, combination therapy could potentially provide both short-term and long-term benefits. However, the consensus group recommends avoiding the use of PRP therapy in close proximity to corticosteroid injection and recommends PRP therapy for at least 6 weeks after intra-articular corticosteroid use (20).

### **Combined Use of PRP and Hyaluronic Acid**

Research in the literature on whether the combination of PRP and hyaluronic acid is effective in the treatment of osteoarthritis

of the knee generally shows that this combination generally gives better results than PRP or hyaluronic acid treatments alone (49,50). However, the consensus group stated that more data are needed before recommending the combination of PRP with hyaluronic (20).

## CONCLUSION

Numerous clinical and preclinical studies on the efficacy of PRP in knee osteoarthritis have demonstrated the benefits of PRP application, especially in terms of pain control, functional improvement, and delay in surgical interventions. However, considering the heterogeneity of preparation protocols, patient characteristics, application protocols, and other treatment-related factors that affect the efficacy of PRP, the need to optimize the treatment is emphasized. Available data from the literature and consensus reports support the use of PRP as an effective and safe treatment modality, particularly in individuals with mild-to-moderate knee osteoarthritis.

The potential of PRP in clinical practice as a powerful alternative to traditional methods as an orthobiologic approach in the treatment of osteoarthritis of the knee is increasingly being recognized. However, standardization of treatment protocols and evaluation of long-term effects in larger studies are critical for the integration of PRP into clinical practice. In this context, the study of PRP applications in a larger patient group with randomized controlled trials designed to achieve high sensitivity and long-term follow-up will determine the future use of this method in the treatment of knee osteoarthritis.

## Footnotes

### Authorship Contributions

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

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## REFERENCES

- Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393:1745-59.
- Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum*. 2008;58:26-35.
- Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine*. 2020;29-30:100587.
- Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019;27:1578-89.
- Boffa A, Salerno M, Merli G, De Girolamo L, Laver L, Magalon J, et al. Platelet-rich plasma injections induce disease-modifying effects in the treatment of osteoarthritis in animal models. *Knee Surg Sports Traumatol Arthrosc*. 2021;29:4100-21.
- Cheng NC, Tu YK, Lee NH, Young TH. Influence of human platelet lysate on extracellular matrix deposition and cellular characteristics in adipose-derived stem cell sheets. *Front Cell Dev Biol*. 2020;8:558354.
- Yan J, Chen X, Pu C, Zhao Y, Liu X, Liu T, et al. Synovium stem cell-derived matrix enhances anti-inflammatory properties of rabbit articular chondrocytes via the SIRT1 pathway. *Mater Sci Eng C Mater Biol Appl*. 2020;106:110286.
- Hefka Blahnova V, Dankova J, Rampichova M, Filova E. Combinations of growth factors for human mesenchymal stem cell proliferation and osteogenic differentiation. *Bone Joint Res*. 2020;9:412-20.
- Jia J, Wang SZ, Ma LY, Yu JB, Guo YD, Wang C. The differential effects of leukocyte-containing and pure platelet-rich plasma on nucleus pulposus-derived mesenchymal stem cells: implications for the clinical treatment of intervertebral disc degeneration. *Stem Cells Int*. 2018;2018:7162084.
- Hesari R, Keshvarinia M, Kabiri M, Rad I, Parivar K, Hoseinpoor H, et al. Comparative impact of platelet rich plasma and transforming growth factor- $\beta$  on chondrogenic differentiation of human adipose derived stem cells. *Bioimpacts*. 2020;10:37-43.
- Ziegler CG, Van Sloun R, Gonzalez S, Whitney KE, DePhillipo NN, Kennedy MI, et al. Characterization of growth factors, cytokines, and chemokines in bone marrow concentrate and platelet-Rich plasma: a prospective Analysis. *Am J Sports Med*. 2019;47:2174-87.
- Hu B, Wang L, Sun N, Rui G, Lin S. Leukoreduced PRP enhanced proliferation and ECM production yet inhibited senescence, inflammation, and multi-differentiation potential of AFSCs by downregulating HMGB1. *Immunopharmacol Immunotoxicol*. 2023;45:730-41.
- Park SI, Lee HR, Kim S, Ahn MW, Do SH. Time-sequential modulation in expression of growth factors from platelet-rich plasma (PRP) on the chondrocyte cultures. *Mol Cell Biochem*. 2012;361:9-17.
- Moussa M, Lajeunesse D, Hilal G, El Atat O, Haykal G, Serhal R, et al. Platelet rich plasma (PRP) induces chondroprotection via increasing autophagy, anti-inflammatory markers, and decreasing apoptosis in human osteoarthritic cartilage. *Exp Cell Res*. 2017;352:146-56.
- Hahn O, Kieb M, Jonitz-Heincke A, Bader R, Peters K, Tischer T. Dose-ich plasma powder on chondrocytes in vitro. *Am J Sports Med*. 2020;48:1727-34.
- Zhuang W, Li T, Li Y, Zhang Y, Gao J, Wang X, et al. The varying clinical effectiveness of single, three and five intraarticular injections of platelet-rich plasma in knee osteoarthritis. *J Orthop Surg Res*. 2024;19:284.
- Patel S, Gahlaut S, Thami T, Chouhan DK, Jain A, Dhillion MS. Comparison of conventional dose versus superdose platelet-rich plasma for knee osteoarthritis: a prospective, triple-blind, randomized clinical trial. *Orthop J Sports Med*. 2024;12:23259671241227863.
- Görmeli G, Görmeli CA, Ataoglu B, Çolak C, Aslantürk O, Ertem K. Multiple PRP injections are more effective than single injections and

- hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Knee Surg Sports Traumatol Arthrosc.* 2017;25:958-65.
19. Yurtbay A, Say F, Çinka H, Ersoy A. Multiple platelet-rich plasma injections are superior to single PRP injections or saline in osteoarthritis of the knee: the 2-year results of a randomized, double-blind, placebo-controlled clinical trial. *Arch Orthop Trauma Surg.* 2022;142:2755-68.
  20. Laver L, Filardo G, Sanchez M, Magalon J, Tischer T, Abat F, et al. The use of injectable orthobiologics for knee osteoarthritis: A European ESSKA-ORBIT consensus. Part 1-Blood-derived products (platelet-rich plasma). *Knee Surg Sports Traumatol Arthrosc.* 2024;32:783-97.
  21. Dashore S, Chouhan K, Nanda S, Sharma A. Preparation of platelet-rich plasma: national IADVL PRP taskforce recommendations. *Indian Dermatol Online J.* 2021;12:S12-23.
  22. Legiawati L, Yusharyahya SN, Bernadette I, Novianto E, Priyanto MH, Gliselida KC, et al. Comparing Single-spin versus double-spin platelet-rich plasma (PRP) centrifugation methods on thrombocyte count and clinical improvement of androgenetic alopecia: a preliminary, randomized, double-blind clinical trial. *J Clin Aesthet Dermatol.* 2023;16:39-44.
  23. Oh JH, Kim W, Park KU, Roh YH. Comparison of the cellular composition and cytokine-release kinetics of various platelet-rich plasma preparations. *Am J Sports Med.* 2015;43:3062-70.
  24. Roh YH, Kim W, Park KU, Oh JH. Cytokine-release kinetics of platelet-rich plasma according to various activation protocols. *Bone Joint Res.* 2016;5:37-45.
  25. Castillo-Macías A, Zavala J, Ortega-Lara W, García-Herrera SM, Valdez-García JE. Optimizing platelet and leucocyte-rich plasma as biomaterials for ophthalmic applications: impact of centrifugation speed. *Clin Ophthalmol.* 2023;17:3787-97.
  26. Goodale MB, Phelps HA, Barnhard JA, Shoben AB, Brunke MW. Lower centrifugation speed and time are positively associated with platelet concentration in a canine autologous conditioned plasma system. *J Am Vet Med Assoc.* 2023;261:1-6.
  27. Hamilton B, Tol JL, Knez W, Chalabi H. Exercise and the platelet activator calcium chloride both influence the growth factor content of platelet-rich plasma (PRP): overlooked biochemical factors that could influence PRP treatment. *Br J Sports Med.* 2015;49:957-60.
  28. Cavallo C, Roffi A, Grigolo B, Mariani E, Pratelli L, Merli G, et al. Platelet-rich plasma: the choice of activation method affects the release of bioactive molecules. *Biomed Res Int.* 2016;2016:6591717.
  29. Yaradilmis YU, Demirkale I, Safa Tagral A, Caner Okkaoglu M, Ates A, Altay M. Comparison of two platelet rich plasma formulations with viscosupplementation in treatment of moderate grade gonarthrosis: A prospective randomized controlled study. *J Orthop.* 2020;20:240-6.
  30. Kim JH, Park YB, Ha CW, Roh YJ, Park JG. Adverse reactions and clinical outcomes for leukocyte-poor versus leukocyte-rich platelet-rich plasma in knee osteoarthritis: a systematic review and meta-analysis. *Orthop J Sports Med.* 2021;9:23259671211011948.
  31. Di Martino A, Boffa A, Andriolo L, Romandini I, Altamura SA, Cenacchi A, et al. Leukocyte-rich versus leukocyte-poor platelet-rich plasma for the treatment of knee osteoarthritis: a double-blind randomized trial. *Am J Sports Med.* 2022;50:609-17.
  32. Anitua E, Zalduendo M, Troya M, Padilla S, Orive G. Leukocyte inclusion within a platelet rich plasma-derived fibrin scaffold stimulates a more pro-inflammatory environment and alters fibrin properties. *PLoS One.* 2015;10:e0121713.
  33. Tian J, Lei XX, Xuan L, Tang JB, Cheng B. The effects of aging, diabetes mellitus, and antiplatelet drugs on growth factors and anti-aging proteins in platelet-rich plasma. *Platelets.* 2019;30:773-92.
  34. Edelberg JM, Lee SH, Kaur M, Tang L, Feirt NM, McCabe S, et al. Platelet-derived growth factor-AB limits the extent of myocardial infarction in a rat model: feasibility of restoring impaired angiogenic capacity in the aging heart. *Circulation.* 2002;105:608-13.
  35. Khoshbin A, Leroux T, Wasserstein D, Marks P, Theodoropoulos J, Ogilvie-Harris D, et al. The efficacy of platelet-rich plasma in the treatment of symptomatic knee osteoarthritis: a systematic review with quantitative synthesis. *Arthroscopy.* 2013;29:2037-48.
  36. Chopin C, Geoffroy M, Kanagaratnam L, Dorilleau C, Ecarnot F, Siboni R, et al. Prognostic Factors Related to Clinical Response in 210 Knees Treated by Platelet-Rich Plasma for Osteoarthritis. *Diagnostics (Basel).* 2023;13:760.
  37. Wiciński M, Szwedowski D, Wróbel Ł, Jeka S, Zabrzyński J. The influence of body mass index on growth factor composition in the platelet-rich plasma in patients with knee osteoarthritis. *Int J Environ Res Public Health.* 2022;20:40.
  38. Bansal H, Leon J, Pont JL, Wilson DA, Bansal A, Agarwal D, et al. Platelet-rich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy. *Sci Rep.* 2021;11:3971.
  39. Pintat J, Silvestre A, Magalon G, Gadeau AP, Pesquer L, Perozziello A, et al. Intra-articular injection of mesenchymal stem cells and platelet-rich plasma to treat patellofemoral osteoarthritis: preliminary results of a long-term pilot study. *J Vasc Interv Radiol.* 2017;28:1708-13.
  40. Fernandez Cuadros ME, Albaladejo Florin MJ, Lopez RA, Perez Moro OS. Efficiency of platelet-rich plasma (PRP) compared to ozone infiltrations on patellofemoral pain syndrome and chondromalacia: a non-randomized parallel controlled trial. *diversity and equality in health and care.* 2017;14:203-11.
  41. El-Desouky II. Effectiveness of intra-articular injection of platelet-rich plasma in isolated patellofemoral arthritis. *The Egyptian Orthopaedic Journal.* 2022;57:152-6.
  42. Chouhan DK, Dhillon MS, Patel S, Bansal T, Bhatia A, Kanwat H. Multiple Platelet-Rich plasma injections versus single platelet-rich plasma injection in early osteoarthritis of the knee: an experimental study in a guinea pig model of early knee osteoarthritis. *Am J Sports Med.* 2019;47:2300-7.
  43. Lewis E, Merghani K, Robertson I, Mulford J, Prentice B, Mathew R, et al. The effectiveness of leukocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: the PEAK randomized controlled trial. *Bone Joint J.* 2022;104-B:663-71.
  44. Subramanyam K, Alguvelly R, Mundargi A, Khanchandani P. Single versus multi-dose intra-articular injection of platelet rich plasma in early stages of osteoarthritis of the knee: A single-blind, randomized, superiority trial. *Arch Rheumatol.* 2021;36:326-34.
  45. Varma HS, Lodhi JS, Vidyarthi A, Jayaprakasan V. Single versus three doses of intraarticular platelet-rich plasma injection in treatment of early osteoarthritis knee joint-a prospective comparative study. *international journal of recent surgical and medical sciences.* 2022;9:561-7.
  46. Frey C, Yeh PC, Jayaram P. Effects of antiplatelet and nonsteroidal anti-inflammatory medications on platelet-rich plasma: a systematic review. *Orthop J Sports Med.* 2020;8:2325967120912841.
  47. Schippinger G, Prüller F, Divjak M, Mahla E, Fankhauser F, Rackemann S, et al. Autologous platelet-rich plasma preparations: influence of nonsteroidal anti-inflammatory drugs on platelet function. *Orthop J Sports Med.* 2015;3:2325967115588896.

48. Nachmias VT, Sullender JS, Fallon JR. Effects of local anesthetics on human platelets: filopodial suppression and endogenous proteolysis. *Blood*. 1979;53:63–72.
49. Baria MR, Vasileff WK, Borchers J, DiBartola A, Flanigan DC, Plunkett E, et al. Treating knee osteoarthritis with platelet-rich plasma and hyaluronic acid combination therapy: a systematic review. *Am J Sports Med*. 2022;50:273-81.
50. Zhao J, Huang H, Liang G, Zeng LF, Yang W, Liu J. Effects and safety of the combination of platelet-rich plasma (PRP) and hyaluronic acid (HA) in the treatment of knee osteoarthritis: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2020;21:224.

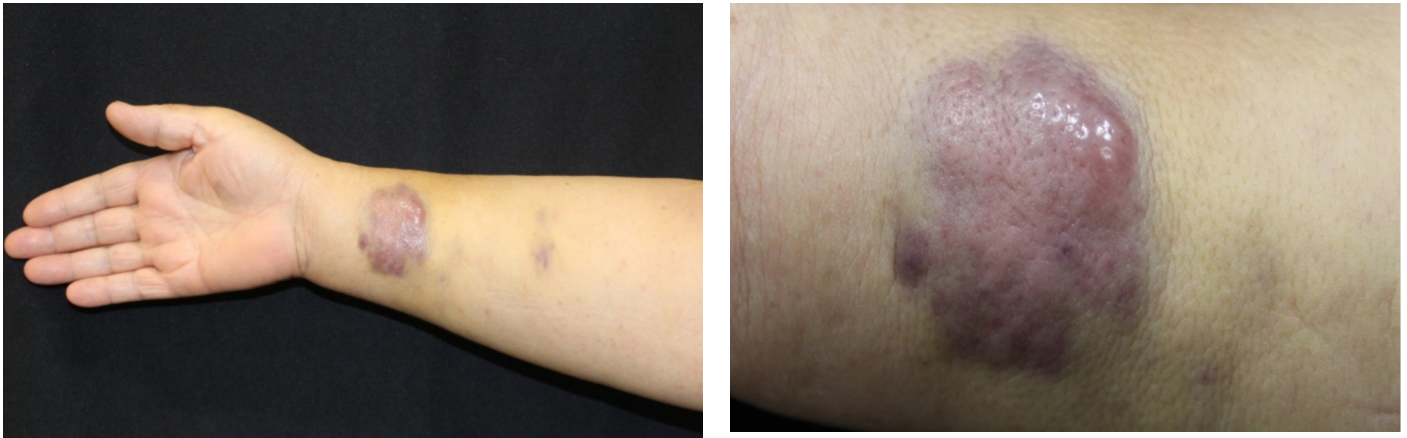
# Lymphangiosarcoma: A Tumoral Lesion Developing on the Forearm After Mastectomy

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**Keywords:** Forearm, nodule, lymphangiosarcoma



**Figure 1.** The indurated, irregular, blue-purple hard nodular lesion on the right forearm.

A 77-year-old female patient was admitted to our clinic due to swelling on the right forearm. The patient was diagnosed with breast cancer 10 years ago, and mastectomy was underwent. Additionally, all of the lymph nodes were removed. After that chemotherapy and radiotherapy were performed. In her dermatological examination, an indurated hard nodular lesion, approximately 5x5 cm in size, with irregular blue-purple borders was found on the ventral surface of the right forearm (Figure 1) (Necessary permissions were obtained from the patient and her children for verbal and visual sharing of the case).



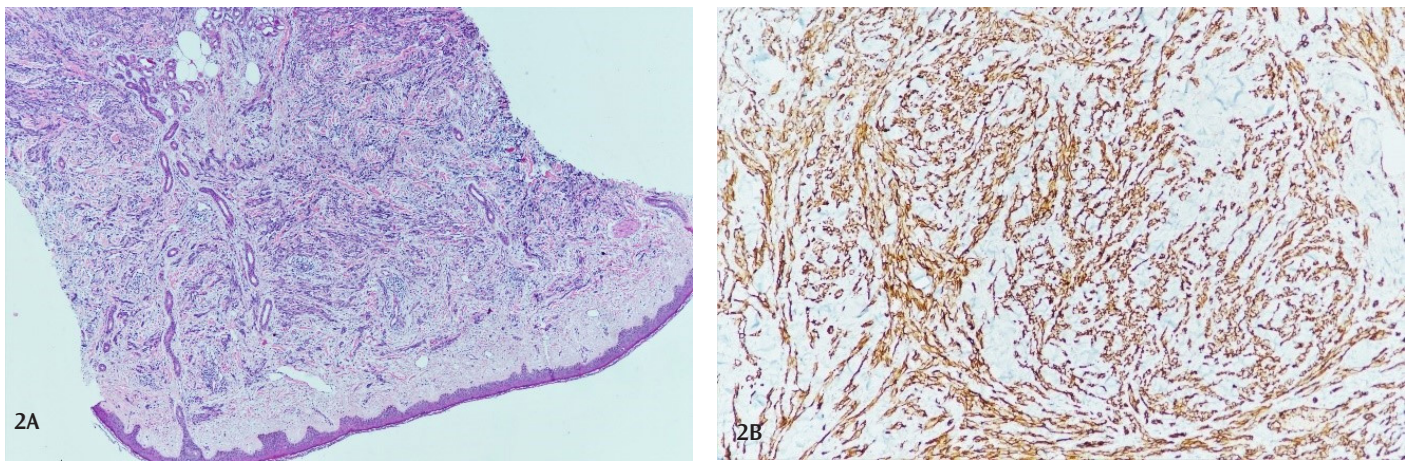
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**Figure 2.** (A, B) Histopathological image of the biopsy sample taken from the patient at 40 and 100 magnifications.

A 4mm punch biopsy sample was obtained from the lesion. Anastomosing vascular channel structures with infiltrative architecture located in the dermis were observed, HE staining x40 ( Figure 2A). Tumor cells with sometimes spindle-like, sometimes epithelioid appearance, pleomorphic, high atypia, and high mitotic activity were observed, Ki67 staining x100 (Figure 2B). Immunohistochemical examination revealed CD31 (scytex/EP78) positive, CD34 (Leica/ QBEnd-10) negative, Factor8 positive, D2 40 (/Cell-Marque/monoclonal positive, CKPan ( BioGenex/AE1-AE3) negative, HHV-8 (Cell-Marque /13b10) negative, Ki67 (Cell marque-SP6) 45-50% were detected (X20). The patient was diagnosed with lymphangiosarcoma based on these findings. She was referred to the Plastic Surgery Department for the operation. Our patient underwent “Transhumeral Amputation” in the plastic surgery department. The post-operative photo of the patient is shown in Figure 3.



**Figure 3.** Image of the patient’s arm a few days after the operation.

In cancers of bone and soft tissues, amputation may be performed for therapeutic purposes in cases where the tumor cannot be separated from the surrounding normal tissues. Transhumeral amputation can occur at any length of the humerus. The ideal level is 4-5 cm proximal to the elbow joint (1,2). Closed amputation; It is performed if there is enough skin tissue to cover the wound in the amputated area. After surgical limb amputation, the tissues and skin in the surgical wound are closed, and the amputation process is completed. Without leaving any open wounds (1,2). This surgical technique was also used in our case. In the literature, malignancies such as Kaposi’s sarcoma, squamous cell carcinoma, and malignant lymphoma and melanoma may develop on the basis of chronic lymphedema have been indicated (3,4). The development of lymphangiosarcoma has been reported in 10% of patients with lymphedema on the arms after mastectomy and lymphadenectomy. It is commonly used in seen on the proximal upper extremity, forearm, elbow, and anterior chest wall (5,6). The time from the formation of lymphedema to the development of lymphangiosarcoma is reported as approximately 5-27 years (7). In our case, this period was 10 years. Patients with lymphedema on their arms, especially after mastectomy, should be closely followed, and the necessary tests and examinations should be performed in the presence of suspicious lesions. Early diagnosis and treatment significantly affect patient prognosis and increase the chance of survival.



## Ethics

**Informed Consent:** Necessary permissions were obtained from the patient and her children for verbal and visual sharing of the case.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: E.H.T., S.Ö.A., Concept: E.H.T., S.Ö.A., Design: E.H.T., S.Ö.A., Data Collection or Processing: E.H.T., S.Ö.A., Analysis or Interpretation: E.H.T., S.Ö.A., Literature Search: E.H.T., N.Ö., S.E., S.T., İ.O.T., S.Ö.A., Writing: E.H.T., S.Ö.A.

**Conflict of Interest:** İlteriş Oğuz Topal, MD, is a Section Editor in the European Archives of Medical Research. She had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Other authors have nothing to disclose.

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## REFERENCES

1. <https://read.qxmd.com/read/19730305/targeted-reinnervation-for-transhumeral-amputees-current-surgical-technique-and-update-on-results?redirected=slug>
2. <https://read.qxmd.com/read/26527583/functional-and-clinical-outcomes-of-upper-extremity-amputation?redirected=slug>
3. Mizuno S, Yamada Y, Yamada K, Nomura N, Wakamatsu N. Clinical variability in a Japanese hereditary lymphedema type I family with an FLT4 mutation. *Congenit Anom (Kyoto)*. 2005;45:59-61.
4. Szuba A, Rockson SG. Lymphedema: classification, diagnosis and therapy. *Vasc Med*. 1998;3:145-56.
5. Komorowski AL, Wysocki WM, Mituś J. Angiosarcoma in a chronically lymphedematous leg: an unusual presentation of Stewart-Treves syndrome. *South Med J*. 2003;96:807-8.
6. Chung KC, Kim HJ, Jeffers LL. Lymphangiosarcoma (Stewart-Treves syndrome) in postmastectomy patients. *J Hand Surg Am*. 2000;25:1163-8.
7. Aygıt AC, Yildirim AM, Dervisoglu S. Lymphangiosarcoma in chronic lymphoedema. Stewart-Treves syndrome. *J Hand Surg Br*. 1999;24:135-7.

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