e-ISSN:2602-2079

Volume 9
Issue 10
2025

JOURNAL of Surgery and Medicine

International Medical Journal

JOSAM

Editorial Team

Kuwait City, Hawally, Kuwait
Website
Email

Fahmi Khan, MB, BS, CABMs
Hamad Medical Corporation | HMC
Department of Medicine (Hamad General Hospital)
Doha, Qatar
Website
Email

Elroy Patrick Weledji, Professor, BSc, MBBChBAO, MSc, FRCS(Edinburgh)
Department of Medicine
University of Buea
Buea, Cameroon
Website
Email

Prasenjit Das, Professor, MD, DNB, MNAMS, MNASc
Department of Pathology
All India Institute of Medical Sciences
New Delhi, India
Website
Email

Seyed Vahid Hosseini, Professor
Shiraz University of Medical Sciences, Shiraz, Iran
Website
Email

Vol. 9 No. 10 (2025)

Published: 2025-10-29

Research Article

Medical error tendency levels and associated factors in surgical nurses from different generations

Tendency to medical error levels and associated factors

Aylin Aydın Sayılan, Selin Orhan, Nurşen Kulakaç, Neriman Akyolcu

172-175

PDF 63 42 Citations 0

Comparison of triple triage system and CTAS (Canadian Triage and Acuity Scale) system in the emergency department

Triage and CTAS: Emergency department comparisons

Mehmet Koşargelir, Güleser Akpınar

176-180

PDF 206 62 Citations 0

Esophageal cancer surgery 5-year survival rate and predictors of operative mortality—a single-center analysis

Esophageal cancer surgery survival rate

Vítor Patrício Correia, José Paulo Freire, Luís Castro, Helder Matos, Andreia Barão, Teresa Braga, Rosário Rosa, Luís Miranda

181-186

PDF 112 97 Citations 0

Comparison of orally administered misoprostol and membrane sweeping for labor induction among women with singleton postdate pregnancies in South-South, Nigeria

Labor induction among women with singleton postdate pregnancies

Omonigho Esemuede, Osamudia Okhionkpamwonyi, Innocent Okoacha, Akhator Aimiehinor, Patrick Ifeanyi Okonta

187-192

PDF 49 17 Citations 0

Can the probe movement direction affect pain in patients undergoing transrectal ultrasound-guided prostate biopsy?

Probe direction and pain in prostate biopsy

Ali Akkoç, Murat Topçuoğlu, Murat Uçar, Erkan Karadağ, Semih Keskin, Deniz Demir

193-198

Review

Neurobiological and behavioral correlates of excessive social media use in adolescents

Impact of social media use on adolescents

Daniel Ogun

199-206

What are the applications of stem cell therapy for infertility? A literature review

What has been achieved so far in the field of reproductive medicine?

Nawar Al-khafaji

207-212

Case Report

Rare case of small bowel inflammatory myofibroblastic tumor

Rare small bowel inflammatory myofibroblastic tumor

Nemanja Trifunović, Nebojša Mitrović, Dejan Stevanović, Damir Jašarović, Jovana Trifunović

213-215

Omental torsion, a rare acute abdominal syndrome: A case report

Omental torsion

Tutkun Talih, Umut Sercan Eser, Kamile Eser, Gamze Talih

216-218

Deep venous thrombosis after brown recluse spider bite: A rare case report

DVT after brown recluse spider bite

Reshma Pydi, NFN Soumya, Sania Thite, Jigyasha Pradhan, Kaitlyn Hoyt, Hanasoge Girishkumar

219-221

J Surg Med. 2025;9(10):172-175.
https://doi.org/10.28982/josam.8142

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Research article
https://jsurgmed.com/

Medical error tendency levels and associated factors in surgical nurses from different generations

Aylin Aydın Sayılan [1], Selin Orhan [2], Nursen Kulakac [3], Neriman Akyolcu [4]

[1] Kirklareli University Faculty of Health Sciences, Nursing Department, Kirklareli, Turkey
[2] Kirklareli University Institute of Health Sciences, Nursing Department, Kirklareli, Turkey
[3] Gümüşhane University Faculty of Health Sciences, Nursing Department, Gümüşhane, Turkey
[4] İstinye University Faculty of Health Sciences, Nursing Department, İstanbul, Turkey

ORCID of the author(s)

AAS: https://orcid.org/0000-0003-0576-8732
SO: https://orcid.org/0009-0000-6543-5388
NK: https://orcid.org/0000-0002-5427-1063
NA: https://orcid.org/0000-0003-2194-8637

Corresponding Author
Aylin Aydin Sayilan
Kirklareli University Faculty of Health Science, Nursing Department, Kirklareli, Turkey
E-mail: aylin.sayilan@klu.edu.tr

Ethics Committee Approval
The study was approved by the Kırklareli University Health Sciences Institute ethical committee, Türkiye (PR0462R01-2023). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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

Published
2025 October 4

Abstract

Background/Aim: Since experience is acquired over time, characteristics deriving from intergenerational differences play an important role in medical errors. This study was performed to determine tendency to medical error levels and associated factors in surgical nurses from two different generations (Y and Z).

Methods: This cross-sectional, correlational study was conducted with 168 nurses working in a public and a training and research hospital between 1 May and 30 June, 2023, and selected using the random sampling method. A sociodemographic data form and the Medical Error Tendency Scale were employed for data collection. The data analysis was performed with number, percentage, and mean values and using Student's t test, ANOVA, and Pearson's correlation analysis.

Results: Seventy-two percent of the nurses were from Generation Y. Mean tendency to medical error scores were 231.23 (11.25) in the nurses from Generation Y and 225.59 (11.76) in those from Generation Z. The difference in mean total Medical Error Tendency Scale scores between the two generations was statistically significant (P=0.005). A significant difference in favor of Generation Y was observed in the Medical Error Tendency Scale 'drug and transfusion practices' (P=0.006), 'prevention of infections' (P=0.004), and 'patient monitoring and equipment safety' subdimensions (P=0.008). Nurses who enjoyed working in their clinics and who had sufficient sleep status also registered higher mean Medical Error Tendency Scale scores (P<0.05).

Conclusions: The nurses in this study exhibited a moderate tendency to medical error, the difference between the two groups being significantly in favor of Generation Y. Enjoying their work and sufficient sleep status had a positive effect on nurses' performance by reducing their tendency to medical error.

Keywords: surgical nurse, generational (Y, Z) difference, medical error, patient safety, nursing workforce

How to cite: Aydın Sayılan A, Orhan S, Kulakac N, Akyolcu N. Medical error tendency levels and associated factors in surgical nurses from different generations. J Surg Med. 2025;9(10):172-175.

Introduction

Medical error is defined as the exhibition of unethical behavior inappropriate to a professional providing a health service, with a patient suffering harm due to inadequate and/or neglectful behaviors in medical practice [1]. Incorrect medical practice emerges as the result of neglect, inattention, lack of knowledge, skills deficits, and inadequate patient care [2,3].

A retrospective study of medical errors between 2000 and 2007 determined that 49.4% of individuals exposed to such errors died, while 31.4% suffered disability. That research also showed that 13.4% of errors led to another disease and 1.7% to an infectious disease [4]. Although adequate and recent data concerning the reporting of medical errors in Türkiye are not fully available, studies of patient safety have increased in recent years. The Turkish Ministry of Health Safety Reporting System report and analysis for 2016 reported a medical error rate of approximately 16.6%, and concluded that this was compatible with those of other countries [5].

Preventing medical errors and the effects thereof is the main aim of patient safety. Preventing such errors before they affect patients is a responsibility incumbent on all health professionals. From that perspective, determining the attitudes of health professionals in different medical spheres is of great importance to lowering the rates of such errors, and thus ensuring patient safety and improving trust in health institutions [6]. Nurses, who constitute the majority of individuals working in health care, are more frequently at risk of medical errors due to factors such as their numerous dependent and independent tasks, their being in constant contact with patients, and intense working hours [7].

The most frequent error reports in the Turkish Ministry of Health Safety Reporting System report and analysis for 2016 were those deriving from nurses [5]. The reported causes of errors made by nurses include low numbers of working nurses, the imposition of non-core duty tasks, fatigue, and inexperience [8-11]. Previous studies have also shown that nurses with fewer years' professional experience have a greater tendency to medical errors [12].

Since experience is acquired over time, characteristics deriving from inter-generational differences play an important role in this process, and this also impacts on individuals' attitudes toward events, cases, and concepts. The essentially age-dependent concept of the 'generation' is applied to groups of individuals born within a specific period, who are affected by events within that time frame, and who share common characteristics and perspectives as a result. Generations' characteristics and expectations are reported to be capable of leading to intergenerational variation [13-15].

Different generations in nursing are affected by curriculum models that emphasize different aspects of care, and this can potentially increase inter-generation variation. When nurses from different generations work together, differences between them can therefore affect their professional well-being, performance, and productivity [16].

Although generations X, Y, and Z are currently actively present in the workforce, this study was performed for the purpose of determining differences in surgical nurses' tendency to medical errors and associated factors by examining generations Y and Z.

The research questions were;

1. What are nurses' tendency to medical error levels?
2. Do nurses' sociodemographic and working characteristics affect their tendencies to medical error?

Materials and methods

Type of research

This descriptive, correlational study was performed in order to determine the tendency to medical error levels and associated factors of surgical nurses from different generations.

Research Population and Sample

The research population consisted of nurses working in surgical clinics in Türkiye. Data were collected from nurses consenting to take part in the study between 01 May and 30 July, 2023, using the random sampling method. Data collection forms produced by means of Google Forms were sent to nurses' mobile phones via messaging software. The data from 168 nurses were included in the research. The inclusion criteria were voluntary participation in the study, age 18 years or older, working in a surgical unit, and answering all the questions fully. The response rate was 87.96%.

Data Collection Tools and Data Collection

The research data were collected using a nurse description form and the Medical Error Tendency Scale.

Nurse description form*:* This contained five questions investigating sociodemographic characteristics such as age, sex, marital status, sleep status, and contentment with working in the particular unit.

Medical Error Tendency Scale: This scale measures health professionals' tendencies to commit medical errors. This five-point Likert-type tool was developed by Özata and Altunkan and consists of 49 items [9]. The lowest possible score is 49 and the highest 245. The scale consists of five subdimensions – 'Drug and transfusion practices,' 'Prevention of infections,' 'Prevention of Falls,' 'Patient monitoring and equipment safety,' and 'Communication.' It has no cut-off point, but higher scores indicate a lower tendency among nurses to commit medical errors. The scale has a Cronbach alpha coefficient of 0.95 [9]. The Cronbach alpha coefficient in the present study was 0.93.

Ethical Considerations

Approval for the study was received from the Kırklareli University Health Sciences Institute ethical committee, Türkiye (PR0462R01-2023). Consent was received from all participants in the first part of the questionnaire prior to commencement. Participants were able to discontinue the questionnaire at any time, with no justification being required. The study was performed in compliance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed on Statistical Package for the Social Sciences (SPSS) version 23 software. Descriptive statistical methods such as frequency, percentage, mean, and standard deviation were employed during the data analysis, and the Kolmogorov-Smirnov test was used to examine normality of distribution. The data were found to be normally distributed. Relationships between nurses of different generations' descriptive characteristics and two or more variables were

evaluated using the chi-square test. Student's t test was applied to determine relationships between the nurses' scale scores and sociodemographic variables. Multivariate linear regression analysis (method: enter) was applied to identify factors associated with nurses' tendency to commit medical errors. *P*-values <0.05 were considered statistically significant.

Results

The mean age of the participants was 35.30 (8.72) years. Women represented 62.8% of the Generation Y nurses enrolled in the study and 72.3% of the Generation Z nurses. No statistically significant differences were determined between the generations in terms of sociodemographic characteristics (*P*>0.05) (Table 1).

The mean total Medical Error Tendency Scale scores of the nurses working in surgical units were 231.23 (11.25) for Generation Y and 225.59 (11.76) for Generation Z. The mean total score was significantly higher in the nurses from Generation Y (*P*=0.005) (Table 2).

A significant weak, positive correlation was observed between age and Medical Error Tendency Scale scores in the nurses working in surgical units (*P*<0.001) (Table 3).

The multilinear regression results show that the tendencies to commit medical errors of nurses working in surgical units were positively and significantly affected by age (VIF: 1.014), increased sleep hours (VIF: 1.057), and contentment with working in the particular unit (VIF:1.059) (*P*<0.05). These variables explained 15% of the total variance (Table 4).

Table 1: A comparison of the surgical unit nurses' demographic characteristics by generations (n=168)

		Generation Y (n=121)		Generation Z (n=47)		Statistics
		n	%	n	%	
Sex	**Female**	76	62.8	34	72.3	$\chi2$ =1.360
	Male	45	37.2	13	27.7	*P*=0.224
Marital status	**Married**	37	31.4	6	12.8	$\chi2$ =2.417
	Single	83	68.6	41	87.2	*P*=0.120
Sufficient sleep	**Yes**	17	14	6	9.9	$\chi2$ =0.047
	No	104	86	41	90.1	*P*=0.828
Content working in the unit	**Yes**	92	76	32	68.1	$\chi2$ =1.106
	No	29	24	15	31.9	*P*=0.293

Table 2: A comparison of surgical unit nurses' Medical Error Tendency Scale scores by generations

Medical Error Tendency Scale	Generation Y	Generation Z	Statistics
	Mean (SD	Mean (SD	
Drug and transfusion practices	82.19 (4.47	79.74 (4.41	*P*=0.006
Prevention of infections	58.00 (2.94	56.35 (3.58	*P*=0.004
Prevention of falls	24.01 (1.78	23.64 (1.84	*P*=0.157
Patient monitoring and equipment safety	42.85 (2.80	41.44 (3.04	*P*=0.008
Communication	24.49 (1.11	24.38 (1.04	*P*=0.473
Total score	231.55 (11.36	225.56 (11.28	*P*=0.005

Table 3: Correlations between surgical unit nurses' sociodemographic characteristics and Medical Error Tendency Scale scores

		1	2	3
(1)	**Medical Error Tendency Scale**	1		
(2)	**Age**	r=0.236 ***P*<0.001**	1	
(3)	**Weekly working hours**	r=-0.010 *P*=0.875	r=-0.153 *P*=0.157	1

Table 4: Multilinear regression analysis findings between surgical unit nurses' tendencies to medical errors and independent variables

Model	B	SE	β	t	*P*-value	VIF
Fixed	242.162	3.493		69.328	<0.001	
Age	4.186	1.496	0.159	2.798	0.006	1.014
Sleep hours	6.608	1.496	0.257	4.417	<0.001	1.057
Contentment with working in the unit	-4.902	1.476	-0.193	-3.322	0.001	1.059

Model R=0.388; R^2=0.150; Adjusted R^2=0.141; F=15.688; *P*<0.001; Durbin Watson=1.655. Independent variable: Medical Error Tendency Scale, Independent variables (contentment with working in the unit: 1 yes, 2 no)

Discussion

Generations are regarded as referring to a period of 15-20 years. The nurses in this study were from generations Y and Z.

The total Medical Error Tendency Scale scores of the surgical unit nurses in this study were significantly higher for the Generation Y nurses, at 231.23 (11.25), compared to those from Generation Y at 225.59 (11.76) (*P*=0.005). Differences in perception among nurses from different age groups and who were raised under different conditions also affect their attitudes toward medical errors. Generation Y is described as disposed to teamwork and self-confident [17]. Some studies have reported low tendencies to medical error levels irrespective of generations [2, 18-20], while one study reported a high medical error tendency [21]. However, there are also studies concluding that the age factor does not affect the tendency to medical error [22]. The variation in our study results may derive from the tendency to medical error being multifactorial in nature.

Tendencies to commit medical errors associated with drug and transfusion practices (*P*=0.006), prevention of infections (*P*=0.004), and patient monitoring and equipment safety (*P*=0.008) were lower in the nurses from Generation Y than in those from Generation Z. One study of tendencies to medical errors involving nurses and physicians reported that such errors most frequently involved administration of the wrong drug or administration to the wrong patient. The authors also concluded that age was not a factor affecting medical errors practices, and that the basic cause was lack of communication [23]. Similarly, another study reported that nurses most frequently committed drug administration errors, although errors involving sharp object injuries, the prevention of infections, and transfusion errors also occurred. Factors such as excessive workloads and lack of communication were described as the main causes of error [24]. Lack of communication may be the principal reason for nurses most frequently making errors in drug administration in those studies.

Due to the rapid development of the workforce and global change, workplaces can contain several different generations. There are approximately 20 years between each generation, and perspectives change according to life events. Specifically in terms of nursing, research has reported inter-generation differences in areas such as leadership, patient safety, flexibility and accessibility, and professional approach. It is important for managers and leaders to consider these difference in the workplace and to make arrangements accordingly [25, 26].

A significant weak, positive correlation was observed between age and Medical Error Tendency Scale scores among the surgical unit nurses in this study, with older nurses exhibiting lower tendencies to medical error. In their study examining surgical nurses' attitudes and tendencies to medical errors, Kandemir and Yüksel [22] reported significantly lower tendencies to such errors among nurses aged 35 or older. Another study from the Turkish Republic of Northern Cyprus also reported that the tendency to medical error decreased in line with factors such as age and work experience [24]. A different study reported a lower tendency to medical errors among individuals with 13 or more years' professional experience [27]. Our findings are compatible with the previous literature and suggest that the tendency to

medical error is positively affected by factors such as age and greater professional experience.

Multilinear regression analysis showed that the tendency to medical error among surgical unit nurses was positively and significantly affected by greater age, increased sleep hours, and contentment with working in the particular unit. These variables explained 15% of the total variance. A Japanese study investigating the importance of nurse health and its potential impact on patient services found that insufficient sleep, shift working, and poor mental health increased the tendency to medical error [28]. Another study, involving nurses working in Canada, also found a lower medical error rate among individuals who enjoyed their work and reported a healthy working environment [29]. Other research from Australia, a county where tendencies to medical errors appear to be widespread, reported a significant increase in such tendencies among nurses with lengthy experience in the profession and those with insufficient sleep [30]. Studies have shown that sleep adequacy also affects job satisfaction. It is important to plan appropriate measures and to regulate nurses' working hours to ensure that they obtain enough sleep [31,32]. Our finding was consistent with the previous literature and showed that the tendency to medical error is positively affected by such factors as age, sufficient sleep, and contentment with one's work.

Limitations

The data from this research involve only two hospitals and are cross-sectional in nature. They cannot therefore be generalized to all surgical unit nurses. Additionally, the method of survey distribution (Google Forms) may introduce potential biases.

Conclusion

The tendency to medical error in this study was at a moderate level, and Generation Y exhibited a better performance than Generation Z. Greater age, sufficient sleep, and contentment with working in their particular unit reduced nurses' tendencies to medical error. Considering the high circulation in surgical unit staff, and that these may have a high tendency to medical errors, it is of great importance that nurses' generational differences be taken into account. We would also recommend that nurses work in the units they prefer, that their working hours be regulated, and that obstacles to their obtaining sufficient sleep be identified. Finally, we recommend that further studies involving different generations and wider samples now be performed.

References

1. The Joint Commission, 2010. Available from: https://www.jointcommission.org/about/jointcommissionfaqs.aspx?faq#324. Accessed: 20 October 2023.
2. Ta'an W. Medical error prevalence, nursing power, and structural empowerment: A serial mediation analysis. Scientific World Journal. 2024;1554373. doi: 10.1155/2024/1554373.
3. Gaffney TA, Hatcher BJ, Milligan R. Nurses' role in medical error recovery: an integrative review. J Clin Nurs. 2016;25(7-8):906-17. doi: 10.1111/jocn.13126.
4. Ertem G, Oksel E, Akbıyık A. Hatalı tıbbi uygulamalar (malpraktis) ile ilgili retrospektif bir inceleme. Dirim Tıp Dergisi. 2009;84(1):1-10.
5. Turkish Ministry of Health. GRS Güvenlik raporlama sistemi 2016 yılı istatistik ve analiz raporu, 2016. Available from: http://grs.saglik.gov.tr/BM/Reports/GRS2016rapor_R1.pdf. Accessed: 22 April 2023.
6. Kalra J, Kalra N, Baniak N. Medical error, disclosure and patient safety: a global view of quality care. Clin Biochem. 2013;46(13-14):1161-9. doi: 10.1016/j.clinbiochem.2013.03.025.
7. Oliveira AC, Garcia PC, Nogueira LS. Nursing workload and occurrence of adverse events in intensive care: a systematic review. Rev Esc Enferm USP. 2016;50(4):683-94. doi: 10.1590/S0080-623420160000500020.
8. Al-Kandari F, Thomas D. Adverse nurse outcomes: correlation to nurses' workload, staffing, and shift rotation in Kuwaiti hospitals. Applied Nursing Research. 2008;21:139-46.
9. Özata M, Altunkan H. Frequency of medical errors in hospitals, determination of medical error types and medical errors: Konya sample. Medical Research Journal. 2010;8(2):100-11.
10. Mauti G, Githae M. Medical error reporting among physicians and nurses in Uganda. Afr Health Sci. 2019;19(4):3107-17. doi: 10.4314/ahs.v19i4.33.
11. Mohsenpour M, Hosseini M, Abbaszadeh A, Shahboulaghi FM, Khankeh H. Nursing error: an integrated review of the literature. Indian J Med Ethics. 2017;2(2):75-81. doi: 10.20529/ijme.2017.020.
12. Dikmen DY, Yorgun S, Yeşilçam N. Hemşirelerin tıbbi hatalara eğilimlerinin belirlenmesi. Hacettepe Üniversitesi Hemşirelik Fakültesi Dergisi. 2014;32(1):44-56.
13. So Hee L, Yeojin Y. Work values and communication styles among Generation X, Y, and Z nurses: A cross-sectional study. Int Nurs Rev. 2024;71(1):115-21. doi: 10.1111/inr.12863.
14. Şenturan Ş, Köse A, Dertli E, Başak S, Şentürk N. X ve Y kuşağı yöneticilerinin iş değerleri algısı ve farklılıkları üzerine inceleme. Business & Economics Research Journal. 2016;7(3):171-82.
15. Tan SHE, Chin GF. Generational effect on nurses' work values, engagement, and satisfaction in an acute hospital. BMC Nurs. 2023;22(1):88. doi: 10.1186/s12912-023-01256-2.
16. Grubb VM. The new workplace reality. In clash of the generations. Hoboken, NJ, USA: John Wiley & Sons, 2016.
17. Haydari SM, Kocaman G, Tokat MA. Farklı kuşaklardaki hemşirelerin işten ve meslekten ayrılma niyetleri ile örgütsel ve mesleki bağlılıklarının incelenmesi. Sağlık ve Hemşirelik Yönetimi Dergisi. 2016;3(3):119-31.
18. Işık Andsoy I, Kar G, Öztürk Ö. Hemşirelerin tıbbi hata eğilimlerine yönelik bir çalışma. Sağlık Bilimleri Ve Meslekleri Dergisi. 2015;1(1):17-27. doi: 10.17681/hsp.06267.
19. Yüksel A, Akbulut T, Bahadır Yılmaz E. Hemşirelerde stresle baş etme ve tıbbi hataya eğilim düzeyleri arasındaki ilişkinin belirlenmesi. Sağlık Akademisyenleri Dergisi. 2016;6(4):288-94.
20. Karacabay K, Savcı A, Çömez S, Çelik N. Cerrahi hemşirelerinin iş yükü algilari ile tıbbi hata eğilimleri arasindaki ilişkinin belirlenmesi. Mersin Üniversitesi Sağlık Bilimleri Dergisi. 2020;13(3):404-17.
21. Şahin ZA, Özdemir FK. Hemşirelerin tıbbi hata yapma eğilimlerinin incelenmesi. Hemşirelikte Eğitim ve Araştırma Dergisi. 2015;12(3):210-4.
22. Kandemir A, Yüksel S. Cerrahi hemşirelerinin tıbbi hata tutum ve eğilimlerinin belirlenmesi. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi, 2020;23(2):287-9.
23. Topcu I, Turkmen AS, Sahiner NC, Savaser S, Sen H. Physicians' and nurses' medical errors associated with communication failures. J Pak Med Assoc. 2017;67(4):600-4.
24. Bilgic N, Altun S. Determination of nurses' tendency to medical error and the factors affecting this in the Turkish Republic of Northern Cyprus. J Pak Med Assoc. 2022;72(7):1335-9.
25. Stevanin S, Voutilainen A, Bressan V, Vehviläinen-Julkunen K, Rosolen V, Kvist T. Nurses' generational differences related to workplace and leadership in two European Countries. West J Nurs Res. 2020;42(1):14-23.
26. Huber P, Schubert HJ. Attitudes about work engagement of different generations-A cross-sectional study with nurses and supervisors. J Nurs Manag. 2019;27(7):1341-50.
27. Özen N, Onay T, Terzioğlu F. Hemşirelerin tıbbi hata eğilimlerinin ve etkileyen faktörlerin belirlenmesi. Sağlık Bilimleri ve Meslekleri Dergisi. 2019;6(2):283-92.
28. Arimura M, Imai M, Okawa M, Fujimura T, Yamada N. Sleep, mental health status, and medical errors among hospital nurses in Japan. Ind Health. 2010;48(6):811-7.
29. Phillips LA, de Los Santos N, Ntanda H, Jackson J. The impact of the work environment on the health-related quality of life of Licensed Practical Nurses: a cross-sectional survey in four work environments. Health Qual Life Outcomes, 2022;20(1):44.
30. Dorrian J, Lamond N, van den Heuvel C, Pincombe J, Rogers AE, Dawson D. A pilot study of the safety implications of Australian nurses' sleep and work hours. Chronobiol Int. 2006;23(6):1149-63.
31. Labrague LJ. Pandemic fatigue and clinical nurses' mental health, sleep quality and job contentment during the covid-19 pandemic: The mediating role of resilience. J Nurs Manag. 2021;29(7):1992-2001.
32. Karagozoglu S, Bingöl N. Sleep quality and job satisfaction of Turkish nurses. Nurs Outlook. 2008;56(6):298-307.e3.

J Surg Med. 2025;9(10):176-180.
https://doi.org/10.28982/josam.8315

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Research article
https://jsurgmed.com/

Comparison of triple triage system and CTAS (Canadian Triage and Acuity Scale) system in the emergency department

Mehmet Koşargelir, Güleser Akpınar

Istanbul Başakşehir Çam and Sakura City Hospital Emergency Medicine Department, Istanbul, Turkey

ORCID of the author(s)

MK: https://orcid.org/0000-0003-1948-022X
GA: https://orcid.org/0000-0001-8559-5098

Corresponding Author
Güleser Akpınar
Istanbul Başakşehir Çam and Sakura City Hospital Emergency Medicine Department, Basaksehir Neighborhood G-434 Street No: 2L Postal Code: 34480 Basaksehir, Istanbul, Turkey
E-mail: guleserakpinarduman@gmail.com

Ethics Committee Approval
The study was approved by the Istanbul Medipol University Ethics Committee on June 29, 2021 with decision number 765.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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

Published
2025 October 3

Abstract

Background/Aim: Triage systems are crucial for determining patient care priorities and efficiently utilizing resources in emergency departments. The aim of this study is to compare the effectiveness of the three-stage triage system (TR) and the Canadian Triage and Acuity Scale (CTAS) system in terms of patient safety, resource management, and alignment with expert opinions in an adult emergency department.

Methods: A prospective, cross-sectional, single-blind clinical study was conducted in an adult emergency department between October 1 and October 15, 2021. Patients aged 15 years and older with a Glasgow Coma Scale (GCS) score of 15 were included in the study. Trauma patients, patients transported by ambulance, and patients under 15 years of age were excluded from the study.

CTAS was applied by a single emergency medicine resident on odd days of the month, while TR was applied on the even days. The specialist physician who provided the reference triage categories was unaware of the initial assessments. Primary outcomes included inter-rater agreement (weighted kappa coefficient), triage accuracy, and resource utilization patterns. Statistical analysis used the Kruskal-Wallis H test, Fisher's exact test, and a weighted kappa coefficient with a significance level set at $P<0.05$.

Results: A total of 620 patients were evaluated (TR: n=290, CTAS: n=330). CTAS demonstrated significantly higher agreement with expert opinion compared to TR ($\kappa=0.375$, $P<0.001$) ($\kappa=0.835$, $P<0.001$). In CTAS, the rate of inadequate triage was significantly lower (12%) compared to TR (28%). CTAS demonstrated a more balanced patient distribution across emergency levels and rational resource utilization, resulting in appropriate requests for radiological examinations at T3 level (32.35% compared to 78.95% in the yellow zone of TR, $P<0.001$). Hospital admission rates were higher in CTAS (seven patients) compared to TR (one patient).

Conclusion: The CTAS system demonstrated significantly higher compliance and lower triage error rates compared to the TR system, with expert consensus, thereby showing superior performance in terms of patient safety and resource management. The implementation of CTAS in emergency departments may improve the quality of patient care and optimize resource utilization.

Keywords: CTAS Emergency, TR, Triage

How to cite: Koşargelir M, Akpınar G. Comparison of triple triage system and CTAS (Canadian Triage and Acuity Scale) system in the emergency department. J Surg Med. 2025;9(10):176-180.

Introduction

Triage in emergency departments is crucial for determining the priority of patient care and efficiently utilizing resources [1,2]. Due to increasing patient volumes and limited resources, the use of an accurate and reliable triage system has become increasingly important [3].

Among the triage systems widely used worldwide are the three-phase triage system (TR), the Australian Triage Scale (ATS), the Manchester Triage System (MTS), the Emergency Severity Index (ESI), and the Canadian Triage and Acuity Scale (CTAS) [4,5]. Each system has its own advantages and disadvantages. The TR triage system is preferred for its simplicity and quick implementation, while its five-point system provides a more detailed assessment [6,7].

CTAS is an internationally recognized triage system developed in Canada in the late 1990s [8]. Its reliability and validity have been studied in many countries, with high agreement rates reported [9,10]. CTAS has been shown to be particularly successful in predicting patient outcomes and resource utilization [11,12].

The TR system is widely used, particularly in developing countries and busy emergency departments [13]. Its main advantages include simplicity, ease of understanding, minimal training requirements, and rapid implementation. However, insufficient detail in patient assessment and low triage risk are considered disadvantageous [14].

Studies comparing triage systems have generally focused on the reliability, validity, and resource utilization of the systems [15]. In recent years, with the increasing importance of patient safety, the rates of inadequate triage and overtriage have also been closely examined [16]. Inadequate triage refers to the low-priority assessment of high-risk patients, while overtriage refers to the high-priority assessment of low-risk patients [17].

The aim of this study was to compare the effectiveness of the TR and CTAS triage systems in an adult emergency department in terms of patient safety, resource management, and compliance with expert opinions.

Materials and methods

Study Design and Population:

This prospective, cross-sectional, single-blind clinical study was conducted in the adult emergency department of Haydarpaşa Numune Training and Research Hospital. Ethical approval was obtained from the Istanbul Medipol University Ethics Committee on June 29, 2021 with decision number 765. The study was conducted between October 1 and October 15, 2021, from 8:00 a.m. to 5:00 p.m. A total of 10,833 patients who presented to the emergency department during the study period were evaluated, of whom 3,136 were patients who presented during the specified hours.

Inclusion and Exclusion Criteria: Patients with a Glasgow Coma Scale (GCS) score of 15, aged 15 years or older, and who consented to participate in the study were included. Trauma patients, patients transported by ambulance, medical cases under the age of 15, and patients who refused to participate in the study were excluded.

Application Protocol

Triage assessments were performed by a single emergency medical technician trained in both triage systems. The CTAS triage system was applied on odd days of the month (1, 3, 5...), and the TR triage system was applied on even days (2, 4, 6...).

The specialist physician assigning the reference triage category was not informed of the initial triage assessment performed by the assistant. Vital signs and clinical assessments were performed using standard protocols.

Clinical Assessment Parameters

- Pulse: 60–100 beats/minute (normal range)
- Respiratory rate: >20/min considered abnormal
- Body temperature: 36–37.5°C (normal range)
- Oxygen saturation: <95% abnormal for TR system, <92% abnormal for CTAS
- Pain assessment: 1–3 (mild), 4–7 (moderate), 8–10 (severe)

Oxygen saturation measurements were performed using the MD300C2 finger-type pulse oximeter device manufactured by Beijing Choice Electronic Technology Co., Ltd. (Beijing, China).

Data Collection and Evaluation

Demographic information, clinical complaints, applied triage system, triage category, laboratory and imaging tests, consultation requirements, treatment methods, and discharge status from the emergency department were recorded using a standard data collection form. Patient admission complaints were classified according to the clinical categories provided in Table 1.

The final treatment and follow-up category was determined by an independent specialist physician based on a comprehensive patient assessment, final diagnosis, and actual status (discharge, admission to the ward, admission to the intensive care unit). This served as the reference standard for measuring triage accuracy.

After patients were discharged from the emergency department, the triage categories determined by the triage physician and the specialist physician were compared using a weighted kappa coefficient. Differences between the final treatment area category and the initial triage category were classified as “overtriage” and “undertriage.”

Triage Accuracy Assessment

Overtriage: The triage category assigned during the initial assessment is higher (more urgent) than the final treatment and follow-up area category.

Undertriage: The triage category assigned during the initial assessment is lower (less urgent) than the final treatment and follow-up area category.

Statistical analysis

SPSS version 23 (SPSS Inc., Armonk, NY) software was used for statistical analysis. For the comparison of TR and CTAS levels, the Kruskal-Wallis H test, a non-parametric test, was applied with post-hoc analysis using the adjusted Dunn test. Fisher's exact test was used to evaluate the relationships between categorical variables. The weighted kappa coefficient was calculated to evaluate the agreement of triage systems with expert consensus. The statistical significance level was set at $P<0.05$.

Results

Demographic Characteristics and Triage Distribution

A total of 620 patients were evaluated in the study. The TR group included 290 patients (mean age 44.60 [19.06], 57.93% female) and the CTAS group included 330 patients (mean age 46.61 [19.63], 52.73% female).

In the TR triage system, most patients were classified as green code (86.55%, n=251), while fewer patients were classified as yellow (12.07%, n=35) and red (1.38%, n=4) categories. In contrast, the CTAS system showed a more balanced distribution of emergency levels: T5 Non-urgent (58.79%, n=194), T4 Non-urgent (20.00%, n=66), T3 Urgent (17.27%, n=57), T2 Urgent (3.03%, n=10), and T1 Resuscitation (0.91%, n=3) (Table 2).

Gender distributions were similar across triage categories in both systems. In the TR system, patients in the yellow category were significantly younger than those in the green category (P<0.001), while no significant age differences were observed between categories in the CTAS system.

The five most common complaints in both systems were muscle pain, ENT issues, extremity problems, abdominal pain, and eye problems; detailed distributions are presented in Table 3.

Triage Consistency and Accuracy

The CTAS system demonstrated significantly higher consistency compared to the TR system when compared to expert opinion (κ=0.375, P<0.001) (κ=0.835, P<0.001). In the TR system, 80 of the 251 patients initially classified as green were upgraded to yellow following expert review, indicating significant inadequacy in triage (Table 4). In the CTAS system, only 34 of the 194 patients classified as T5 were revised to T4, demonstrating superior accuracy (Table 5). The triage deficiency rate in the TR system (28%) poses a significant patient safety concern compared to CTAS (12%).

This difference highlights the superior reliability of the CTAS system in accurately determining patient urgency levels.

Resource Utilization Models

Analysis of examination request patterns revealed that CTAS demonstrated a more rational approach to resource utilization. In the CTAS system, radiological examination requests for T3 emergency patients were significantly higher than other levels (78.95; P<0.001), while consultation requests were appropriately lower at the T5 level compared to higher urgency levels (P<0.001).

In the TR system, fewer laboratory tests were requested for yellow-coded patients than expected (P<0.001), while more consultation requests were made for red-coded patients (P=0.01). In CTAS, laboratory tests showed an appropriate distribution without significant differences across all levels (P=0.82) (Table 6).

Clinical Outcomes

In terms of patient discharge, 319 patients were discharged, seven patients were admitted, two patients were transferred, and two patients refused treatment in the CTAS group. In the TR group, 287 patients were discharged, one patient was admitted, and two patients refused treatment. The higher admission rate in the CTAS group indicates that patients requiring inpatient treatment were identified more effectively.

Table 1: Complaints of patients included in the study

Abscess and local infection	**Muscle pain**
Headache	ENT problems
Dizziness	Eye problems
Skin problems	Abdominal pain
Palpitations	Bites and stings
Dyspnoea	Vomiting diarrhea
Extremity problems	Syncope
Chest pain	Urinary problems
Pregnancy-gynecological problems	Psychiatric problems
Neurological conditions	GI bleeding-diabetes

ENT problems: Ear, nose and throat problems, GI bleeding: Gastrointestinal bleeding

Table 2: Gender and age characteristics of TR and CTAS groups

System/Category	Female n(%)	Male n(%)	χ^2; P_1	Age, years Median (IQR)	χ^2; P_2
TR					
Emergent	2 (50)	2 (50)	2.02; 0.404	38.00 (9.25-45.75)[a*b]	13.94; 0.001
Urgent	24 (68.57)	11 (31.43)		32.00 (17.00-46.00)[b]	
Standard	142 (56.57)	109 (43.43)		45.00 (31.00-61.00)[a]	
CTAS					
Resuscitation	1 (33.33)	2 (66.67)	1.07; 0.923	22.00 (22.00-67.00)*	6.94; 0.074
Emergent	5 (50)	5 (50)		59.50 (43.75-79.00)	
Urgent	28 (49.12)	29 (50.88)		48.00 (25.00-60.50)	
Less Urgent	36 (54.55)	30 (45.45)		42.00 (29.00-60.25)	
Non-Urgent	104 (53.61)	90 (46.39)		48.00 (31.75-61.25)	

*Categorical data presented as number and percentage, continuous data as median (IQR). p_1: Fisher's exact test, p_2: Kruskal Wallis H test (Post-Hoc: Adj. Dunn's test; a,b: indicates significant difference between groups marked with different letters, P<0.05). *Not included in analysis due to insufficient observations.*

Table 3: Distribution of presenting complaints

Presenting Complaint	TR n(%)	CTAS n(%)
Headache	10 (3.45)	15 (4.55)
Dizziness	6 (2.07)	7 (2.12)
Muscle pain	40 (13.79)	57 (17.27)
ENT problems	35 (12.07)	28 (8.48)
Palpitations	3 (1.03)	1 (0.30)
Dyspnea	18 (6.21)	18 (5.45)
Chest pain	8 (2.76)	10 (3.03)
Eye problems	18 (6.21)	26 (7.88)
Abdominal pain	27 (9.31)	16 (4.85)
Extremity problems	22 (7.59)	33 (10.00)
Falls	12 (4.14)	17 (5.15)
Skin problems	18 (6.21)	8 (2.42)
Bites and stings	15 (5.17)	19 (5.76)
Vomiting-Diarrhea	8 (2.76)	7 (2.12)
Syncope	6 (2.07)	7 (2.12)
Abscess and local infection	4 (1.38)	4 (1.21)
Urinary problems	16 (5.52)	23 (6.97)
Pregnancy and gynecological problems	5 (1.72)	1 (0.30)
Psychiatric problems	2 (0.69)	1 (0.30)
Diabetes	0 (0.00)	1 (0.30)
GI bleeding	0 (0.00)	1 (0.30)
Neurological complaints	2 (0.69)	1 (0.30)
Seizure	0 (0.00)	1 (0.30)
Foreign body aspiration	0 (0.00)	1 (0.30)
Test request	14 (4.83)	21 (6.36)
Admission request	0 (0.00)	2 (0.61)

ENT problems: Ear, nose and throat problems, GI bleeding: Gastrointestinal bleeding

Table 4: TR and Expert consensus comparison

TR Category	Expert Consensus			
	Emergent	Urgent	Standard	Total
Emergent	4	0	0	4
Urgent	0	35	0	35
Standard	0	80	171	251
Total	**4**	**115**	**171**	**290**

Weighted Kappa = 0.375; P <0.001

Table 5: CTAS and Expert consensus comparison

CTAS Category	Expert Consensus					
	Resuscitation	Emergent	Urgent	Less Urgent	Non-Urgent	Total
Resuscitation	3	0	0	0	0	3
Emergent	0	10	0	0	0	10
Urgent	0	0	57	0	0	57
Less Urgent	0	0	0	66	0	66
Non-Urgent	0	0	0	34	160	194
Total	**3**	**10**	**57**	**100**	**160**	**330**

Weighted Kappa = 0.835; P <0.001

Table 6: Distribution of Laboratory Tests, Radiological Examinations and Consultation

Requirements According to TR and CTAS Triage Categories

	Laboratory examination		Radiological examination		Consultation	
	No	Yes	No	Yes	No	Yes
TR						
Emergent	1 (25.00)	3 (75.00)[a]	1 (25.00)	3 (75.00)	1 (25.00)	3 (75.00)[a]
Urgent	30 (88.24)	4 (11.76)[b]	23 (67.65)	11 (32.35)	30 (88.24)	4 (11.76)[b]
Standard	135 (54.00)	115 (46.00)[a]	151 (60.40)	99 (39.60)	182 (72.80)	68 (27.20)[a,b]
Total	166 (57.64)	122 (42.36)	175 (60.76)	113 (39.24)	213 (73.96)	75 (26.04)
X^2; *P*	17.52; <0.001		2.69; 0.245		8.18; 0.013	
CTAS						
Resuscitation	1 (33.33)	2 (66.67)	1 (33.33)	2 (66.67)[a,b]	0 (0.00)	3 (100.00)[a]
Emergent	4 (40.00)	6 (60.00)	4 (40.00)	6 (60.00)[a,b]	5 (50.00)	5 (50.00)[a,b]
Urgent	30 (52.63)	27 (47.37)	12 (21.05)	45 (78.95)[a]	29 (50.88)	28 (49.12)[a]
Less Urgent	37 (56.06)	29 (43.94)	42 (63.64)	24 (36.36)[b]	49 (74.24)	17 (25.76)[a,b]
Non-Urgent	107 (55.15)	87 (44.85)	122 (62.89)	72 (37.11)[b]	157 (80.93)	37 (19.07)[b]
Total	179 (54.24)	151 (45.76)	181 (54.85)	149 (45.15)	240 (72.73)	90 (27.27)
X^2; *P*	1.67; 0.817		35.59; <0.001		28.43; <0.001	

Discussion

The CTAS system demonstrated significantly higher agreement with expert opinion (κ=0.84) compared to the TR system (κ=0.38), indicating the superior reliability of the five-level triage system. This finding is consistent with previous multicenter studies reporting consistently high reliability rates for CTAS across various healthcare settings [4,18].

The significant difference in lower triage rates between TR (28%) and CTAS (12%) represents a critical advantage in terms of patient safety. Sub-triage poses significant risks by causing delays in appropriate care for patients with high urgency. The lower sub-triage rate observed with CTAS is consistent with previous studies emphasizing the importance of minimizing this risk for optimal patient outcomes [11,19].

Resource utilization analysis demonstrates that CTAS promotes more rational allocation of healthcare resources. The significantly higher rate of radiological examinations in T3 patients compared to lower urgency levels indicates the system's ability to align resource intensity with patient urgency appropriately. This contrasts with the TR system, where resource allocation models are less aligned with patient needs.

The more balanced patient distribution observed in CTAS compared to the patient distribution concentrated in the green category in TR indicates that the five-level system provides more detailed patient categorization. This enhanced level of detail enables better resource planning and workflow management in emergency departments [20].

While the TR system offers advantages in terms of simplicity and rapid implementation, these advantages should be evaluated in comparison with proven patient safety concerns and inadequate resource utilization models. The learning curve and implementation time required for CTAS can be overcome with structured training programs, as demonstrated in previous implementation studies [7].

Limitations

This study was conducted at a single center and only during daytime hours, which may limit its generalizability to different implementation settings and patient populations. The design, which varied the days, minimized bias but may have introduced temporal differences in patient presentations. Future multicenter studies including night shift evaluations will strengthen the evidence base for triage system comparisons.

Conclusion

This study demonstrates that the CTAS system significantly outperformed the TR system in several critical areas of emergency department operations. Superior alignment with expert opinions, significantly lower triage error rates, and more rational resource utilization models supported the implementation of CTAS in emergency departments aiming to optimize patient safety and operational efficiency.

The findings indicated that while the TR system offered simplicity in practice, the advantages demonstrated by CTAS in patient safety and resource management justify the additional training and implementation requirements. Healthcare institutions considering triage system optimization should prioritize patient safety outcomes and resource efficiency over ease of implementation.

Future research should focus on validating these findings in a multicenter setting and exploring implementation strategies that can facilitate the successful adoption of CTAS while minimizing transition challenges.

References

1. Farrohknia N, Castrén M, Ehrenberg A, Lind L, Oredsson S, Jonsson H, et al. Emergency department triage scales and their components: a systematic review of the scientific evidence. Scand J Trauma Resusc Emerg Med. 2011;19(1):42.
2. Christ M, Grossmann F, Winter D, Bingisser R, Platz E. Modern triage in the emergency department. Dtsch Arztebl Int. 2010;107(50):892-8.
3. Bullard MJ, Unger B, Spence J, Grafstein E, CTAS National Working Group. Revisions to the Canadian emergency department triage and acuity scale (CTAS) adult guidelines. CJEM. 2008;10(2):136-42.
4. Dong SL, Bullard MJ, Meurer DP, Blitz S, Ohinmaa A, Holroyd BR, et al. Reliability of computerized emergency triage. Acad Emerg Med. 2006;13(3):269-75.
5. Bullard MJ, Chan T, Brayman C, Warren D, Musgrave E, Unger B; Members of the CTAS National Working Group. Revisions to the Canadian Emergency Department Triage and Acuity Scale (CTAS) Guidelines. CJEM. 2014 Nov;16(6):485-9.
6. Fernandes CM, Tanabe P, Gilboy N, Johnson LA, McNair RS, Rosenau AM, et al. Five-level triage: a report from the ACEP/ENA Five-level Triage Task Force. J Emerg Nurs. 2005;31(1):39-50.
7. Beveridge R, Ducharme J, Janes L, Beaulieu S, Walter S. Reliability of the Canadian emergency department triage and acuity scale: interrater agreement. Ann Emerg Med. 1999;34(2):155-9.
8. Van der Wulp I, Van Baar ME, Schrijvers AJP. Reliability and validity of the Manchester Triage System in a general emergency department patient population in the Netherlands: results of a simulation study. Emerg Med J. 2008;25(7):431-4.
9. Storm-Versloot MN, Ubbink DT, Kappelhof J, Luitse JS. Comparison of an informally structured triage system, the emergency severity index, and the manchester triage system to distinguish patient priority in the emergency department. Acad Emerg Med. 2011;18(8):822-9.
10. FitzGerald G, Jelinek GA, Scott D, Gerdtz MF, Jelinek GA, Knott J, et al. Emergency department triage revisited. Emerg Med J. 2010;27(2):86-92.
11. Grossmann FF, Zumbrunn T, Frauchiger A, Delport K, Bingisser R, Nickel CH. At risk of undertriage? Testing the performance and accuracy of the emergency severity index in older emergency department patients. Ann Emerg Med. 2012;60(3):317-25.
12. Gräff I, Goldschmidt B, Glien P, Bogdanow M, Fimmers R, Hoeft A, et al. The German Version of the Manchester Triage System and its quality criteria--first assessment of validity and reliability. PLoS One. 2014;9(2):e88995.
13. Kuriyama A, Urushidani S, Nakayama T. Five-level emergency triage systems: variation in assessment of validity. Emerg Med J. 2017;34(11):703-10.
14. Jiménez JG, Murray MJ, Beveridge R, Pons JP, Cortés EA, Garrigós JBF, et al. Implementation of the Canadian Emergency Department Triage and Acuity Scale (CTAS) in the Principality of Andorra: Can triage parameters serve as emergency department quality indicators? CJEM. 2003;5(5):315-22.
15. Zachariasse JM, Seiger N, Rood PP, Alves CF, Freitas P, Smit FJ, et al. Validity of the Manchester Triage System in emergency care: A prospective observational study. PLoS One. 2017;12(2):e0170811.
16. Ng CJ, Yen ZS, Tsai JCH, Chen LC, Lin SJ, Sang YY, et al. Validation of the Taiwan triage and acuity scale: a new computerised five-level triage system. Emerg Med J. 2011;28(12):1026-31.
17. Fernandes CM, McLeod S, Krause J, Shah A, Jewell J, Smith B, et al. Reliability of the Canadian Triage and Acuity Scale: interrater and intrarater agreement from a community and an academic emergency department. CJEM. 2013;15(4):227-32.
18. Storm-Versloot MN, Ubbink DT, Choi VC, Luitse JSK. Observer agreement of the Manchester Triage System and the Emergency Severity Index: a simulation study. Emerg Med J. 2009;26(8):556-60.
19. Mirhaghi A, Heydari A, Mazlom R, Ebrahimi M. The reliability of the Canadian Triage and Acuity Scale: meta-analysis. N Am J Med Sci. 2015;7(7):299-305.

20. Van der Wulp I, Schrijvers AJP, Van Stel HF. Predicting admission and mortality with the Emergency Severity Index and the Manchester Triage System: a retrospective observational study. Emerg Med J. 2009;26(7):506-9.

J Surg Med. 2025;9(10):181-186.
https://doi.org/10.28982/josam.8326

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Research article
https://jsurgmed.com/

Esophageal cancer surgery 5-year survival rate and predictors of operative mortality—a single-center analysis

Vítor Patrício Correia, José Paulo Freire, Luís Castro, Helder Matos, Andreia Barão, Teresa Braga, Rosário Rosa, Luís Miranda

Department of Surgery, Hospital de Santa Maria, Unidade Local de Saúde Santa Maria, Av. Prof. Egas Moniz, 1649-028 Lisboa – Portugal

ORCID of the author(s)

VPC: https://orcid.org/0000-0002-9308-4586
JPF: https://orcid.org/0000-0002-9739-9585
LC: https://orcid.org/0000-0002-7017-1791
HM: https://orcid.org/0000-0001-7614-560X
AB: https://orcid.org/0000-0002-5952-5544
TB: https://orcid.org/0009-0005-7893-0798
RR: https://orcid.org/0000-0003-0964-1069
LM: https://orcid.org/0000-0003-4281-3627

Corresponding Author
Vítor Daniel Teixeira Patrício Correia
Av. Prof. Egas Moniz , 1649-028, Lisboa – Portugal
E-mail: vitordanielcorreia@hotmail.com

Ethics Committee Approval
All procedures were carried out in accordance with the requirements set forth by the institutional ethics committee, as well as those outlined in the 1964 Declaration of Helsinki and its subsequent amendments. Before each procedure, individual, free, informed, and clarified consent was obtained from each patient.

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

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

Published
2025 October 9

Abstract

Background/Aim: Esophagectomy remains the primary curative option for esophageal cancer; however, survival outcomes vary based on treatment strategies, tumor staging, and surgical techniques. This study evaluated the survival rates of patients undergoing esophagectomy and assessed factors influencing postoperative prognosis.

Methods: A retrospective observational study was conducted of 75 patients undergoing esophagectomy between 2017 and 2024 at a single tertiary center. Fifty-nine patients had esophageal and gastroesophageal junction malignancies and were non-randomly allocated to one of three treatment arms: primary surgery, neoadjuvant chemoradiotherapy (CROSS) followed by surgery, and perioperative chemotherapy (FLOT) followed by surgery. Survival analysis was performed using Kaplan-Meier estimates, and prognostic factors were assessed using multivariate statistical tests.

Results: The overall 5-year survival rate was 32%. Patients in the FLOT group had a higher survival rate than patients in the CROSS and primary surgery groups. However, the difference was not statistically significant (P=0.121). Pathological staging significantly impacted survival, with stage I patients having a 52% 5-year survival rate. McKeown esophagectomy was associated with the lowest survival rate (11%); transhiatal esophagectomy exhibited the highest anastomotic leak rate (50%). The Surgical Apgar Score (SAS) was a strong predictor of perioperative risk (AUC=0.94, P<0.001).

Conclusion*:* Postoperative pathological staging remains the strongest predictor of survival in esophageal cancer surgery. While neoadjuvancy showed promising trends, additional studies are necessary to optimize patient selection and evaluate the role of active surveillance strategies in long-term outcomes.

Keywords: esophagus, esophageal neoplasms, esophagectomy, survival rate, neoadjuvant therapy

How to cite: Correia VP, Freire JP, Castro L, Matos H, Barão A, Braga T, Rosa R, Miranda L. Esophageal cancer surgery 5-year survival rate and predictors of operative mortality—a single-center analysis. J Surg Med. 2025;9(10):181-186.

Introduction

Esophageal cancer, the eighth most common malignancy, is one of the most aggressive neoplasms of the digestive system; it has a generally poor prognosis and high mortality rates worldwide [1,2]. Surgical resection remains the primary curative approach, particularly in early-stage disease, although it is widely accepted that its combination with preoperative chemoradiation greatly improves outcomes [3].

On the other hand, despite true gastroesophageal junction (GEJ) adenocarcinoma (ADC) (Siewert type II) being a rare, distinct entity that is difficult to treat, there has been a growing trend in favor of perioperative chemotherapy instead of chemoradiation [4,5]. In either case, from a surgical standpoint GEJ cancer surgery implies an esophagectomy. Practitioners are increasingly adopting a more extensive esophageal resection approach providing a margin of safety and lymphadenectomy improvements [4,5].

The survival rate of patients undergoing esophagectomy varies significantly depending on multiple factors, including tumor stage, histological subtype, surgical technique, and perioperative management [6].

Despite advances in surgical techniques and perioperative care, esophagectomy is associated with significant morbidity and mortality. Postoperative complications, including anastomotic leaks, infections, and pulmonary complications, can severely impact short- and long-term survival [7,8]. The implementation of minimally invasive surgical techniques has demonstrated some benefits in terms of reducing postoperative complications. However, the impact of such techniques on operative mortality and long-term survival remains a subject of ongoing research [9,10].

Several studies have analyzed the survival rates of esophageal cancer patients post-surgery, with 5-year survival rates ranging from 15–50% [11,12]. Most studies cite sub-25% survival rates that depend on tumor characteristics and treatment protocols [13,14]. Understanding the factors that influence survival outcomes can provide valuable insights into optimizing patient selection, improving surgical strategies, and enhancing perioperative management to maximize survival benefits.

One valuable tool for assessing perioperative risk and predicting postoperative outcomes is the Surgical Apgar Score (SAS). The SAS, originally developed by Gawande et al. [15], is based on intraoperative parameters such as estimated blood loss, lowest mean arterial pressure, and lowest heart rate. Studies have shown that lower SAS scores correlate with higher rates of postoperative complications and mortality across various surgical disciplines, including gastrointestinal surgery [16]. Recent research suggests that SAS may be a useful predictor of short- and long-term survival following esophagectomy, allowing for better risk stratification and postoperative management [17].

In addition to surgical interventions, recent trials have explored non-surgical management approaches for esophageal cancer. The Surgery As Needed for Oesophageal cancer (SANO) trial introduced a “watch-and-wait” strategy for patients with a complete clinical response following neoadjuvant chemoradiotherapy (NCRT), thereby avoiding immediate surgery unless tumor recurrence is detected [18]. The trial findings suggested that a non-operative approach may lead to similar survival outcomes while reducing surgical morbidity, challenging the traditional paradigm of mandatory esophagectomy after NCRT [19]. However, long-term follow-up is necessary to confirm the longitudinal nature of this strategy and its impact on overall survival and quality of life [20,21].

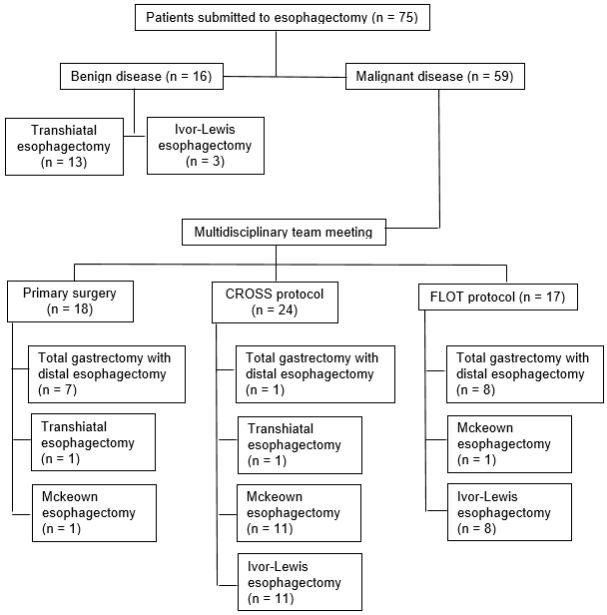
This study analyzes the survival rates of patients who have undergone surgical treatment for esophageal and GEJ cancer at a single tertiary center, considering various prognostic factors such as staging, procedure choice, and patient characteristics that may influence overall survival. By examining clinical and pathological variables, including perioperative risk scores such as SAS, this research seeks to contribute to improved patient management and treatment decision-making.

Materials and methods

Study design

This retrospective observational study focused on 75 patients who underwent esophagectomy between 2017 and 2024. Patient allocation was non-random and dictated by several clinical factors. Sixteen of the patients underwent transhiatal (n=13) or Ivor-Lewis esophagectomy (n=3) due to benign disease, such as end-stage achalasia, severe caustic injury with non-healing strictures, non-responsive esophageal strictures and benign neoplasms, and were therefore excluded from the oncological sample analysis. All oncological patients (n=59) were evaluated at a tertiary center multidisciplinary meeting with General Surgeons, Gastroenterologists, Medical and Radiation Oncologists, Pathologists and Radiologists, in which each case was individually discussed and a treatment strategy was selected according to tumor location, histological subtype, clinical staging, patient comorbidities, and performance status, among other factors. That processes therefore introduced a clinically mandated selection bias. These patients were selected for primary surgery (n=18), neoadjuvant chemoradiotherapy followed by surgery according to the CROSS protocol6 (n=24), or perioperative chemotherapy followed by surgery according to the FLOT protocol5 (n=17) [figure 1].

Figure 1. Patients included in the study



CROSS: Chemoradiotherapy for Oesophageal cancer followed by Surgery Study protocol, FLOT: Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel protocol

This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure transparency, completeness, and accuracy in reporting observational research.

Outcomes

Primary goals encompassed calculation and plotting of 5-year survival curves for the overall sample as well as for the oncological group. Survival was then compared between treatment strategy allocation arms, procedure-related allocation and according to postoperative staging.

Secondary goals included analysis of predicted versus observed mortality as well as complications, namely the anastomotic leak rate.

Statistical analysis

Data analysis was conducted using SPSS software version 26 (IBM Corp, Armonk, NY, USA). We applied the Shapiro-Wilk test to all of the variables to assess their normality. Nominal variables were expressed as absolute values and percentages and compared using the Pearson's chi-squared test with the post-hoc correction according to Bonferroni. Numerical variables were expressed as means ± standard deviation, if normally distributed, and subsequently compared with recourse to analysis of variance (ANOVA) and Tukey's post-hoc testing. Numerical data found to be non-parametric were expressed as medians (minimum – maximum) and compared using the Kruskal-Wallis test and Dunn's post-hoc correction.

Survival analysis was performed using Kaplan-Meier estimates, complemented by survival curve comparisons using the log-rank (Mantel-Cox) test to determine the presence of statistically significant differences.

Expected-versus-observed morbidity and mortality was assessed by plotting the Receiver Operating Characteristics (ROC) curves and calculating the Area Under the Curve (AUC) to determine sensitivity cut-off scores.

A *P*-value less than 0.05 was considered to indicate statistical significance.

Results

The 59 patients with esophageal malignant disease included in the study between 2017 and 2024 were assigned non-randomly to one of three treatment strategies [table 1]. However, the allocation differences were not statistically significant (X2 (2, n=59) = 2.169), *P*=0.338): 18 patients (30.5%) were directed being to primary surgery, 24 patients (40.7%) were directed to pre-operative chemoradiotherapy according to the CROSS protocol followed by surgery, and 17 patients (28.8%) were directed to peri-operative chemotherapy with the FLOT protocol followed by surgery.

The gender pool was asymmetric; however, this distribution remained homogenous between the treatment arms (*P*=0.085) [table 1].

Age at treatment was significantly different among the treatment groups (F (2, 56) = 5.442), *P*=0.007); post-hoc testing revealed that the patients in the primary surgery group were significantly older than the patients allocated to CROSS protocol.

Due to the treatment allocation being clinically oriented, the distribution was found to be significantly different between the study's groups (X2 (4, n=59) = 32.614), *P*<0.001); FLOT treatment was primarily chosen for GEJ ADC (n=16; 53.3%), and the CROSS treatment was primarily chosen for esophageal Squamous Cell Carcinoma (SCC) (n=14; 82.4%). Tumor location followed suit and exhibited a similar distribution pattern [table 1].

No significant differences in postoperative pathological staging (American Joint Committee on Cancer (AJCC) 8th edition) distributions were noted among the treatment arms (X2 (8, n=58) = 8.172, *P*=0.417) [table 1]. However, of the eight patients observed to have pathological complete response (13.8%), seven were in the CROSS group, and all of them were being treated for esophageal SCC (*P*=0.021).

The median follow-up duration was 13 months (range: 0–91 months); follow-up duration was similar for all of the treatment arms (H (2, n=59) = 4.128, *P*=0.127). All cause-mortality within the follow-up period was 54.2% (n=32) overall and 66.7% (n=12) for the primary surgery group; it was 58.3% (n=14) for the CROSS study arm and 35.3% (n=6) for the FLOT group (X2 (4, n=59 = 3.740, *P*=0.154) [table 1].

Mortality was plotted against follow-up time to obtain a survival function according to Kaplan-Meier; we recovered a median survival time of 20.0 months (95% CI 11.889; 28.111) and a 32% overall survival rate at 5 years [figure 2A]. Survival functions were also plotted for the treatment arms [figure 2B]; we did not find any significant differences among the groups according to the log-rank (Mantel-Cox) test (*P*=0.121). The primary surgery patients had a median survival duration of 19.0 months (95% CI 1.913; 36.087) and a 5-year survival rate of 23.5%. We found that 58% of the FLOT patients were alive 60 months after the procedure. The median survival duration for the CROSS group was 20.0 months (95% CI 11.294; 28.706); the survival rate at 60 months was 19.5%.

Figure 2A: Kaplan-Meier survival curve for the overall oncological patient sample

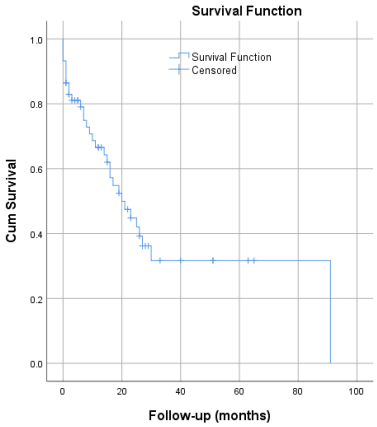


Figure 2B: Kaplan-Meier survival function based on treatment strategy allocation

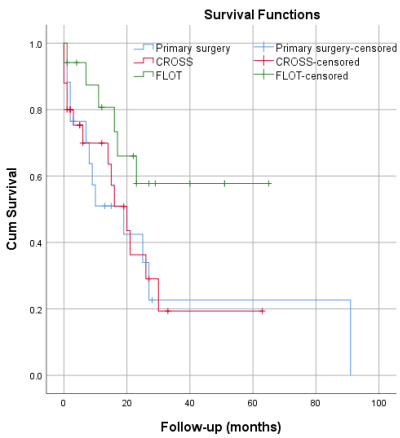


Table 1: Oncological sample characteristics

	Total sample	Primary surgery	CROSS	FLOT	*P*-value
N	59 (100%)	18 (30.5%)	24 (40.7%)	17 (28.8%)	0.338
Male	50 (84.7%)	15 (83.3%)	21 (87.5%)	14 (82.35%)	
Female	9 (15.3%)	3 (16.7%)	3 (12.5%)	3 (17.65%)	0.085
Age (years)	64 ±9.8	68.9 ±10.7	59.6 ±6.2	65 ±10.8	0.007
Histology					
Esophageal ADC	12 (20.3%)	3 (16.7%)	8 (33.3%)	1 (5.9%)	
GEJ ADC	30 (50.8%)	12 (66.6%)	2 (8.33%)	16 (94.1%)	<0.001
Esophageal SCC	17 (28.8%)	3 (16.7%)	14 (58.33%)	0	
Location					
Upper/Middle third	8 (13.5%)	0	8 (33.3%)	0	
Lower third	22 (37.3%)	6 (33.3%)	16 (66.7%)	0	<0.001
GEJ	29 (49.2%)	12 (66.7%)	0	17 (100%)	
Post-op staging					
I	18 (31.0%)	8 (44.5%)	5 (20.8%)	5 (29.4%)	
II	16 (27.6%)	4 (22.2%)	7 (29.2%)	6 (35.3%)	
III	14 (24.1%)	4 (22.2%)	5 (20.8%)	5 (29.4%)	0.417
IV	2 (3.4%)	2 (11.1%)	0	0	
Complete response	8 (13.8%)	0	7 (29.2%)	1 (5.9%)	0.021
Procedure					
TGDE	19 (32.2%)	10 (55.6%)	1 (4.2%)	8 (47.05%)	
TE	8 (13.6%)	7 (38.9%)	1 (4.2%)	0	
Mckeown	13 (22.0%)	1 (5.5%)	11 (45.8%)	1 (5.9%)	<0.001
Ivor-Lewis	19 (32.2%)	0	11 (45.8%)	8 (47.05%)	
Follow-up (months)	13 (0-91)	9.5 (0-91)	9 (0-63)	22 (1-65)	0.127
All-cause mortality	32 (54.2%)	12 (66.7%)	14 (58.3%)	6 (35.3%)	0.154

ADC: Adenocarcinoma, GEJ: Gastroesophageal Junction, SCC: Squamous Cell Carcinoma, TGDE: Total gastrectomy with distal esophagectomy, TE: Transhiatal esophagectomy

Table 2: Oncological sample procedure-related metrics

	TGDE	TE	Ivor-Lewis	Mckeown	*P*-value
(n=59)	19 (32.2%)	8 (13.6%)	19 (32.2%)	13 (22.0%)	
Location					
Upper/Middle third	0	0	2 (10.5%)	6 (46.2%)	
Lower third	1 (5.3%)	6 (75%)	9 (47.4%)	6 (46.2%)	<0.001
GEJ	18 (94.7%)	2 (25%)	8 (42.1%)	1 (7.6%)	
Lymphadenectomy	23.5 (15-50)	23 (3-33)	23 (7-53)	26 (7-54)	0.309
Intervention (min)	256 (152-454)	201 (152-329)	289 (238-401)	322 (285-429)	0.001
Hospital stay (days)	9 (3-24)	25 (10-56)	14 (8-87)	17 (4-62)	0.005
Follow-up (months)	15 (0-65)	9 (2-91)	11 (1-40)	16 (0-63)	0.938
Surgical Apgar Score	7 (4-9)	7 (4-8)	7 (4-9)	8 (5-9)	0.110
Anastomotic leak *(n=13)*	1 (5.3%)	4 (50%)	6 (31.6%)	2 (15.4%)	0.037
30-day mortality *(n=8)*	3 (15.8%)	0	1 (5.3%)	4 (30.8%)	0.125
All-cause mortality *(n=32)*	10 (52.6%)	5 (62.5%)	7 (36.8%)	10 (76.9%)	0.154

GEJ: Gastroesophageal Junction, TGDE: Total Gastrectomy with Distal Esophagectomy, TE: Transhiatal Esophagectomy

It is recognized that cancer staging is inversely related to survival, independent of treatment strategy [1]. That observation stands true for our study sample (P=0.02); we noted a cumulative 5-year survival rate of 52% for stage I patients (median: 51.0 months; 95% CI 30.964; 72.946) and a cumulative 5-year survival rate of 25% for stage II patients (at 52 months of follow-up). All stage III and IV patients had died by 30 and 2 months of follow-up, respectively. Individuals with a complete response after neoadjuvant therapy exhibited a survival rate of 75% (median cumulative survival not reached) [figure 3].

We also examined statistics pertaining to surgical procedure choice, which depended on tumor location and pre-operative characteristics; we noted significant differences in allocation (P<0.001) [table 2]. A median lymphadenectomy of 24 nodes (range: 3–54 nodes) was obtained; there were no significant differences among the four types of surgical procedures (H (3, n=59) = 3.593, P=0.309) [table 2].

We found that both Ivor-Lewis and McKeown esophagectomy were significantly lengthier procedures than transhiatal esophagectomy and total gastrectomy with distal esophagectomy (P=0.001); the latter was characterized by a shorter median hospital stay (9 days; range: 3–24 days) (H (3, n=59) = 13.018, P=0.005) [table 2].

The rate of complications, namely anastomotic leaks, was 50% (n=4) among patients who underwent transhiatal esophagectomy (n=8); it was 32% (n=6) among patients who underwent Ivor-Lewis esophagectomies. The latter rate is significantly higher than that of other procedures (X2 (3, n=59) = 8.467, P=0.037) [table 2]. Anastomotic dehiscence was treated endoscopically for the majority of cases; it was associated with a very high success rate and few re-operations. There was no mortality directly attributed to this cause.

Operative and all-cause mortality were identical among the procedures (P=0.125 and P=0.154, respectively). We produced Kaplan-Meier curves to compare the survival of the procedure-stratified groups [figure 4]. Patients who underwent total gastrectomy with distal esophagectomy had a 30% survival rate at the 5-year mark. Patients in the transhiatal esophagectomy arm exhibited a survival rate of 44% at 60 months; patients in the Ivor-Lewis group exhibited a survival rate of 48% at 40 months. The McKeown esophagectomy patients fared the worst; only 11% were alive after five years. However, the test of equality of survival distribution (i.e., the Mantel-Cox log rank) revealed no overall difference in survival rate (P=0.544).

We obtained SAS data for all patients (median score: 7; range: 4–9). We plotted those data against observed operative, 30-day mortality (n=8, which was found to be non-significantly different among the surgical procedures, P=0.125). The resultant ROC curve revealed an AUC of 94% (95% CI 0.887,1.0; P<0.001) [figure 5].

Figure 3: Kaplan-Meier survival function based on postoperative pathological staging

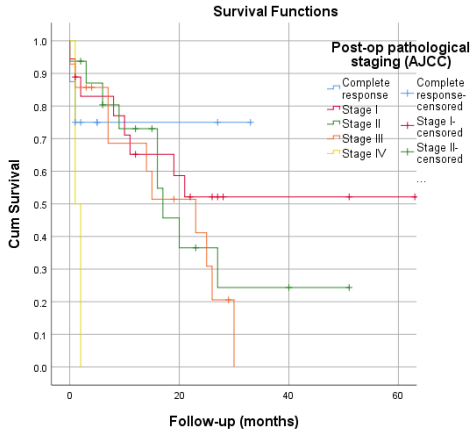


Figure 4: Kaplan-Meier survival function based on surgical procedure

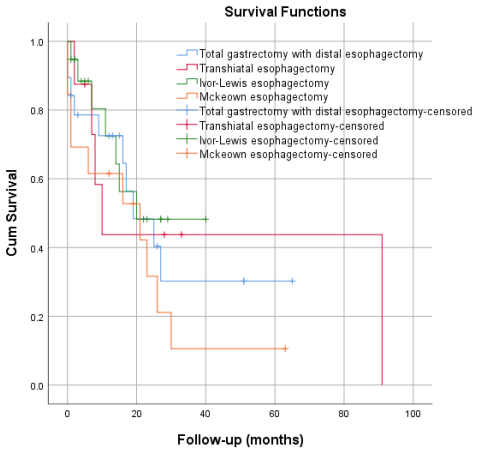
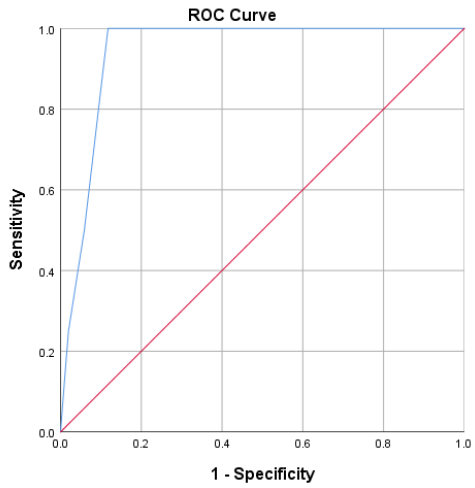


Figure 5: ROC curve for SAS against 30-day mortality



Discussion

This study provides a detailed analysis of survival outcomes following esophagectomy for esophageal and GEJ cancer at our institution. We evaluated multiple prognostic factors, including treatment strategies, tumor staging, surgical techniques, and perioperative risk assessments. Our findings reinforce the notion that survival outcomes are significantly influenced by the chosen treatment protocol, tumor pathology, and patient-specific factors such as age and comorbidities.

The overall 5-year survival rate of 32% that we observed is consistent with the previous literature, which has reported survival rates ranging between 15% and 50% depending on staging and treatment modalities [1,2]. Notably, patients in the perioperative chemotherapy (FLOT) group exhibited higher survival rates than patients in the primary surgery and neoadjuvant chemoradiotherapy (CROSS) groups. However, the differences among the groups were not statistically significant (P=0.121). The more positive outcomes observed in the FLOT cohort are consistent with recent trials that demonstrated the efficacy of perioperative chemotherapy at improving overall survival for gastroesophageal junction adenocarcinoma.6,14 However, additional longitudinal studies are necessary to ascertain the enduring nature of these findings and potential long-term complications associated with this approach.

One of the most influential prognostic factors identified in this study was postoperative pathological staging, which showed a clear inverse correlation with survival outcomes. Stage I patients exhibited a 52% 5-year survival rate; patients with stage III and IV diseases had significantly lower survival rates—no stage IV patients survived more than 2 months. These results corroborate previous findings that highlight early-stage disease as a key determinant of improved survival following esophagectomy [11]. Furthermore, the observation that patients achieving complete pathological response post-neoadjuvant therapy had a 75% survival rate suggests that tumor downstaging plays a critical role in improving survival rates [19,21].

Surgical technique also appeared to influence outcomes, with patients undergoing McKeown esophagectomy exhibiting the lowest 5-year survival rates (11%) compared with other procedures. However, this difference was not statistically significant (P=0.544). Complication rates, particularly anastomotic leaks, varied among the procedures; transhiatal esophagectomy exhibited the highest incidence of complications (i.e., 50%). Despite these complications, overall perioperative mortality was comparable across all of the surgical techniques. This finding highlights the importance of individual patient selection when determining the most appropriate surgical approach [7,13].

The implementation of the SAS in our cohort further validated its utility at predicting operative risk. The ROC curve analysis (AUC=0.94) suggests that SAS may serve as a robust tool for identifying high-risk patients who may benefit from intensified perioperative monitoring. This finding is consistent with previous studies demonstrating the predictive value of SAS in gastrointestinal surgeries [15,17].

While our study contributes to the growing debate regarding the necessity of immediate surgery following neoadjuvant therapy, it also has several limitations. First, its single-center, non-randomized design inherently introduces selection bias, particularly in the allocation of treatment strategies; treatment strategies were based on clinical judgment rather than standardized randomization. Second, the relatively small sample size of our cohort, especially when stratified across three distinct treatment arms and multiple surgical techniques, limits our statistical power to detect significant differences in survival outcomes. Additionally, heterogeneity in tumor histology and location, while reflective of real-world clinical practice, may have confounded direct comparisons among the groups. Lastly, although the SAS exhibited strong predictive value in our patient population its generalizability still remains uncertain. Multi-center prospective studies with larger cohorts and longer follow-up durations are necessary to validate these findings and explore the

integration of SAS into routine preoperative assessment algorithms to enhance surgical risk stratification.

Conclusions

This study underscores the complexity of managing esophageal and gastroesophageal junction cancers and reveals the significant impact of pathological staging on postoperative survival outcomes. Our findings show that postoperative pathological staging remains the strongest predictor of survival, confirming that earlier stages correlate with better prognoses. The use of perioperative chemotherapy, particularly the FLOT protocol, is correlated with improved survival outcomes, suggesting a potential shift in treatment paradigms for these malignancies. However, we did not measure statistically significant differences among the groups, which highlights the need for additional research.

Moreover, the SAS has shown to be a valuable predictor of perioperative risk; it offers a reliable way of anticipating patient outcomes post-surgery. The variation in survival rates among the various surgical techniques, although not statistically significant, suggests that individual surgical approaches should be tailored based on specific patient and disease characteristics.

References

1. Lagergren J, Smyth E, Cunningham D, Lagergren P. Oesophageal cancer. Lancet. 2017 Nov 25;390(10110):2383-96. doi: 10.1016/S0140-6736(17)31462-9. Epub 2017 Jun 22. PMID: 28648400.
2. World Health Organization. Global burden of disease: 2021 update [Internet]; [cited 2025 Mar 1]. Available from: https://www.who.int/data/gho
3. Lordick F, Mariette C, Haustermans K, Obermannová R, Arnold D; ESMO Guidelines Committee. Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2016 Sep;27(suppl 5):v50-v57. doi: 10.1093/annonc/mdw329. PMID: 27664261.
4. Lin D, Khan U, Goetze TO, Reizine N, Goodman KA, Shah MA, et al. Gastroesophageal Junction Adenocarcinoma: Is There an Optimal Management? Am Soc Clin Oncol Educ Book. 2019 Jan;39:e88-e95. doi: 10.1200/EDBK_236827. Epub 2019 May 17. PMID: 31099690.
5. Hölscher AH, Bollschweiler E, Fetzner UK, Babic B. Surgical approach to advanced Siewert II cancer: beyond the borders? The West Side. Updates Surg. 2023 Feb;75(2):329-33. doi: 10.1007/s13304-022-01363-w. Epub 2022 Aug 24. PMID: 36001282.
6. Shapiro J, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, CROSS study group, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol. 2015 Sep;16(9):1090-8. doi: 10.1016/S1470-2045(15)00040-6. Epub 2015 Aug 5. PMID: 26254683.
7. van der Sluis PC, van der Horst S, May AM, Schippers C, Brosens LAA, Joore HCA, Kroese, et al. Robot-assisted Minimally Invasive Thoracolaparoscopic Esophagectomy Versus Open Transthoracic Esophagectomy for Resectable Esophageal Cancer: A Randomized Controlled Trial. Ann Surg. 2019 Apr;269(4):621-30. doi: 10.1097/SLA.0000000000003031. PMID: 30308612.
8. Low DE, Kuppusamy MK, Alderson D, Cecconello I, Chang AC, Darling G, et al. Benchmarking Complications Associated with Esophagectomy. Ann Surg. 2019 Feb;269(2):291-8. doi: 10.1097/SLA.0000000000002611. PMID: 29206677.
9. Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet. 2012 May 19;379(9829):1887-92. doi: 10.1016/S0140-6736(12)60516-9. Epub 2012 May 1. PMID: 22552194.
10. Luketich JD, Pennathur A, Awais O, Levy RM, Keeley S, Shende M, et al. Outcomes after minimally invasive esophagectomy: review of over 1000 patients. Ann Surg. 2012 Jul;256(1):95-103. doi: 10.1097/SLA.0b013e3182590603. PMID: 22668811; PMCID: PMC4103614.
11. Wright CD, Kucharczuk JC, O'Brien SM, Grab JD, Allen MS; Society of Thoracic Surgeons General Thoracic Surgery Database. Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. J Thorac Cardiovasc Surg. 2009 Mar;137(3):587-95; discussion 596. doi: 10.1016/j.jtcvs.2008.11.042. Erratum in: J Thorac Cardiovasc Surg. 2009 Jun;137(6):1581. PMID: 19258071.
12. Lagergren J, Lagergren P. Recent developments in esophageal adenocarcinoma. CA Cancer J Clin. 2013 Jul-Aug;63(4):232-48. doi: 10.3322/caac.21185. PMID: 23818335.
13. Takeuchi H, Miyata H, Gotoh M, Kitagawa Y, Baba H, Kimura W, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. Ann Surg. 2014 Aug;260(2):259-66. doi: 10.1097/SLA.0000000000000644. PMID: 24743609.
14. Mariette C, Markar SR, Dabakuyo-Yonli TS, Meunier B, Pezet D, Fédération de Recherche en Chirurgie (FRENCH) and French Eso-Gastric Tumors (FREGAT) Working Group, et al. Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. N Engl J Med. 2019 Jan 10;380(2):152-62. doi: 10.1056/NEJMoa1805101. PMID: 30625052.
15. Gawande AA, Kwaan MR, Regenbogen SE, Lipsitz SA, Zinner MJ. An Apgar score for surgery. J Am Coll Surg. 2007 Feb;204(2):201-8. doi: 10.1016/j.jamcollsurg.2006.11.011. Epub 2006 Dec 27. PMID: 17254923.
16. Regenbogen SE, Lancaster RT, Lipsitz SR, Greenberg CC, Hutter MM, Gawande AA. Does the Surgical Apgar Score measure intraoperative performance? Ann Surg. 2008 Aug;248(2):320-8. doi: 10.1097/SLA.0b013e318181c6b1. PMID: 18650644; PMCID: PMC2562699.
17. Zheng C, Luo C, Xie K, Li JS, Zhou H, Hu LW, et al. Surgical Apgar score could predict complications after esophagectomy: a systematic review and meta-analysis. Interact Cardiovasc Thorac Surg. 2022 Jun 15;35(1):ivac045. doi: 10.1093/icvts/ivac045. PMID: 35293571; PMCID: PMC9714643.
18. van der Wilk BJ, Noordman BJ, Neijenhuis LKA, Nieboer D, Nieuwenhuijzen GAP, Sosef MN, et al. Active Surveillance Versus Immediate Surgery in Clinically Complete Responders After Neoadjuvant Chemoradiotherapy for Esophageal Cancer: A Multicenter Propensity Matched Study. Ann Surg. 2021 Dec 1;274(6):1009-16. doi: 10.1097/SLA.0000000000003636. PMID: 31592898.
19. Noordman BJ, Wijnhoven BP, Lagarde SM, Boonstra JJ, Coene PP, Dekker JW, et al. Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: A stepped-wedge cluster randomised trial. BMC Cancer. 2018 Feb 6;18(1). doi:10.1186/s12885-018-4034-1
20. Noordman BJ, Verdam MGE, Onstenk B, Heisterkamp J, Jansen WJBM, Martijnse IS, et al. Quality of Life During and After Completion of Neoadjuvant Chemoradiotherapy for Esophageal and Junctional Cancer. Ann Surg Oncol. 2019 Dec;26(13):4765-72. doi: 10.1245/s10434-019-07779-w. Epub 2019 Oct 16. PMID: 31620943; PMCID: PMC6864114.
21. van der Wilk BJ, Eyck BM, Wijnhoven BPL, Lagarde SM, Rosman C, SANO Study Group. Neoadjuvant chemoradiotherapy followed by active surveillance versus standard surgery for oesophageal cancer (SANO trial): a multicentre, stepped-wedge, cluster-randomised, non-inferiority, phase 3 trial. Lancet Oncol. 2025 Apr;26(4):425-36. doi: 10.1016/S1470-2045(25)00027-0. Epub 2025 Mar 17. PMID: 40112851.

J Surg Med. 2025;9(10):187-192.
https://doi.org/10.28982/josam.8097

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Research article
https://jsurgmed.com/

Comparison of orally administered misoprostol and membrane sweeping for labor induction among women with singleton postdate pregnancies in South-South, Nigeria

Omonigho Esemuede [1], Osamudia Okhionkpamwonyi [1,2], Innocent Okoacha [1,2], Akhator Aimiehinor [1,2], Patrick Ifeanyi Okonta [1,2]

[1] Department of Obstetrics and Gynecology, Delta State University Teaching Hospital, Oghara, Delta State, Nigeria
[2] Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, Delta State University, Abraka, Delta State, Nigeria

ORCID of the author(s)

OE: https://orcid.org/0009-0006-8280-5196
OO: https://orcid.org/0000-0003-0520-6836
IO: https://orcid.org/0000-0002-0232-3378
AA: https://orcid.org/0009-0007-8651-7666
PIO: https://orcid.org/0000-0001-6209-7336

Corresponding Author
Omonigho Esemuede
Department of Obstetrics and Gynecology, Delta State University Teaching Hospital, PMB 07, Oghara, Nigeria
E-mail: esemuedeomonigho@yahoo.com

Ethics Committee Approval
Ethical approval for the study were obtained from the institutional Ethical Review Committee of both hospitals. The reference numbers for the ethical approval of both hospitals are HREC/PAN/2022/003/0452 and CHW/ECC VOL 1/251 for Delta State Teaching Hospital, Oghara and Central Hospital, Warri, respectively. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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

Published
2025 October 7

Abstract

Background/Aim: Postdate pregnancy is an indication for induction of labor to prevent post-term pregnancy with its associated complications. Labor induction processes require hospital admission, resulting in additional costs in managing patients. Therefore, safe and effective outpatient techniques that help reduce the need for inpatient induction of labor are beneficial. The aim of this study is to compare and evaluate the safety and effectiveness of two outpatient methods: a single 50 µg dose of oral misoprostol and membrane sweeping in preventing post-term pregnancy. It also examines the impact on reducing the need for hospital admission for labor induction in postdate singleton pregnancies across two tertiary hospitals in Delta State, Nigeria.

Methods: This two-center randomized controlled trial was conducted on women with uncomplicated postdate singleton pregnancies in an outpatient setting. A total of 157 participants were randomly assigned to one of two intervention groups: the oral misoprostol (OM) group or the membrane sweeping (MS) group. Participants in the OM group received a single 50 µg dose of oral misoprostol, while those in the MS group underwent a one-time membrane sweeping procedure at the antenatal clinic after 40 weeks of gestation.

Results: The participants' baseline sociodemographic and clinical characteristics were similar in both groups. This study found that the proportion of women that achieved spontaneous onset of labor in the OM group (92.1%) was more than in the MS group (85.3%), but this difference was not statistically significant (P=0.21). This study showed that both 50 µg OM and MS are effective and safe methods for inducing labor on an outpatient basis in post-term pregnancies, with OM offering the benefits of a shorter latency period, decreased reliance for oxytocin augmentation in labor, and reduced overall labor duration (P<0.001, P=0.003 and P<0.001, respectively).

Conclusion: The study showed that both OM and MS are effective and safe outpatient agents in preventing post-term pregnancy, although the proportion of women achieving spontaneous onset of labor was greater in the OM group. The two outpatient induction methods were similar regarding neonatal outcomes and the need for Neonatal Intensive Care Unit (NICU) admission with no recorded maternal adverse effects. Both interventions demonstrated good safety profiles for outpatient care; however, a higher proportion of patients in the OM group reported a positive perception of the intervention compared to those in the MS group.

Keywords: oral misoprostol, membrane sweeping, outpatient basis, postdate pregnancies

How to cite: Esemuede O, Okhionkpamwonyi O, Okoacha I, Aimiehinor A, Okonta PI. Comparison of orally administered misoprostol and membrane sweeping for labor induction among women with singleton postdate pregnancies in South-South, Nigeria. J Surg Med. 2025;9(10):187-192.

Introduction

One desired obstetric outcome is the prevention and management of prolonged gestation in order to circumvent the many associated complications. Post-term pregnancy is a high-risk pregnancy that is associated with maternal and perinatal morbidity and mortality [1]. It has been shown that women with otherwise uncomplicated pregnancies have increased risk of maternal and perinatal morbidity and mortality from the gestational age of 42 weeks and longer [2,3]. Fetal complications associated with post-term pregnancy include intrapartum asphyxia from progressive decline in placenta function, oligohydramnios and cord compression in labor, fetal macrosomia, shoulder dystocia, fetal dysmaturity syndrome and unexplained intrauterine fetal death. Maternal complications include anxiety, cephalopelvic disproportion, genital trauma associated with fetal macrosomia, as well as increased caesarean section rate. Neonatal complications are increased risk of birth trauma, meconium aspiration syndrome, and early neonatal seizures [2-4].

Postdate pregnancy occurs in 10-14% of pregnancies [3,4]. The incidence decreases as the accuracy of the dating criteria used increases. It is the most common indication for induction of labor in many centers in Nigeria and other developing countries [4-6].

The cause of postdate pregnancy is unknown. Predisposing factors include inaccurate dating; history of prolonged pregnancy; congenital fetal anomalies like congenital absence of fetal pituitary glands, anencephaly, and congenital fetal adrenal hypoplasia; placenta sulfatase deficiency; extra uterine pregnancy; family history; male fetuses; nulliparity; and obesity [2].

The management of a postdate pregnancy is either expected or an elective delivery of the baby. However, current evidence favors a policy of induction of labor after 41 weeks, as this has been associated with reduced incidence of perinatal mortality, meconium staining of the amniotic fluid, and caesarean section delivery compared with expected management, which has no observed increase in the risk of instrumental delivery, maternal analgesic requirements, or fetal heart rate abnormality [2,4,7,8].

Labor induction success is largely influenced by the readiness of the cervix. An unfavorable cervix requires ripening, which could be achieved with membrane sweeping or mechanical methods like laminaria tent, or extra-amniotic Foley‘s catheter placement. It could also be accomplished through pharmacological methods like prostaglandin E2 vaginal pessaries and gels, prostaglandin E1 analogue like misoprostol, and sometimes low dose oxytocin infusion [3].

Membrane sweeping is a procedure in which the fetal membranes are gently separated from the lower uterine segment using a circular motion of the examining fingers [9]. This technique is commonly performed to reduce the risk of post-term pregnancy and minimize the need for other induction methods, such as Foley's catheter insertion, misoprostol administration, or oxytocin infusion [10]. It is usually carried out after 40 weeks’ gestation, and performed before 42 weeks of gestation. It has been found to stimulate the local release of prostaglandins F2a, the activity of phospholipase A2, the mechanical dilatation of the cervix, and the frequency of uterine contractions [11,12]. Misoprostol, a prostaglandin E1 analogue, is widely used for cervical ripening and labor induction. Its advantages include affordability, broad availability, and stability at room temperature.

Misoprostol can be administered through oral, vaginal, sublingual, or buccal routes. However, the sublingual and buccal routes are not currently recommended for labor induction due to limited supporting data [13]. Oral administration achieves peak plasma concentration more rapidly, typically within 30 minutes, whereas the vaginal route takes approximately one hour [14-16]. Cervical ripening and labor induction processes require inpatient care, resulting in additional costs in managing patients. Hence, any safe and effective interventions that helps in the reduction of the cost of management of patients are, therefore, beneficial. In a study conducted between April 2007 and March 2010 at Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria, Adeniji et al. [17], reported that both 50 μg oral misoprostol and membrane sweeping administered on an outpatient basis, are safe and effective agents for inducing labor in uncomplicated postdate singleton pregnancies. The study showed that oral misoprostol has a shorter latency period advantage, reduced need for oxytocin augmentation in labor, and a shorter labor duration. Similar studies need to be conducted to document the validity of this finding and add to the body of knowledge.

Therefore, the aim of the study is to compare the efficacy and safety of the two outpatient techniques of single-dose 50 μg oral misoprostol and membrane sweeping in preventing post-term pregnancies and reducing the need for inpatient induction of labor in uncomplicated postdate singleton pregnancies.

Materials and methods

This study was a randomized controlled trial of a single dose of 50 μg OM and MS in uncomplicated singleton postdate pregnancies. Participants recruited for the study had early ultrasound dating from 8 to 14 weeks of their pregnancy in addition to their last menstrual period, utilised for the determination of the expected delivery date.

The study was conducted between February 1, 2022 and December 31, 2022 at the department of Obstetrics and Gynaecology, Delta State University Teaching Hospital (DELSUTH), Oghara, and its affiliate, Central Hospital, Warri both in Delta State, South-South Nigeria. Patients with singleton and postdate pregnancies were recruited after providing informed consent.

Participants were randomly allocated into either of the two study arms (OM arm or MS arm) in a 1:1 ratio using a random permutated blocking technique with a block size of ten. For each block, ten computer generated three-digit random numbers were arranged on a spreadsheet with five rows and two columns. Each of the random numbers was cut into a piece of 5cm x 5cm paper, and sealed in an opaque brown envelope, which was identical for all the random numbers. If the random number picked by the participant matched the OM column, the participant was allocated to the OM study arm. If the random number matched the MS column, the participant was allocated to the MS study arm.

Ethical approval for the study was obtained from the institutional Ethical Review Committee of both hospitals. The reference numbers for the ethical approval of both hospitals are HREC/PAN/2022/003/0452 and CHW/ECC VOL 1/251 for Delta

State Teaching Hospital, Oghara and Central Hospital, Warri, respectively. Inclusion criteria included a parturient with a singleton live fetus, postdate pregnancy from 40 weeks and 1 day to 40 weeks and 9 days, intact fetal membranes, Bishop's score ≤5 and cephalic presentation. Patients excluded were those whose pregnancies were postdate pregnancies (of ≥40 weeks and 10 days), multiple pregnancies, grand multiparity, cephalopelvic disproportion, previous caesarean section or a uterine scar, fetal malpresentation, fetal distress, antepartum hemorrhage, premature rupture of the membranes and medical disorders.

The Study Group

This study was a two-center randomized controlled trial of women with uncomplicated postdate singleton pregnancies. One hundred fifty-seven patients with singleton postdate pregnancies were randomized into two groups: The first group was the oral misoprostol (OM) group, while the second group was the membrane sweeping (MS) group. The OM group received a single oral dose of 50 µg misoprostol on an outpatient basis, while the MS group underwent a one-time membrane sweeping procedure at the antenatal clinic. Cases where cervical access was not possible due to a non-yielding cervix were classified as "failed MS." In this study, spontaneous labor was defined as a participant's self-presentation to the labor ward with regular, painful uterine contractions occurring at least once every ten minutes. Failure to achieve spontaneous labor by 41 weeks and 3 days of gestation was classified as a prolonged pregnancy. Participants in this category were managed according to departmental protocols for cervical ripening and labor induction, which included intravaginal misoprostol and oxytocin titration, to facilitate delivery before 42 weeks of gestation or caesarean section as deemed appropriate.

The primary outcome measure was the proportion of women who achieved spontaneous onset of labor before 41 weeks and 3 days gestation. The secondary outcome measures were time interval from the initiation of intervention to the onset of labor (latency period), time interval from the onset of labor to delivery, route of delivery, need for oxytocin augmentation, and neonatal outcomes.

Statistical analysis

Data entry and analysis were accomplished using the Statistical Package for Social Sciences (SPSS) version 26 (IBM ® Inc, Il Chicago. USA). Analysis was by intention to treat (ITT). The descriptive statistics of the study population were presented as frequency tables as illustrated below. Categorical variables were expressed as frequencies and percentages. Continuous variables that were normally distributed were expressed as mean (standard deviations), while non-normally distributed continuous variables were expressed as medians and interquartile range. Comparisons of participants' baseline characteristics and outcome measures between the two arms of the study were conducted using the chi square tests for categorical variables (with Fisher's exact test where applicable). Student's T test was used for continuous variables that were normally distributed, and the Mann Whitney U test was employed for continuous variables where normal distribution could not be assumed. The level of significance was set at 5%.

Results

There were 205 patients who were assessed for eligibility for the study, from. which 48 were excluded. Of the 48 patients excluded, 27 did not meet the inclusion criteria while 21 declined to participate in the study. The remaining 157 participants were randomized into 78 participants in the OM arm and 79 participants in the MS arm. Three participants were lost to follow-up, two in the OM arm and one in the MS arm. The intervention was discontinued in three participants in the MS arm due to a failed MS. All 157 randomized participants were finally analyzed.

Table 1 shows the baseline sociodemographic and clinical characteristics of the participants. The majority of the participants were within the age range, 25-29 years. However, there were no statistically significant difference in the mean age between the two study groups (30.78 [6.43] for the OM group and 31.01 [6.11] for the MS group). Most of the participants had post-primary education (69 [90.7%] and 71 [94.7%] for the OM group and MS group, respectively); and there was no statistically significant difference in the distribution of educational attainment between the groups.

The participants were also mostly in the Para 1-4 group {66 (86.8%) and 60 (80.0%) for the OM group and MS group, respectively}, and parity distribution between the OM group and the MS group were not statistically different (P=0.28). Also, the difference between the mean gestational age in the two groups (40.22 [0.42] for the OM group and 40.23 [0.42] for the MS group) was not statistically significant (P=0.97).

Table 1: Baseline demographic and clinical characteristics of participants

		OM-Group (n = 76)		MS-Group (n = 75)		Total (n = 151)		χ^2/t	*P*-value
		n	%	n	%	n	%		
Age group (years)	<20 years	1	1.3	2	2.7	3	2.0	2.686	0.748
	20-24 years	11	14.5	10	13.3	21	13.9		
	25-29 years	26	34.2	22	29.3	48	31.8		
	30-34 years	11	14.5	17	22.7	28	18.5		
	35-39 years	19	25.0	19	25.3	38	25.2		
	≥40 years	8	10.5	5	6.7	13	8.6		
	Mean (SD)	30.78 (6.43)		31.01 (6.11)		30.89 (6.25)		-0.232	0.817
Marital Status	Single	5	6.6	10	13.3	15	9.9	1.925§	0.185
	Married	71	93.4	65	86.7	136	90.1		
Level of Education	Primary	7	9.2	4	5.3	11	7.3	0.859	0.651
	Secondary	41	53.9	43	57.4	84	55.6		
	Tertiary	28	36.8	28	37.3	56	37.1		
Parity	0	10	13.2	15	20.0	25	16.6	1.279§	0.281
	1 – 4	66	86.8	60	80.0	126	83.4		
	Mean (SD)	1.83 (1.15)		1.49 (1.07)		1.66 (1.12)		1.859	0.065
GA (weeks)	Mean (SD)	40.22 (0.42)		40.23 (0.42)		40.23 (0.42)		-0.044	0.965

Age Range: 16 – 44 years. χ^2 Chi Squared test, t: Independent sample t-test, §: Fischer's exact test

Table 3: Comparison of the agents of induction with regard to latency period

		OM-Group (n=70)		MS-Group (n=64)		Total (n=134)		χ^2/t	*P*-value
		n	%	n	%	n	%		
Latency Period (hours)	***< 12***	35	50.0	17	26.6	52	38.8	18.313	***<0.001**
	>12 – 24	32	45.7	30	46.9	62	46.3		
	>24 – 36	1	1.4	15	23.4	16	11.9		
	>36 – 48	-	-	-	-	-	-		
	>48	2	2.9	2	3.1	4	3.0		
Intervention to onset of Labor	***Mean (SD)***	12.50 (8.59)		18.99 (10.02)		15.60 (9.82)		-4.008	***<0.001**

χ^2=Chi Squared test | t=Independent sample t-test

Table 4: Comparison of events and outcomes of labor in the study groups

		OM-Group (n=70)		MS-Group (n=64)		Total (n=134)		χ^2	*P*-value
		n	%	n	%	n	%		
Need for Oxytocin (n=136)	***Yes***	14	20.0	29	45.3	43	32.1	9.830	***0.003**
	No	56	80.0	35	54.7	91	67.9		
Mode of Delivery (n=136)	***VD***	65	92.9	54	84.4	119	88.8	2.420	0.170
	CS	5	7.1	10	15.6	15	11.2		

VD: Vaginal Delivery, CS: Caesarean Section, χ^2 Chi Squared test

Table 5: Comparison of labor duration in the study groups

		OM-Group (n=70)		MS-Group (n=64)		Total (n=134)		χ^2/t	*P*-value
		n	%	n	%	n	%		
Duration of Labor (hours)	***< 4***	-	-	-	-	-	-		
	>5 – 8	43	61.4	19	29.7	62	46.3	18.993	***<0.001**
	>9 – 12	22	31.4	24	37.5	46	34.3		
	>12	5	7.1	21	32.8	26	19.4		
Duration of Labor	***Mean (SD)***	7.74 (2.25)		9.97 (3.01)		8.80 (2.86)		-4.824	***<0.001**
Intervention to Delivery	***Mean (SD)***	20.24 (10.08)		28.92 (12.10)		24.39 (11.88)		-4.489	***<0.001**

χ^2 Chi Squared test, t: Independent sample t-test

Table 6: Neonatal outcomes in the study groups

		OM-Group		MS-Group		Total		χ^2/t	*P*-value
		Mean (SD		*Mean (SD*		*Mean (SD*			
		n	*%*	*n*	*%*	*n*	*%*		
Birth weight (kg) *Mean (SD)*		3.26 (0.30)		3.19 (0.32)		3.23 (0.31)		1.294	0.198
APGAR score (1ST min) [n=141]	**< 7**	31	44.3	33	51.6	64	47.8	0.710	0.489§
	≥ 7	39	55.7	31	48.4	70	52.2		
Mean (SD)		6.86 (1.24)		6.50 (1.35)		6.68 (1.30)		1.579	0.117
APGAR score (5TH min) [n=141]	**< 7**	2	2.9	8	12.5	10	7.5	4.502	***0.048§**
	≥ 7	68	97.1	56	87.5	124	92.5		
Mean (SD)		8.84 (1.12)		8.42 (1.37)		8.64 (1.26)		1.924	0.057
APGAR score (10TH min) *Mean (SD)*		9.86 (0.51)		9.62 (0.79)		9.74 (0.68)		1.737	0.086
NICU Admission (n=141)	***Yes***	4	5.7	10	15.6	14	10.4	3.510§	0.089
	No	66	94.3	54	84.4	120	89.6		

NICU: Neonatal Intensive Care Unit, χ^2 Chi Squared test, t: Independent sample t-test, §: Fischer's exact test

Table 1 shows there was no statistically significant difference in the distribution of participants in each component between the two study groups.

Table 2 shows that the proportion of participants that achieved spontaneous onset of labor in the OM group (n=70; 92.1%) was more than in the MS group (n=64; 85.3%); however, there was no statistically significant difference (*P*=0.21).

Table 2: The Primary outcome measure which is the proportion of participants who had spontaneous labor

		OM-Group (n = 76)		MS-Group (n = 75)		Total (n = 151)		χ^2	*P*-value
		n	%	n	%	n	%		
Spontaneous Labor	***Yes***	70	92.1	64	85.3	134	88.7	1.733§	0.209
	No	6	7.9	11	14.7	17	11.3		

χ^2 Chi Squared test

Table 3 shows that the mean of the latency period was shorter among participants in the OM group (12.50 [8.59] hours) than those in the MS group (18.99 [10.02] hours) and the difference was statistically significance (*P*<0.001).

Table 4 shows that more participants in the MS group (n=29; 45.3%) required oxytocin augmentation compared to those in the OM group (n=14; 20.0%), and this was statistically significant (*P*=0.003). It was observed that more women in the OM group (n=65; 92.9%) had vaginal deliveries compared to participants in the MS group (n=54; 84.4%). However, this was not statistically significant (*P*=0.170).

Table 5 shows that the majority of the participants' duration of labor ranged from four to eight hours. However, the mean labor duration was significantly shorter among participants in the OM group (7.74 [2.25] hours) than those in the MS group (9.97 [3.01] hours); and the difference was statistically significant (*P*<0.001).

Table 6 shows that there were similarities in the neonatal outcomes in both the OM and MS groups, with more babies in the MS group (n=8; 12.5%) compared to the OM group (2; 2.9%) having moderate birth asphyxia at the fifth minute after birth. In addition, the neonates that were admitted in the Neonatal Intensive Care Unit in the MS group (n=10; 15.6%) were more than in the OM group (n=4; 5.2%); and there was no statistically difference (*P*=0.09).

Discussion

This study compared the efficacy of two outpatient techniques of single-dose 50 µg oral misoprostol and membrane sweeping in preventing post-term pregnancies and reducing the need for hospital admission for induction of labor in postdate singleton pregnancies in two tertiary hospitals in Delta State, Nigeria. The findings of this study showed that the results of the comparison of the sociodemographic and clinical characteristics in both study groups were not statistically significant. This demonstrates that the randomization process was effective in ensuring that probable confounding variables were equally distributed in both groups and, therefore, unlikely to affect the results of the study.

The main objective of the study was to determine and compare the proportion of women who would achieve spontaneous onset of labor before 41 weeks and 3 days gestation in participants with postdate pregnancies who had single-dose 50 µg oral misoprostol and those who had membrane sweeping. The study revealed that the proportion of participants that achieved spontaneous onset of labor in the OM group (92.1%) was greater compared to the MS group (85.3%). However, the results showed no statistically significant difference between the two groups (P=0.209).

This is in keeping with a study reported by Adeniji and Akintola et al. [17]. Their findings indicated that there was no statistical difference between the proportion of participants that achieved spontaneous onset of labor in both the OM and MS groups. Manipulation of the cervix during digital vaginal examination or membrane sweeping has been shown to trigger the onset of labor by stimulating the release of localized prostaglandins F2α, phospholipase A2, and cytokines from intrauterine tissues [32]. Additionally, misoprostol, a prostaglandin E1 (PGE1) analogue, undergoes rapid de-esterification into its active free acid metabolites, leading to a faster onset of action compared to the local prostaglandin production expected with membrane sweeping [33]. This difference may be attributed to the combined effect of the pre-recruitment digital vaginal examination used to assess the Bishop score (≤5) prior to randomization and the administration of a single 50 µg oral dose of misoprostol in the OM group.

This study also demonstrated that both 50 µg OM and MS were effective for inducing labor on an outpatient basis in postdate pregnancies. However, the OM group demonstrated advantages, including a shorter latency period, reduced need for oxytocin augmentation, and a shorter duration of labor. Within 12 hours of intervention initiation, 44.9% of participants in the OM group reported being in labor, compared to 21.5% in the MS group. By 24 hours, the proportions increased to 85.9% and 59.5%, respectively. Orally administered misoprostol reaches its peak plasma concentration more rapidly than the vaginal route, achieving maximum levels within 30 minutes [14,15]. This also explained the combined effect of the endogenous locally released prostaglandins from the manipulation of the cervix during the pre-recruitment Bishop score assessment and the exogenous prostaglandins (OM) when compared with only endogenous prostaglandins from manipulation of the cervix and MS.

The study further revealed that more participants in the MS group, (45.3%), required additional need for oxytocin augmentation when compared to participants in the OM group (20.0%) and this was statistically significant. This finding is in line with several studies that have demonstrated less need for oxytocin augmentation in patients who received misoprostol when compared to patients that had MS [17-19,21]. The duration of labor was significantly shorter in the OM group, in which 61.4% of those who had a vaginal delivery achieved it within eight hours, compared with 29.7% in the MS group, and this was statistically significant. These findings agreed with similar studies conducted by Adeniji and Akinola in Osogbo, Nigeria [17] and Kamal et al. in Cairo, Egypt [18]. Their reports showed that participants who received misoprostol had a shorter latency period, less oxytocin use for augmentation, and a shorter duration of labor.

In addition, this study showed that more participants in the OM group (92.9%) had vaginal deliveries compare to participants in the MS group (84.4%). This is in keeping with study done by Kamal et al. [18], but in contrast with the study done by Adeniji and Akinola [17], where the proportions of vaginal deliveries were similar in both the OM and MS groups. This finding is probably due to the difference in the methodology and the fact that their study utilized a smaller sample size, which may have introduced performance and detection bias.

Safety was defined in this study as any adverse effects that could jeopardize the life of the mother and or that of the fetus from the use of OM and MS. The reported maternal adverse effects of misoprostol, such as fever, diarrhea, vomiting, tachysystole, hyperstimulation, uterine rupture or postpartum hemorrhage were not observed in this study, possibly because of the single oral dose administered and a membrane sweeping. However, the neonatal outcomes in both OM and MS groups were similar, which agreed with studies done by Adeniji and Akintola [17] and Kamal et al. [18]. Furthermore, more babies in the MS group (12.5%) compared to OM group (2.9%) had moderate birth asphyxia at the fifth minute after birth. The birth asphyxia occurred in babies of relatively low birth weight and whose mothers had oxytocin augmentation of labor. There is documented evidence that low birth weight of neonates and oxytocin augmentation of labor contribute to the higher risk of perinatal asphyxia [34,35]. The neonates that were admitted in the Neonatal Intensive Care Unit in both groups were only monitored for observation and were discharged within 24 hours.

Strength of the Study

One strength of the study is that it was a randomized controlled trial in which there was a randomized allocation of participants to the two study groups. This minimized selection bias and unequal allocation of confounders among the participants. In addition, it was a two-centre study enhancing the generalizability of the findings.

This research provided a high level of evidence on the performances of oral misoprostol and membrane sweeping as an outpatient technique in preventing post-term pregnancies in our environment, thereby enriching the growing body of knowledge and offering the women the best possible management.

Limitations

This study also has limitations. It was not possible for either group in the study to be blinded to the participants. Nor was it possible for the investigator and the research assistants who were involved in data collection and analysis, as the interventions

in both groups were completely different. Nevertheless, the variables being measured were fairly objective, and the investigator and research assistants were as objective as possible.

Conclusion

This study determined that the proportion of women that achieved spontaneous onset of labor in the OM group was greater compared to MS group, although there was no statistically significant difference. This study demonstrated that patients who received a single-dose oral misoprostol (OM) had a shorter latency period, reduced need for oxytocin augmentation, and a shorter duration of labor compared to those who underwent membrane sweeping (MS) on an outpatient basis. Both induction methods showed comparable neonatal outcomes, including the need for admission with no recorded maternal adverse effects.

Recommendations

It is clear from the findings of this study that a greater proportion of participants achieved spontaneous onset of labor with a shorter latency period, reduced need for oxytocin augmentation and a reduced labor duration in participants given single-dose OM compared with MS on an outpatient basis. Therefore, it is recommended that OM can be used as an appropriate outpatient technique for labor induction in order to prevent post-term pregnancies and reduced the need for inpatient induction of labor in postdate pregnancies.

Furthermore, a larger multicenter study is recommended to further validate or refute the advantages of oral misoprostol observed in this study.

References

1. Doherty L, Norwitz ER. Prolonged pregnancy: When should we intervene? Curr Opin Obstet Gynecol. 2008;20(6):519–27.
2. Spong CY. Defining “term” pregnancy: Recommendations from the defining “term” pregnancy workgroup. JAMA - J Am Med Assoc. 2013;309(23):2445–6.
3. Leduc D, Biringer A, Lee L, Dy J, Corbett T, Duperron L, et al. Induction of Labour. J Obstet Gynaecol Canada [Internet]. 2013;35(9):840–57.
4. Middleton P, Shepherd E, Crowther CA. Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database Syst Rev. 2018;2018(5).
5. Lawani OL, Onyebuchi AK, Iyoke CA, Okafo CN, Ajah LO. Obstetric Outcome and Significance of Labour Induction in a Health Resource Poor Setting. Obstet Gynecol Int. 2014;2014:1–5.
6. Bako BG, Obed JY, Sanusi I. Methods of induction of labour at the University of Maiduguri Teaching Hospital, Maiduguri: a 4-year review. Niger J Med. 2008;17(2):139–42.
7. Factors E, Risks N. Management of late-term and postterm pregnancies. Obstet Gynecol. 2014;124(2):390–6.
8. Souter V, Painter I, Sitcov K, Caughey AB. Maternal and newborn outcomes with elective induction of labor at term. Am J Obstet Gynecol [Internet]. 2019;220(3):273.e1-273.e11.
9. Yildirim G, Güngördük K, Karadağ ÖI, Aslan H, Turhan E, Ceylan Y. Membrane sweeping to induce labor in low-risk patients at term pregnancy: A randomised controlled trial. J Matern Neonatal Med. 2010;23(7):681–7.
10. Ugwu EO, Obi SN, Iferikigwe ES, Dim CC, Ezugwu FO. Membrane stripping to prevent post-term pregnancy in Enugu, Nigeria: A randomized controlled trial. Arch Gynecol Obstet. 2014;289(1):29–34.
11. Tan PC, Khine PP, Sabdin NH, Vallikkannu N, Sulaiman S. Effect of membrane sweeping on cervical length by transvaginal ultrasonography and impact of cervical shortening on cesarean delivery. J Ultrasound Med. 2011;30(2):227–33.
12. Montis M, Tibaldi V, Santangelo G, Pajno C, Corno S, D’aniello D, et al. The use of misoprostol and mifepristone in second trimester interruption of pregnancy: State of art. Clin Obstet Gynecol Reprod Med. 2020;6(2):1–4.
13. Management C, For G. ACOG practice bulletin no. 107: Induction of labor. Obstet Gynecol. 2009;114(2 PART 1):386–97.
14. Raymond EG, Harrison MS, Weaver MA. Efficacy of Misoprostol Alone for First-Trimester Medical Abortion: A Systematic Review. Obstet Gynecol. 2019;133(1):137–47.
15. Ashmawy NE, Assar TM, Taha SM, Helmy EA. Original Article Effect of Membrane Sweeping on Induction of Labour a Randomized Controlled Trial. Benha J Appl Sci. 2020;5(2):1–7.
16. Vogel JP, Osoti AO, Kelly AJ, Livio S, Norman JE, Alfirevic Z. Pharmacological and mechanical interventions for labour induction in outpatient settings. Cochrane Database Syst Rev. 2017;2017(9).
17. Adeniji AO, Akinola SE. A comparison of orally administered misoprostol and membrane sweeping for labour induction in uncomplicated singleton post-term pregnancies. S Afr J Obstet Gynaecol. 2013;19(1):4–7.
18. Kamal H, Youssef A, Elias A. Stripping of membranes versus vaginal misoprostol in induction of labor. J Med Sci Res. 2019;2(2):174.
19. Javadekar D, Rokade A. Can term gestation be induced by misoprostol on OPD basis?Journal of Evolution of Medical and Dental Sciences. 2013; 2(22); 3929-36.
20. PonMalar J, Benjamin SJ, Abraham A, Rathore S, Jeyaseelan V, Mathews JE. Randomized double-blind placebo controlled study of preinduction cervical priming with 25 µg of misoprostol in the outpatient setting to prevent formal induction of labour. Arch Gynecol Obstet. 2017;295(1):33–8.
21. Pal R, Deora S, Resident S. Comparative Evaluation of Pre-Induction Use of Misoprostol in Post-Term Pregnancies for Cervical Ripening on Outpatient Basis. Int J Heal Sci Res [Internet]. 2017;7(4):171. Available from: www.ijhsr.org
22. Nyamzi M G, Isah D A, Offiong R A, Isah A Y. Effectiveness of sweeping of membranes in reducing the incidence of elective induction of labor for postdate pregnancies. Arch Med Surg 2019;4:15-21.
23. Dare FO, Oboro VO. The role of membrane stripping in prevention of post-term pregnancy: A randomised clinical trial in Ile-Ife, Nigeria. J Obstet Gynaecol (Lahore). 2002;22(3):283–6.
24. Boulvain M, Fraser WD, Marcoux S, Fontaine JY, Bazin S, Pinault JJ, et al. Does sweeping of the membranes reduce the need for formal induction of labour? A randomized controlled trial. BJOG An Int J Obstet Gynaecol. 1998;105(1):34–40.
25. Wong SF, Hui SK, Choi H, Ho LC. Does sweeping of membranes beyond 40 weeks reduce the need for formal induction of labour? BJOG An Int J Obstet Gynaecol. 2002;109(6):632–6.
26. Azubuike IJ, Bassey G, Okpani AOU. Comparison of 25 and 50 microgram of misoprostol for induction of labour in nulliparous women with postdate pregnancy in Port Harcourt. Niger J Clin Pract. 2015;18(2):263–7.
27. Elhassan EM, Mirghani OA, Adam I. Cervical ripening and labor induction with 25 µg vs. 50 µg of intravaginal misoprostol. Int J Gynecol Obstet. 2005;90(3):234–5.
28. Kipikasa JH, Adair CD, Williamson J, Breen JM, Medford LK, Sanchez-Ramos L. Use of misoprostol on an outpatient basis for postdate pregnancy. Int J Gynecol Obstet. 2005;88(2):108–11.
29. Hazra A, Gogtay N. Biostatistics series module 5: Determining sample size. Indian J Dermatol. 2016;61(5):496–504.
30. Searle G.D. LLC. Cytotec. Division of Pfizer Inc.NY, NY 10017. Revised : Feb 2018.
31. Jobe AH. Apgar score imprecision. J Pediatr. 2006;149(4):32887.
32. Blackburn S. Maternal, Fetal, & Neonatal Physiology - A Clinical Perspective. 3rd Edition. Missouri: Saunders Elsevier, 2013.
33. Tang OS, Schweer H, Seyberth HW, Lee SWH, Ho PC. Pharmacokinetics of different routes of administration of misoprostol. Hum Reprod 2002;17(2):332-6.
34. Li Z-n, Wang S-r, Wang P. Associations between low birth weight and perinatal asphyxia: A hospital-based study. Medicine 2023;102:13(e33137).
35. Litorp H, Sunny AK, Kc A. Augmentation of labor with oxytocin and its association with delivery outcomes: A large-scale cohort study in 12 public hospitals in Nepal. Acta Obstet Gynecol Scand. 2021;100:684–93.

J Surg Med. 2025;9(10):193-198.
https://doi.org/10.28982/josam.8416

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Research article
https://jsurgmed.com/

Can the probe movement direction affect pain in patients undergoing transrectal ultrasound-guided prostate biopsy?

Ali Akkoç, Murat Topçuoğlu, Murat Uçar, Erkan Karadağ, Semih Keskin, Deniz Demir

Department of Urology, School of Medicine, Alanya Alaaddin Keykubat University, Alanya, Turkey

ORCID of the author(s)

AA: https://orcid.org/0000-0002-4325-1075
MT: https://orcid.org/0000-0003-2155-5171
MU: https://orcid.org/0000-0002-8690-0485
EK: https://orcid.org/0009-0009-2197-7359
SK: https://orcid.org/0009-0005-7887-0203
DD: https://orcid.org/0009-0007-8730-7660

Corresponding Author
Ali Akkoç
Department of Urology, School of Medicine, Alanya Alaaddin Keykubat University, Alanya, Turkey
E-mail: aliakkoc@gmail.com

Ethics Committee Approval
The study was approved by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee on June 25, 2025, with the decision number 11-06.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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

Published
2025 October 28

Abstract

Background/Aim: Prostate biopsy is the gold standard for prostate cancer diagnosis, but patient discomfort remains a major limitation. While numerous studies have investigated anesthesia and analgesia, the influence of transrectal ultrasound probe movement direction has not yet been examined in clinical studies. This study aimed to evaluate whether the direction of transrectal ultrasound probe movement affects pain perception and complication rates during systematic prostate biopsy.

Methods: In this retrospective cohort study, 246 patients undergoing 12-core transrectal ultrasound-guided biopsy between 2019 and 2025 were analyzed. Patients were stratified into three groups according to the probe movement sequence applied by the performing urologist. Pain was assessed using the visual analogue scale (VAS; 0–10) at five time points: probe insertion, probe manipulation, needle puncture, 30 minutes post-biopsy, and two hours post-biopsy. Complications within 30 days were recorded, including rectal bleeding, hematuria, fever, and urinary retention. Statistical analyses included one-way ANOVA with effect size estimation (η^2) for continuous variables and χ^2 or Fisher's exact test for categorical variables.

Results: Baseline characteristics and cancer detection rates were comparable across groups. Pain scores during probe manipulation (VAS 2), needle puncture (VAS 3), and 30 minutes post-biopsy (VAS 4) differed significantly among the groups, with Group B reporting the lowest values and Group A the highest (all $P<0.001$). No significant differences were observed for probe insertion (VAS 1, $P=0.30$) or two hours post-biopsy (VAS 5, $P=0.19$). Hematuria occurred in 40–42% of cases, rectal bleeding in 9.6–19.5%, and fever in 2.4–5.2%. Although these differences were not statistically significant (rectal bleeding, $P=0.09$; fever, $P=0.47$; hematuria, $P=0.94$; urinary retention, $P=0.86$), both rectal bleeding and fever were most frequent in Group A and least frequent in Group B.

Conclusion: Beyond anesthetic technique, probe maneuver direction significantly influences pain perception during transrectal ultrasound-guided biopsy. Group B's shorter cumulative probe trajectory (≈22–24% reduction) corresponded with consistently lower pain and fewer complications. To our knowledge, this is the first study to identify probe movement strategy as a determinant of biopsy tolerance. Incorporating this approach offers a simple, low-cost modification with potential to improve patient comfort and safety.

Keywords: prostate cancer, biopsy, VAS, pain, probe direction

How to cite: Akkoç A, Topçuoğlu M, Uçar M, Karadağ E, Keskin S, Demir D. Can the probe movement direction affect pain in patients undergoing transrectal ultrasound-guided prostate biopsy? J Surg Med. 2025;9(10):193-198.

Introduction

Prostate cancer is one of the leading causes of morbidity and mortality among men worldwide, and histopathological confirmation remains the cornerstone for establishing a definitive diagnosis [1]. Among the diagnostic modalities, transrectal ultrasound-guided biopsy (TRUS-Bx) continues to be the most widely performed. Although the transperineal approach has gained increasing attention in recent years due to its lower risk of infectious complications, its longer procedure time and the need for specialized equipment have limited its routine use. By contrast, TRUS-Bx remains the predominant technique in clinical practice, owing to its practicality, accessibility, and diagnostic efficacy [2].

Despite its widespread adoption, TRUS-Bx is often associated with considerable discomfort and pain. Such pain is multifactorial, arising not only from needle punctures but also from probe insertion and manipulation during the procedure [3]. Indeed, several studies have demonstrated that probe maneuvering may induce greater pain than the needle punctures themselves [4]. Accordingly, optimizing analgesic strategies has become essential for improving patient tolerance and procedural success.

The periprostatic nerve block (PNB) remains the most widely applied analgesic technique during TRUS-Bx [5]. However, PNB alone may be insufficient to adequately relieve discomfort associated with probe insertion and manipulation [6]. Intrarectal local anesthesia (IRLA), which is simple, non-invasive, and well tolerated, has therefore been introduced as an adjunct. IRLA has been shown to effectively reduce pain, particularly during probe-related maneuvers [7]. Evidence suggests that in certain scenarios, IRLA may even provide superior analgesia to PNB without increasing complication rates, thereby maintaining its relevance as a contemporary analgesic method [8, 9].

More recently, combined regimens, most notably the use of PNB together with IRLA, have been proposed to address pain arising at different phases of the biopsy. Prospective studies and systematic reviews indicate that multimodal strategies yield lower pain scores across probe insertion, anesthetic infiltration, and biopsy puncture phases, without compromising safety [9, 10]. These findings highlight the multifactorial nature of TRUS-Bx-related pain and support the rationale for phase-specific multimodal analgesia.

In this context, the present study addresses a largely unexplored factor: the direction of probe movement during TRUS-Bx. Therefore, this study aimed to evaluate whether the direction of transrectal ultrasound probe movement affects patient-reported pain and complication rates during systematic prostate biopsy.

Materials and methods

This retrospective cohort study was conducted at the Department of Urology, Alanya Alaaddin Keykubat University Hospital between January 2019 and June 2025. A total of 246 patients met the inclusion criteria and were enrolled. Demographic and clinical data, including age, body mass index (BMI), serum prostate-specific antigen (PSA) levels, prostate volume, and cancer detection status, were extracted from institutional medical records.

Patients between 45 and 80 years with an abnormal digital rectal examination and/or elevated serum PSA levels (≥4 ng/mL) and complete clinical data were included in the study. Patients with active urinary tract infection, bleeding diathesis, use of anticoagulant or antiplatelet medication without appropriate discontinuation, anal or rectal pathology, previous prostate biopsy, known allergy to local anesthetics, or incomplete medical records were excluded.

The Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee approved the study on June 25, 2025, with the decision number 11-06. All procedures involving human participants were conducted in accordance with the ethical standards of the Declaration of Helsinki and its later amendments.

Although the study had a retrospective design, all patients who underwent prostate biopsy routinely completed a standardized questionnaire including demographic data, pain scores, and post-procedural complications, with prior consent for potential future research use. Therefore, all data were obtained from this preexisting institutional database.

All patients received standard preparation, which included bowel cleansing with a rectal enema and prophylactic oral quinolone antibiotics that were started one day before the procedure and continued for five days after the biopsy.

For patients in all groups, 10 mL of 2% lidocaine gel in a 10 mL syringe was instilled into the rectum approximately 10 minutes before the biopsy.

The procedures were performed in the left lateral decubitus position under transrectal ultrasound guidance using an 18-gauge automatic biopsy gun. Twelve systematic cores were obtained from each patient.

Patients were divided into three groups according to the technique of the performing urologist: Group A (n=77), Group B (n=83), and Group C (n=86), each representing a distinct and consistently applied probe movement strategy that differed in manipulation pattern and the sequential order of biopsy cores, as summarized in Table 1. The corresponding schematic representations of probe trajectories for each group are illustrated in Figure 1.

Each of the three biopsy groups corresponded to a distinct urologist, each having been trained during residency with a different systematic biopsy sequence and probe movement technique. All were experienced and worked in the same department and followed identical preparation, anesthesia, and procedural protocols.

In Group A, biopsies were performed from the base toward the apex, starting on the right side and then proceeding to the left, following a medial-to-lateral order on the right and a lateral-to-medial order on the left.

In Group B, the urologist alternated between the right and left sides at corresponding depths. The sequence began at the base (right lateral, right medial, left medial, and left lateral) followed by the mid-gland in reverse order (left lateral, left medial, right medial, right lateral), and concluded at the apex using the same order as at the base.

In Group C, biopsies were obtained in a sequential right-to-left order at each depth level, consistently progressing from the base toward the apex, with cores taken as right lateral, right medial, left medial, and left lateral at every level.

Figure 1: Schematic representation of simplified geometric models of transrectal ultrasound probe movement directions within the rectum for Groups A, B, and C.

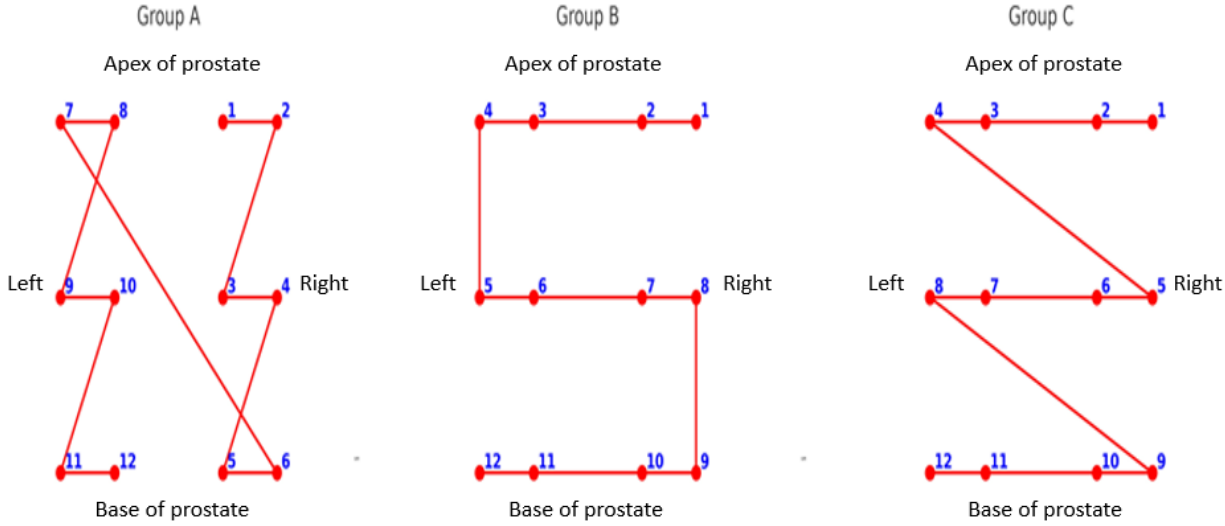


Table 1: Sequential order of transrectal ultrasound-guided prostate biopsy cores according to probe movement technique

Group A	Group B	Group C
1. Right base medial	1. Right base lateral	1. Right base lateral
2. Right base lateral	2. Right base medial	2. Right base medial
3. Right mid medial	3. Left base medial	3. Left base medial
4. Right mid lateral	4. Left base lateral	4. Left base lateral
5. Right apex medial	5. Left mid lateral	5. Right mid lateral
6. Right apex lateral	6. Left mid medial	6. Right mid medial
7. Left base lateral	7. Right mid medial	7. Left mid medial
8. Left base medial	8. Right mid lateral	8. Left mid lateral
9. Left mid lateral	9. Right apex lateral	9. Right apex lateral
10. Left mid medial	10. Right apex medial	10. Right apex medial
11. Left apex lateral	11. Left apex medial	11. Left apex medial
12. Left apex medial	12. Left apex lateral	12. Left apex lateral

Each urologist determined the biopsy order and corresponding probe movement direction according to their prior training and habitual technique acquired during residency.

Pain perception was assessed using the visual analogue scale (VAS; 0–10) at five specific time points. VAS 1 corresponded to probe insertion through the rectum. VAS 2 referred to probe manipulation within the rectum. VAS 3 represented needle puncture into the prostate. VAS 4 was recorded 30 minutes after the biopsy, and VAS 5 was recorded two hours after the biopsy.

Procedure-related complications occurring within 30 days after the biopsy were recorded, including rectal bleeding, hematuria, fever, and urinary retention. Cancer detection status was also noted.

We created a simplified geometric model to schematize the probe movement pattern and resulting cumulative distance ratios in systematic TRUS-guided biopsy. The model was designed on a two-dimensional coordinate grid, analogous to a standard squared mathematics notebook, where each square represented a fixed distance unit. Each biopsy core site was assigned to a specific coordinate corresponding to its anatomical position within the prostate (base, mid-gland, apex; right or left, medial or lateral).

For each group (A, B, and C), these coordinates were sequentially connected according to the biopsy order described in the previous section. The linear distance between consecutive points was then measured and summed to estimate the total probe trajectory. In this schematic system, the distance between two adjacent points on the grid was defined as a single unit, and the total cumulative movement was expressed as the sum of these unit distances.

This geometric modeling was performed with the assistance of an artificial intelligence tool (ChatGPT, OpenAI), which generated schematic figures illustrating the distinct probe trajectories for each biopsy group based on the manually defined coordinates and biopsy sequences provided by the investigators. The resulting diagrams visually demonstrate how probe movement patterns differed among the groups (Figure 1).

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics, version XX (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean (SD) and tested for normality using the Shapiro–Wilk test. For normally distributed continuous data (e.g., age, BMI, PSA, prostate volume, VAS scores), comparisons among the three groups were conducted using one-way analysis of variance (ANOVA). Test statistics were reported as F values with degrees of freedom (df), and effect sizes were expressed as eta squared (η^2). When the overall ANOVA was significant, Bonferroni-adjusted post-hoc tests were applied to identify pairwise group differences.

Categorical variables (e.g., cancer detection, complications such as rectal bleeding, hematuria, fever, urinary retention) were expressed as frequencies and percentages and compared using the χ^2 test. In cases where expected cell counts were <5, Fisher's exact test was applied.

A two-sided *P*-value of <0.05 was considered statistically significant. Effect sizes were interpreted according to conventional thresholds (η^2=0.01 small, 0.06 medium, ≥0.14 large).

Table 2: Baseline demographics and clinical characteristics

Variable	Group A (n=77)	Group B (n=83)	Group C (n=86)	Test statistic	*P*-value
Age, years	66.4 (6.1)	67.3 (6.0)	66.9 (5.8)	F(2,243)=0.55	0.58
BMI, kg/m²	25.3 (2.7)	25.5 (2.6)	25.1 (2.5)	F(2,243)=0.34	0.71
PSA, ng/mL	9.0 (6.4)	9.2 (6.6)	9.1 (6.5)	F(2,243)=0.07	0.93
Prostate volume, mL	42.1 (15.3)	41.8 (14.7)	42.5 (15.1)	F(2,243)=0.13	0.88
Cancer detected, n (%)	36 (46.8)	39 (47.0)	41 (47.7)	χ^2=0.02	0.99

* Values are presented as mean (SD) or n (%). Continuous variables were compared using one-way ANOVA (F values reported), and categorical variables using χ^2 test.

Table 3: VAS pain scores by time point and group

VAS Time Point	Group A (n=77)	Group B (n=83)	Group C (n=86)	F(df=2,243)	p-value	η^2	Post-hoc
VAS 1 – probe insertion	2.3 (1.0)	2.1 (0.9)	2.2 (0.9)	1.21	0.30	0.01	NS
VAS 2 – probe manipulation	3.8 (0.9)	2.0 (0.8)	2.9 (0.9)	28.10	<0.001	0.19	B<C<A
VAS 3 – needle puncture	4.0 (1.0)	2.9 (0.9)	3.4 (0.9)	22.70	<0.001	0.16	B<C<A
VAS 4 – 30 min post	2.0 (0.8)	1.1 (0.6)	1.5 (0.7)	26.40	<0.001	0.18	B<C<A
VAS 5 – 2 h post	0.8 (0.5)	0.7 (0.5)	0.7 (0.5)	1.68	0.19	0.01	NS

* Values are presented as mean (SD). Between-group differences were analyzed using one-way ANOVA (F statistics with degrees of freedom reported). Effect sizes are given as η^2. Post-hoc comparisons were performed with Bonferroni correction. NS=not significant.

Table 4: Procedure-related complications within 30 days

Complication	Group A (n=77)	Group B (n=83)	Group C (n=86)	χ^2	*P*-value
Rectal bleeding, n (%)	15 (19.5)	8 (9.6)	13 (15.1)	4.8	0.09
Fever ≥38 °C, n (%)	4 (5.2)	2 (2.4)	3 (3.5)	1.5	0.47
Hematuria, n (%)	31 (40.3)	34 (41.0)	36 (41.9)	0.1	0.94
Urinary retention, n (%)	2 (2.6)	2 (2.4)	3 (3.5)	0.3	0.86

* Values are presented as n (%). Group comparisons were made using χ^2 test.

Results

A total of 246 patients were included: Group A (n=77), Group B (n=83), and Group C (n=86). The groups were similar in terms of age (*P*=0.58), BMI (*P*=0.71), PSA (*P*=0.93), and prostate volume (*P*=0.88), with no statistically significant differences (Table 2).

Cancer detection rates were comparable among the groups (46.8%, 47.0%, and 47.7% for Groups A, B, and C, respectively), showing no meaningful variation (*P*=0.99) (Table 2).

Pain intensity differed significantly across the groups during probe manipulation, needle puncture, and early post-biopsy phases. VAS 2, VAS 3, and VAS 4 scores were lowest in Group B with mean (SD) values of 2.0 (0.8), 2.9 (0.9), and 1.1 (0.6), respectively, and highest in Group A with mean (SD) values of 3.8 (0.9), 4.0 (1.0), and 2.0 (0.8), respectively. This indicated a consistent gradient of B<C<A (all *P*<0.001). No significant differences were observed for probe insertion (VAS 1, *P*=0.30) or two hours post-biopsy (VAS 5, *P*=0.19) (Table 3).

Rectal bleeding occurred in 19.5%, 9.6%, and 15.1% of patients in Groups A, B, and C, respectively (*P*=0.09); fever in 5.2%, 2.4%, and 3.5% (*P*=0.47); hematuria in 40–42% (*P*=0.94); and urinary retention in 2–3% (*P*=0.86). Although rectal bleeding and fever were numerically higher in Group A and lowest in Group B, these differences were not statistically significant (Table 4).

According to geometric modeling, the estimated cumulative probe trajectory lengths were 20.6 units in the model with the core order corresponding to Group A, 16.0 units in the model corresponding to Group B, and 20.9 units in the model corresponding to Group C. Accordingly, the total distance traveled by the probe in the model fitting the biopsy core order in Group B was approximately 22–24% shorter than in the other two groups.

Discussion

While prostate biopsy is central to prostate cancer diagnosis, the procedure is associated with discomfort and risk. Pain, in particular, continues to limit patient tolerance and may influence willingness to undergo repeated biopsies when clinically indicated [1, 2]. Numerous studies have addressed pain management in TRUS-Bx, most focusing on the role of local anesthesia and analgesic techniques.

In contrast, the present study investigated a novel and previously unexplored determinant of patient discomfort: the direction of probe movement during systematic biopsy. To our knowledge, this is the first study to evaluate whether the cumulative trajectory of the probe, and consequently the manner in which cores are sampled, has a measurable effect on pain perception and complications.

Our results demonstrated that the sequence of probe movement significantly affected pain outcomes. Groups were comparable in baseline demographics, prostate volume, PSA, and cancer detection rates, thereby excluding these as confounding factors. However, VAS scores differed markedly: Group B patients consistently reported the lowest scores at the most painful phases of the biopsy (VAS 2, 3, and 4), whereas Group A patients reported the highest; Group C was intermediate. The differences were both statistically significant and clinically relevant, as indicated by large effect sizes (η^2=0.16–0.19).

Complications, such as rectal bleeding and fever, were numerically more frequent in Group A and least frequent in Group B, while hematuria and urinary retention occurred at similar rates across groups. Although these differences did not achieve statistical significance, the observed trends reinforce the pain data.

The majority of previous studies on TRUS-Bx–related pain have concentrated on anesthetic techniques. PNB has been established as the gold standard for pain control, yet it does not fully address discomfort during probe insertion and manipulation [5, 6]. To overcome these shortcomings, IRLA has been explored with mixed results. Some randomized studies have demonstrated clear benefits, while others have found no significant advantages [7, 8, 11].

Recently, combined regimens of PNB plus IRLA have been recommended, showing superior pain control across multiple

phases of the procedure without increasing complications [9, 10]. Although these interventions reduce pain intensity, they do not address a fundamental mechanical factor: the pattern of probe maneuvering itself.

Several authors have observed that probe insertion and movement may cause more severe discomfort than the biopsy puncture [3, 12]. Our findings not only confirm this observation but also extend it by demonstrating that the sequence of sampling, which dictates the cumulative path of the probe, independently contributes to pain perception. Importantly, while prior reports acknowledged mechanical discomfort, none have systematically analyzed the effect of movement direction on outcomes. Thus, our study adds a novel perspective to the existing body of evidence.

To provide a rational explanation for the observed pain differences, we developed a simplified geometric model to estimate the cumulative distance traveled by the probe in each group. Using a coordinate-based schematic on graph paper, and later digitalized into a grid model, we measured the trajectory length required to complete the 12-core biopsy sequence. The total distance was shortest in Group B (16.0 units) compared with Group A (20.6 units) and Group C (20.9 units), corresponding to a 22–24% reduction in probe travel. This indicates that Group B's technique was approximately 1.3-fold more efficient in terms of probe movement.

These geometric findings closely mirrored our clinical results, demonstrating a parallel relationship between the modeled probe trajectory and patient-reported pain scores. Patients in Group B consistently reported the lowest pain scores, while Groups A and C, whose trajectory lengths were nearly identical, reported higher VAS values. The strong concordance between the calculated probe travel distance and the observed pain outcomes suggests a causal link. Mechanically, a shorter probe trajectory can improve patient comfort by reducing anal canal stretching, mucosal friction, and sphincter irritation, thereby improving patient comfort. Although the model does not account for interindividual variations in prostate size or shape, it provides a reasonable approximation of probe mobility patterns based on directional differences. Therefore, the geometric analysis supports the hypothesis that reduced probe trajectory contributes to lower pain perception observed in Group B.

Future research employing three-dimensional imaging or motion-sensing technology could further validate and refine these findings.

Complication rates in our study were consistent with prior reports. Hematuria was observed in 40–42% of patients, rectal bleeding in 10–20%, and fever in 2–5%. These rates fall within the ranges previously described [2, 13]. Importantly, the numerical differences observed among our groups paralleled the pain results, with Group A showing the highest rates of rectal bleeding and fever, and Group B the lowest.

Although statistical significance was not achieved, the pattern suggests that more extensive probe movement may also increase the risk of mucosal trauma and bacterial translocation, and thus a predisposition to bleeding and infection. This hypothesis is supported by earlier reports highlighting the role of rectal wall trauma in biopsy-related sepsis [14, 15].

Our study provides new insight into a simple, non-pharmacological factor that may improve patient tolerance of TRUS-Bx. While anesthetic methods, such as PNB and IRLA, remain essential, the direction of probe maneuvering appears to be an independent determinant of both pain and potential complications.

From a practical perspective, adopting a biopsy sequence similar to Group B could be readily implemented without additional equipment or cost. Such an adjustment may enhance patient comfort, reduce anxiety associated with repeat biopsies, and ultimately improve adherence to diagnostic and surveillance protocols.

Moreover, this finding adds nuance to the ongoing debate regarding transrectal versus transperineal approaches. Although transperineal biopsy is increasingly favored for its lower infectious risk, transrectal biopsy remains widely used due to its accessibility and efficiency [16, 17]. Optimizing probe maneuver strategies may, therefore, represent an important means of reducing the drawbacks of TRUS-Bx, allowing it to remain a viable option in settings where transperineal biopsy is not readily available.

Limitations

Several limitations of our study warrant consideration. The retrospective, single-center design inherently limits generalizability. Pain assessment was based on VAS scores, which, although widely validated, remain subjective.

A potential operator-related confounding effect cannot be completely excluded, as each biopsy group corresponded to a different urologist who had been trained during residency with a distinct biopsy sequence and probe manipulation technique. Subtle inter-operator differences, such as variations in manual technique, applied pressure, or patient interaction, might have influenced pain perception independently of the probe trajectory. Although all three urologists were experienced and followed identical preparation, anesthesia, and procedural protocols, unrecorded factors, such as procedural tempo, could not be objectively assessed due to the retrospective nature of data collection.

The geometric model used in this study was based on schematic drawings rather than real-time probe tracking and, therefore, represents an approximation of actual movement. Nonetheless, the strong concordance between the calculated trajectory distances and the observed pain outcomes supports the validity of this approach. Finally, although trends in complication rates were observed, the study was not powered to detect statistically significant differences in relatively rare events, such as sepsis or urinary retention.

Conclusion

This study identifies probe movement direction as a previously unrecognized determinant of patient comfort and safety during systematic TRUS-Bx. The findings demonstrate that beyond anesthetic or analgesic methods, the sequence of probe maneuvering itself significantly influences pain perception and may also affect complication rates. Group B, characterized by the shortest cumulative probe trajectory, consistently showed the lowest VAS 2–4 scores and tended to experience fewer complications, such as rectal bleeding and fever, whereas Group A exhibited the highest values. These results indicate that optimizing the procedural technique, specifically the order and direction of probe movement, can meaningfully improve biopsy

tolerance independent of pharmacological intervention. Implementing such a simple, low-cost, and reproducible modification in clinical practice may improve both patient experience and procedural safety. To our knowledge, this is the first report to establish such an association, and prospective multicenter studies with larger cohorts and motion-tracking validation are warranted to confirm these novel findings.

Acknowledgements

The authors would like to thank the staff of the Urology Department at Alanya Alaaddin Keykubat University for their assistance in data collection and patient care during the study period. The authors also acknowledge the use of ChatGPT (OpenAI) for generating a schematic visualization of the geometric model of probe trajectories, which was based on the authors' original manual calculations.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49. doi: 10.3322/caac.21660.
2. Borghesi M, Ahmed H, Nam R, Schaeffer E, Schiavina R, Taneja S, et al. Complications After Systematic, Random, and Image-guided Prostate Biopsy. Eur Urol. 2017;71(3):353-65. doi: 10.1016/j.eururo.2016.08.004.
3. Chang SS, Alberts G, Wells N, Smith JA Jr, Cookson MS. Intrarectal lidocaine during transrectal prostate biopsy: results of a prospective double-blind randomized trial. J Urol. 2001;166(6):2178-80. doi: 10.1016/s0022-5347(05)65529-2.
4. Irani J, Fournier F, Bon D, Gremmo E, Doré B, Aubert J. Patient tolerance of transrectal ultrasound-guided biopsy of the prostate. Br J Urol. 1997;79(4):608-10. doi: 10.1046/j.1464-410x.1997.00120.x.
5. Nash PA, Bruce JE, Indudhara R, Shinohara K. Transrectal ultrasound guided prostatic nerve blockade eases systematic needle biopsy of the prostate. J Urol. 1996;155(2):607-9.
6. Luscombe CJ, Cooke PW. Pain during prostate biopsy. Lancet. 2004;363(9424):1840-1. doi: 10.1016/S0140-6736(04)16392-7.
7. Mallick S, Humbert M, Braud F, Fofana M, Blanchet P. Local anesthesia before transrectal ultrasound guided prostate biopsy: comparison of 2 methods in a prospective, randomized clinical trial. J Urol. 2004;171(2 Pt 1):730-3. doi: 10.1097/01.ju.0000108125.96072.ff.
8. Trucchi A, De Nunzio C, Mariani S, Palleschi G, Miano L, Tubaro A. Local anesthesia reduces pain associated with transrectal prostatic biopsy. A prospective randomized study. Urol Int. 2005;74(3):209-13. doi: 10.1159/000083550.
9. Giannarini G, Autorino R, Valent F, Mogorovich A, Manassero F, De Maria M, et al. Combination of perianal-intrarectal lidocaine-prilocaine cream and periprostatic nerve block for pain control during transrectal ultrasound guided prostate biopsy: a randomized, controlled trial. J Urol. 2009;181(2):585-91. doi: 10.1016/j.juro.2008.10.002.
10. Raber M, Scattoni V, Roscigno M, Dehò F, Briganti A, Salonia A, et al. Topical prilocaine-lidocaine cream combined with peripheral nerve block improves pain control in prostatic biopsy: results from a prospective randomized trial. Eur Urol. 2008;53(5):967-73. doi: 10.1016/j.eururo.2007.09.005.
11. Issa MM, Bux S, Chun T, Petros JA, Labadia AJ, Anastasia K, et al. A randomized prospective trial of intrarectal lidocaine for pain control during transrectal prostate biopsy: the Emory University experience. J Urol. 2000;164(2):397-9.
12. Kravchick S, Peled R, Ben-Dor D, Dorfman D, Kesari D, Cytron S. Comparison of different local anesthesia techniques during TRUS-guided biopsies: a prospective pilot study. Urology. 2005;65(1):109-13. doi: 10.1016/j.urology.2004.08.013.
13. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, Nam R, et al. Systematic review of complications of prostate biopsy. Eur Urol. 2013;64(6):876-92. doi: 10.1016/j.eururo.2013.05.049.
14. Park DS, Hwang JH, Choi DK, Gong IH, Hong YK, Park S, et al. Control of infective complications of transrectal prostate biopsy. Surg Infect (Larchmt). 2014;15(4):431-6. doi: 10.1089/sur.2013.138.
15. Ghafoori M, Shakiba M, Seifmanesh H, Hoseini K. Decrease in infection rate following use of povidone-iodine during transrectal ultrasound guided biopsy of the prostate: a double blind randomized clinical trial. Iran J Radiol. 2012;9(2):67-70. doi: 10.5812/iranjradiol.7561.
16. Guo LH, Wu R, Xu HX, Xu JM, Wu J, Wang S, et al. Comparison between Ultrasound Guided Transperineal and Transrectal Prostate Biopsy: A Prospective, Randomized, and Controlled Trial. Sci Rep. 2015;5:16089. doi: 10.1038/srep16089.
17. Lane BR, Zippe CD, Abouassaly R, Schoenfield L, Magi-Galluzzi C, Jones JS. Saturation technique does not decrease cancer detection during followup after initial prostate biopsy. J Urol. 2008;179(5):1746-50. doi: 10.1016/j.juro.2008.01.049.

J Surg Med. 2025;9(10):199-206.
https://doi.org/10.28982/josam.8211

JOSAM

Review
https://jsurgmed.com/

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Neurobiological and behavioral correlates of excessive social media use in adolescents

Daniel Ogun

College of Science, George Mason University, Fairfax, Virginia, USA

ORCID of the author(s)

DO: https://orcid.org/0009-0005-3084-9974

Corresponding Author
Daniel Ogun
College of Science, George Mason University, Fairfax, Virginia, USA
E-mail: danogun17@gmail.com

Ethics Committee Approval
Since this study is based solely on a literature review, ethics committee approval and informed consent were not required. However, all reviewed studies were sourced from reputable academic journals, institutions, and official reports, ensuring adherence to ethical research standards. Whenever applicable, the original studies included in this review obtained ethical approval from relevant institutional boards and secured informed consent from participants.

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

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

Published
2025 October 17

Abstract

Background/Aim: Millions of teenagers around the world spend more time engaged with their social media accounts than ever before. This situation raises questions about the impact of social media on mental health. This systematic literature review explores the relationships among extreme social media use and addiction, depression, and sleep deprivation.

Methods: A thematic analysis of 38 peer-reviewed studies, all published between 2010 and 2024, was conducted. The selection of studies was based on their significance and relevance to teenage mental health, namely, neurobiological, psychological, and behavioral perspectives. The study categorized findings into three primary themes: compulsive digital behaviors (addiction), emotional distress (depression), and disrupted circadian rhythms (sleep deprivation).

Results: Extended social media exposure alters dopamine regulation, reinforcing addictive tendencies similar to substance dependence. Excessive usage correlates with heightened depressive symptoms, exacerbated by social validation pressures and algorithm-driven content cycles. Furthermore, late-night digital engagement contributes to melatonin suppression and chronic sleep debt, impairing cognitive function and emotional stability.

Conclusion: As serious mental health issues stemming from excessive social media content haunt society, it is essential to initiate effective coping strategies. Given the insights from the present study, the need for an awareness campaign, structured daily usage, and more neuroscientific studies to reduce the long-term impact of social media on adolescent well-being is acute.

Keywords: social media, addiction, depression, sleep deprivation, mental health, teenagers

Figure 1: Social Media Users Since 2000 (Resource: datareportal.com/reports/digital-2024-global-overview-report)

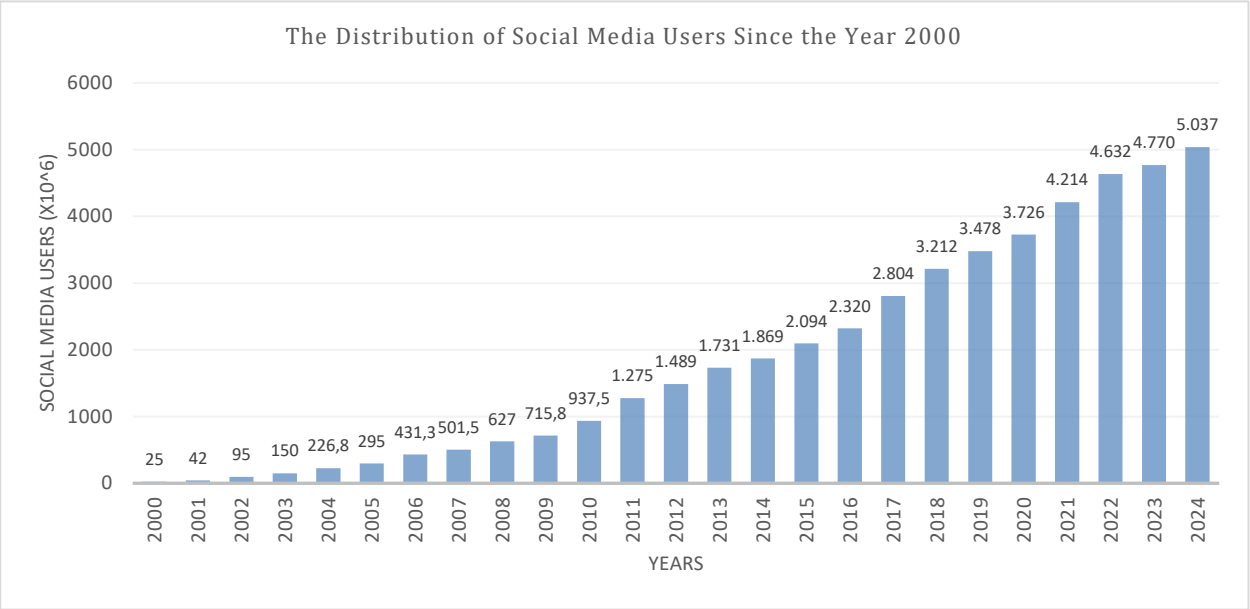
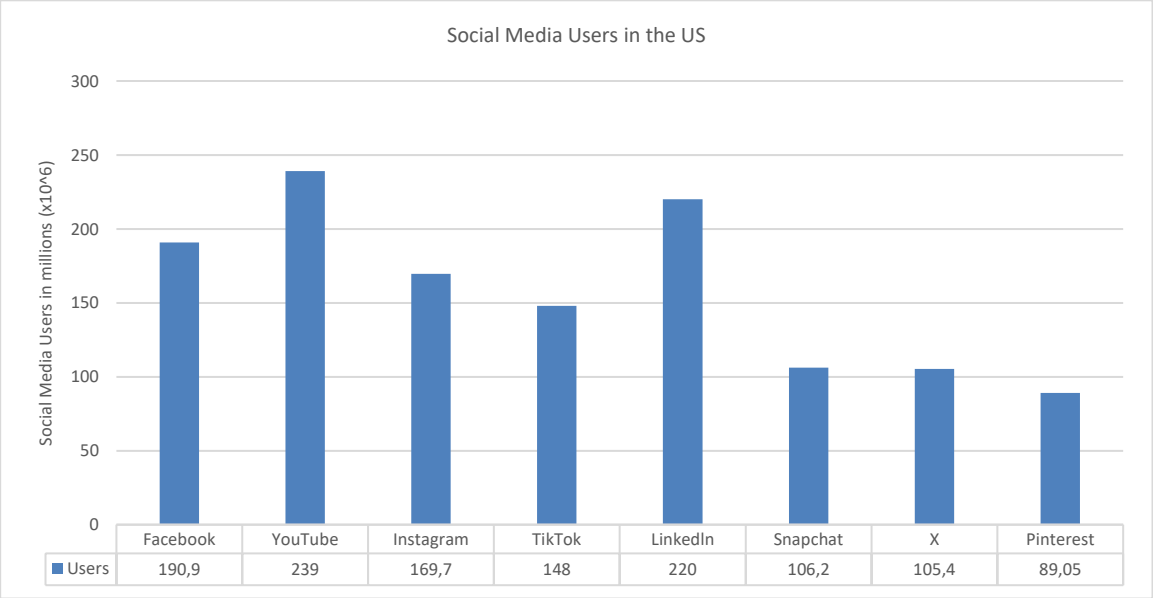


Figure 2: Social Media Users in the United States (Resource: https://datareportal.com/reports/digital-2024-united-states-of-america)



Introduction

As of January 2023, the Global Overview Report [1] noted that the Earth's population is 8.01 billion people, with 57% of people residing in urban areas. The number of internet users globally is 5.16 billion, while active social media users totaling 4.76 billion people. Furthermore, the United Nations World Population Prospects [2] reports that by January 2024, the global population had increased to 8.08 billion people. That is, over one year, the global population increased by 74 million people, reflecting an annual growth rate of 0.9 percent. As of January 2024, there are 5.35 billion internet users and 5.04 billion active users on social media platforms. For a detailed view of the growth in active social media users over the last 24 years, please refer to the figure 1 provided by [3].

As of January 2024, data [3] indicate that the population of the United States is 340.9 million people. Among this population, there are 331.1 million individuals who use the internet; of those, 239 million people are active users of social media. The accompanying figure 2 illustrates the number of social media users in the United States [3].

Social media is a crucial part of the lives of almost everyone, especially teenagers. Nowadays, teenagers can access social media platforms and technology at the tip of their fingertips. In a survey conducted by the Pew Research Center in 2022, 95% of teenagers had access to a smartphone compared with 73% of teenagers in 2014-2015 [4]. Extrapolating these statistics to the population of teenagers in the United States (42 million according to the US Department of Human Services) means that approximately 39.9 million teenagers have access to a cell phone [5]. This number represents a 22% increase over the past 7 years.

Teenagers use social media for a many of reasons, including communication, leisure, and identity. Identity in particular plays an important role in the lives of adolescents, as it defines their sense of self, their values, and their aspirations for the future. The process of establishing one's identity on social media can be likened to selecting one's finest attire for an outing; this goal is to leave a lasting impression [6].

Social media serves as an accessible platform for individuals across the globe. It enables the instantaneous sharing of diverse content, including images, videos, and direct messages, with just a simple click. Given the widespread use of social media

among adolescents, social media platforms have the potential to contribute to various mental health challenges, such as addiction, hormonal imbalances resulting from sleep deprivation, as well as heightened feelings of anxiety, depression, and suicidal ideation [7,34]. Social media and cell phone usage among teenagers has increased in the past couple of years; this usage can result in a wide variety of mental health issues as teenagers grow up to become adults [4]. The purpose of this article is to explore how excessive use of social media on a daily basis affects the mental health of teens (aged 12-20 years old) in North America.

Materials and methods

Study design

We adopted a literature review, which encompasses choosing from a variety of methods and processes for locating, recording, comprehending, meaning-making, and distributing material relevant to a topic of interest [8]. A literature review serves as the foundation for developing a new conceptual model or theory, and it can be useful when attempting to chart the evolution of a certain research topic across time. Due to the fact that literature review combines the conclusions and points of view from multiple empirical studies, such an investigation can often address research subjects better than can a single study [9]. For the purpose of this investigation, 'excessive social media use' is defined as engagement exceeding three hours per day, based on criteria used by Fiellin et al. [14] and Alavi et al. [32]. Other reviewed studies use varying thresholds, including compulsive behaviors or self-reported digital dependence, highlighting the absence of a universally accepted definition.

Data collection

A thorough review was conducted using credible sources such as government reports and institutional studies in addition to peer-reviewed academic sources like PubMed, PsycINFO, Scopus, and Google Scholar. The search terms used were "social media addiction," "teen mental health," "digital dependency," "social media and sleep deprivation," and "social media and depression." To ensure relevance and credibility, studies were chosen based on these criteria:

- Empirical studies published between 2010 and 2024.
- Studies focused on teenagers (ages 12-20 years) in North America.
- Research examining neuroscientific, psychological, or behavioral impacts of social media use.

The selected studies were systematically reviewed using a thematic analysis approach, and the findings were categorized into three primary themes:

- Social Media Addiction & Cognitive Impact: Analyzing alterations in dopamine regulation and brain activity.
- Depression & Anxiety Linked to Social Media: Evaluating the emotional and behavioral effects.
- Sleep Deprivation & Circadian Disruption: Examining the consequences of digital overstimulation and screen time at night.

The study highlights research trends, gaps, and commonalities by synthesizing findings from 38 studies. To guarantee impartiality and balanced representation, a critical evaluation of study limitations, sample sizes, and methodology was carried out.

Analysis

The results of the studies were examined to determine recurring themes and answers to the following research questions:

- Does excessive use of social media result in addiction?
- Does excessive use of social media cause depression?
- Can excessive social media usage lead to sleep deprivation?

Results

Addiction

Excessive use of social media by teenagers is directly linked to behavioral addiction symptoms, according to several studies. Fiellin et al. [14] found that teenagers using social media for more than three hours per day exhibited compulsive usage behaviors similar to those of substance dependence. Specifically, adolescents experienced difficulty controlling their time online, withdrawal-like symptoms when disconnected, and an increased tolerance, requiring more engagement for the same satisfaction.

Alavi et al. [32] further established parallels between adolescent social media addiction and substance addiction, highlighting neurobiological mechanisms such as impaired impulse control. Adolescents addicted to social media exhibited heightened activity in reward-processing brain regions, mirroring patterns observed in cases of drug dependence.

Kuss and Griffiths [11] emphasized the role of reinforcement mechanisms embedded within social media platforms, including instant feedback through likes, comments, and notifications, that contribute to compulsive engagement. These reward structures stimulate dopamine release, reinforcing repetitive behaviors and making disengagement more difficult. Notably, studies examining adolescent brain responses to excessive social media use have detected alterations in dopaminergic pathways similar to those observed in cases of behavioral and substance addictions [11].

Depression

The psychological toll of excessive social media use on adolescents has been well-documented, with growing evidence linking prolonged engagement to increased symptoms of depression. Abi-Jaoude et al. [37] reported that teenagers with high levels of screen time noted lower self-esteem and higher rates of depressive symptoms, especially when social media engagement involved passive scrolling or social comparisons.

Patterns of digital interaction appear to influence emotional well-being, particularly in cases of cyberbullying and fear of missing out (FOMO). Keles et al. [19] conducted a meta-analysis and found consistent evidence of increased depression risk in adolescents spending extended hours on social platforms, particularly when exposure involved stress-inducing factors.

Additionally, the nature of engagement—that is, passive or active—plays a critical role in mental health outcomes. Huang [22] demonstrated that passive social media use, where individuals consume content without active interaction, was more strongly correlated with depressive symptoms compared with direct engagement. This finding underscores the psychological toll of comparison-based behaviors, in which adolescents internalize unrealistic portrayals of happiness and success displayed by their peers online.

Sleep Deprivation

The effect of nighttime social media use on teenagers' sleep patterns is well-documented, with research showing significant disruptions to sleep hygiene and overall rest quality. Carter et al. (2016) observed that adolescents engaging with screens late at night experienced delays in sleep onset, reduced sleep duration, and lower sleep efficiency [27]. These effects were particularly pronounced in individuals who reported compulsive social media use, indicating a behavioral pattern that exacerbates sleep deprivation.

Exposure to blue light from screens plays a critical role in sleep disturbances; blue light interferes with melatonin production and the body's natural sleep-wake cycle [18]. Lemola et al. [30] found that nighttime social media engagement was strongly correlated with increased fatigue and mood instability the following day, largely due to prolonged cognitive stimulation and artificial light exposure disrupting circadian rhythms.

A broader review by Harvard Medical School (2018) reinforced these findings, emphasizing that excessive social media use before bed increases brain activity, delaying melatonin secretion and reducing sleep readiness [6]. This body of research underscores the negative consequences of nighttime digital engagement, suggesting that adolescents with habitual late-night social media usage may be at greater risk for chronic sleep deprivation.

Discussion

The reviewed studies collectively indicate a strong link between excessive social media usage and teenage mental health, particularly in terms of addiction, depression, and sleep deprivation. However, the methodological approaches across these studies vary significantly, which could possibly impact the reliability and applicability of their findings.

Social Media and Addiction

The earliest human records provide evidence of an inclination towards addictive psychoactive drugs. Throughout history, psychoactive substances have been utilized by religious leaders during sacred rituals, medical practitioners for therapeutic reasons, and the general population; such substances include alcohol, nicotine, and caffeine [15]. However, addiction and excessive use of drugs has also been incorporated into the practice of medicine. Levinstein [16,17] conducted one of the first thorough studies of morphine addiction in 1875. He highlighted two critical aspects of opiate addiction that would go on to intrigue researchers: the peculiar nature of withdrawal, which could be rapidly alleviated by administering more of the drug, and the obsessive dependence on the substance, which took precedence over all else, even as the individual's circumstances worsened [17].

Current neuroscientific breakthroughs support the notion that addiction is a brain disorder [18]. However, some experts disagree, stating that addictive behavior is a choice [10]. However, from a neuroscience point of view, addiction can be classified as a physiological disease. The extended amygdala, basal ganglia, and the prefrontal cortex are affected by addiction mainly through certain receptors and neurotransmitters. The prefrontal cortex has both dopamine D1 and D2 receptors. D2 receptors activate at lower dopamine concentrations due to their higher sensitivity to dopamine. Under normal conditions, the prefrontal cortex receives a low-level, consistent supply of dopamine due to the slow, rhythmic activation of dopamine neurons in the ventral tegmental area (VTA), which connects to the cortex. However, dopamine neurons activate more quickly in response to an unexpected occurrence, such as a fun reward or a highly unpleasant event. This rhythmic firing causes a sudden, although brief, rise in dopamine. The large amounts of dopamine obtained during phasic firing can activate D1 receptors, which are believed to be essential for dopamine's rewarding effect [18]. Addiction is a very serious mental disease that affects a person's "brain circuits" and their ability to control themselves when it comes to certain stimuli. (For example, sex, drugs (opioids and cocaine), pornography, gambling, food, and social media [11].) Addiction is a disease that can both cause pleasure and lessen unpleasant or bad effects. Its primary characteristics include an inability to control behavior and the persistence of that activity in the face of adverse consequences [12,20].

Each of the stimuli noted above controls different parts of the brain and is associated with the secretion of different hormones (i.e., neurotransmitters). Several philosophers and psychologists have criticized the neurobiological diagnosis of addiction, as typified by obsessive and recurring drug use [19]. Their critique is based on both empirical evidence and conceptual analysis. Empirical criticism suggests that the disease view lacks support from the empirical evidence cited by its proponents. This critique consists of both observational proof of addicts' recurrent self-destructive conduct and molecular evidence of modifications to the brain's normal functioning brought on by frequent drug use [19]. Abuse-related drugs have a wide range of effects on brain circuitry, including perception, emotion, decision-making, and cognitive function. These effects contribute to the instinctive and compulsive character of drug use [20]. Changes in synaptic connections caused by the drug's activity in these networks may persist long after the drug has cleared a person's system [12,20].

Addiction can have a profound effect on people's well-being, interpersonal connections, and general standard of living. Some of the signs of addiction include [21]:

- Incapability to stop: Individuals may persist with their substance use or participate in detrimental addictive behavior despite their desire to stop.
- Failure to control oneself: Individuals may experience a sense of complete relinquishment of control over their substance use or activities, leading to feelings of helplessness.
- Health concerns and personal difficulties: Addiction affects a person's physical and emotional well-being as well as their relationships, career, and personal relationships.
- Decrease in vitality and motivation: People suffering from addiction may experience a lack of energy or motivation to the things they would normally value [22].

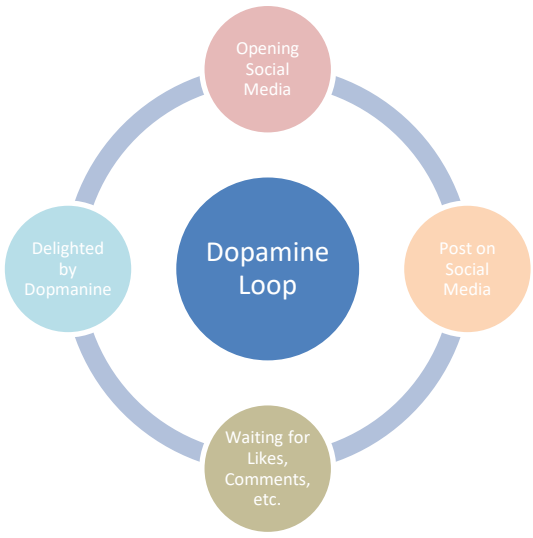
The primary neurotransmitters that influence a person's mental health include dopamine, serotonin, oxytocin, and endorphins [13]. Addiction is also a physiological disease that involves changing the structure of the brain. Anatomical changes in the brain classify addiction as both a physiological and psychological disease [14]. According to Bechara [23], addiction

results from an imbalance between two distinct but interconnected neural systems that regulate decision-making: the prefrontal cortex system, which is reflective and signals pleasure or pain associated with future prospects, and the impulsive amygdala system, which signals immediate prospects' pain [24]. Goodman [25] defined addiction as a state in which a problematic activity is typified by two things: (a) persistent inability to regulate the conduct and (b) persistence in the behavior despite serious negative effects [26].

Dopamine is an important element in people's brains that regulates daily behavior; it may be involved in addiction. Dopamine is intended to send feelings of pleasure, comfort, and happiness to dopamine receptors whenever an action that is pleasurable is thought of and completed. The dopamine system is a "primitive" system that confers a sense to pleasure to repeating a task such as eating food. Indulging in an activity that secretes massive or continuous amounts of dopamine, such as scrolling on social media, causes dopamine receptors to get overwhelmed and adapt to the large amounts of dopamine received over time. To obtain the same feeling of dopamine going forward, a person must use social media for a longer period of time. As time goes on, the receptors get even more adapted to the large amounts of dopamine, resulting in addiction [14]. This situation is often referred to as the dopamine loop [28]. Drugs such as cocaine can block the dopamine transporters in the pre-synaptic nerve, causing a buildup of dopamine in the synaptic cleft between the pre-synaptic nerve and the post-synaptic nerve [18]. This buildup causes a pool of dopamine to accumulate in the synaptic cleft, which in turn travels into the transmitters to provide the dopamine signal [27].

The following figure shows the dopamine loop of social media use [28]:

Figure 3: Loop of Social Media Use (Akshay, Sudha, and Ajit, 2019)



Serotonin is the mood-booster hormone. It changes a person's mood in a positive way and influences behaviors and functions such as memory, fear, stress, digestion, addiction, sexuality, sleep, and homeostasis [29]. (Homeostasis is the state at which the human body remains at equilibrium.) Lower levels of serotonin are correlated with depression in people [29].

Oxytocin is produced in the hypothalamus and secreted from the pituitary gland of the brain. It is often referred to as the "love hormone" and/or the "connection hormone." Oxytocin is like serotonin in terms of mood boosting. It is promoted by increasing the connection between two people. For example, oxytocin is important for pregnant women and mothers to accelerate the process of giving birth and helping to transport milk from nipple ducts [39]. Oxytocin furthermore increases the feelings of relaxation and trust while improving people's mental health [30].

Endorphins are referred to as the "pain tolerance and sex hormone" as they are most prevalent in those situations. These neurotransmitters are produced in the pituitary glands and are then released into the nervous system. Endorphins are secreted into the circulatory system when a person is engaged in physical activity [31].

The majority of teenagers are addicted to social media without being conscious of it. In a survey conducted by the Pew Research Center, many teenagers report difficulty in reducing social media use [4].

Behavioral addiction, like internet addiction, parallels drug addiction; however, instead of dependence on a substance, the individual becomes addicted to the behavior itself or the emotional response it generates [32]. The extreme nature of internet use shares significant parallels with substance addiction. Neuroimaging studies suggest that the underlying causes of this behavior align with those of other addictive disorders. Structural changes in the brain may disrupt executive functions related to planning and reasoning, heightening impulsivity and increasing susceptibility to addiction [33].

It is straightforward for teenagers to become addicted to social media given its usage of colors, notifications, and other habit-forming characteristics. Excessive daily use of social media can contribute to physiological changes in the brain associated with addiction and attention issues [7]. In an article released by Stanford University, 24% of teens reported being online "constantly" [10]. The concept of scrolling on social media platforms such as TikTok, Instagram, or YouTube enables the viewer, in this case a teenager, to spend focus on short videos (i.e., those with a maximum length of one minute). That constant scrolling results in a shortened attention span due to the dopamine physically changing the anatomy of the brain. Dr. Julie Albright, a sociologist, states that the state of scrolling is "almost hypnotic" and a "pleasurable dopamine state" [40]. A study revealed that 50% of TikTok videos are longer than one minute, which may increase cognitive load. Certain social media platforms exploit this fact by providing short videos to scroll through. As a result, this situation can contribute to shortened attention spans and can contribute to other factors such as sleep deprivation [7].

While several studies [14,32] have established behavioral addiction parallels between social media and substance abuse, many have relied on self-reported data. That situation may have introduced bias. Moreover, the lack of longitudinal studies makes it difficult to assess long-term neurological consequences of excessive social media use. The absence of standardized diagnostic criteria for social media addiction further complicates comparisons across studies, making it challenging to distinguish compulsive digital engagement from true clinical addiction.

Sleep Deprivation and Social Media

Social media-induced sleep deprivation can have many effects on teenagers' mental and physical health. Teenagers in this day and age have access to technology and social media that can

affect their sleep schedule. For example, in a survey conducted by the Pew Research Center, 95% of teenagers noted having access to a smartphone compared with just 73% of teenagers in 2014-2015 [4]. We note, however, that sleep deprivation in teenagers can also be due to other issues. For example, the social expectation of succeeding and being admitted to a competitive university drives many teenagers to take challenging Advanced Placement classes. One teenager, Walworth, reports after spending around 4-5 hours on her homework she prefers to go online and chat with her friends and "surf the web." That situation causes her to go to bed later. Constant exposure to illuminated screens at night can throwing the body's circadian rhythm out of whack [30]. The term "circadian rhythm" refers to a biological clock in the body that decides what time someone should go to sleep [34]. The mental effects of sleep deprivation include an inability to focus, concentrate, and remember [29]. Sacrificing sleep to study for an exam is not recommended—the capacity to which a student can remember decreases drastically when he or she is sleep deprived [34]. The effects of sleep deprivation also include an increase in body fat due to hormone imbalances and a weakened immunity to fight bacteria and viruses. When the body is in a rested state, it automatically fights, defends, and destroys "foreign invaders" that could be a cause of disease and or long-term health conditions [35]. The combination of social media and homework can trigger an imbalanced sleep schedule in teenagers, which causes them to be sleep deprived and susceptible to physical and mental conditions that can affect their current and long-term well-being.

Studies have consistently highlighted the negative impact of nighttime screen exposure on melatonin regulation and circadian rhythms [34]. However, sample sizes vary, and few studies have incorporated physiological sleep tracking. That situation limits their ability to quantify the direct neurological effects of sleep deprivation caused by excessive social media use.

Depression and Social Media

With the advent of scrolling, "a few minutes" can easily turn into more than 30 minutes. Impulsivity is strongly associated with addiction, and there are multiple mechanisms through which individuals with impulsive tendencies may be at greater risk of developing addictive behaviors or experiencing addiction with increased severity and duration. One such mechanism involves difficulties assessing or managing both positive and negative emotions, which can result in reduced control over risky actions and poor decision-making [36].

Along with sleep deprivation, social media usage can open the door to anxiety, depression, and suicide in teenagers. Among teenagers, girls are known to exhibit more significant signs of anxiety, depression, and suicide, and girls also tend to spend more time online [37]. The second cause of death among teenagers in Canada is suicide; there was a 110% increase in the number of hospital admissions of intentional self-harm among teenage girls between 2007 and 2014 (Canadian Institute for Health Information, 2018) [41]. An article by the Canadian Medical Association Journal (CMAJ) reported that spending more than 2 hours per day on social media and networking sites was associated with feelings of suicide and depression among teenage girls [38]. Specific subconscious triggers can increase feelings of depression, suicide, and anxiety in teenagers; those triggers include FOMO, which is defined as "a persistent concern that others may be enjoying valuable experiences while one is missing out." Other triggers include feeling like it's necessary to post pictures of yourself to get likes and comments, the feeling of being "replaceable," and physical yet unconscious addictions such as looking at your phone whenever you are bored [38].

The availability of social media opens the door to content that can expose teenagers to sensitive information. For example, viewing distressing images and videos unintentionally related to suicide can promote feelings of anxiety and depression in teenagers who are particularly sensitive. Limiting one's social media apps and using content blockers can allow teenagers to prevent having feelings of depression, anxiety, and suicide [38].

Furthermore, cyberbullying can also promote feelings of suicide in teenagers [38,58]. Humans are social creatures, and teenagers' feelings of negativity in the form of anxiety and depression can be rooted in the lack of real-life social interactions [7]. Consequently, using social media excessively can leave teenagers with feelings of anxiety, depression, and suicide that came up due to conscious and subconscious triggers and cyberbullying.

Similarly, research linking social media use to depression [37,38] often lacks control for confounding variables, such as family dynamics, socio-economic status, and pre-existing mental health conditions. While correlations are evident, establishing causation remains problematic, requiring more robust experimental designs.

Limitations

While this study provides valuable insights into the impact of excessive social media usage on teenagers' mental health, several limitations must be acknowledged. Firstly, the review relies on a limited number of studies (38), which may not fully capture the breadth of the existing research on this topic. A larger dataset would confer a broader understanding of the impact of social media across different demographics. Secondly, the research primarily focuses on data from North America, particularly the United States. This geographical limitation may not reflect the experiences of teenagers in other cultural contexts, where social, economic, and educational factors may influence social media usage differently.

Additionally, the heterogeneity of the reviewed studies poses another challenge. The included research varies in methodologies, sample sizes, and measurement techniques, making it difficult to draw direct comparisons or establish universal conclusions. Some studies rely on self-reported data, which are subject to participant bias and may inflate or distort findings on social media-related addiction, depression, and sleep deprivation.

Furthermore, his review is largely descriptive; it summarizes existing findings rather than conducting statistical analysis or meta-synthesis. This approach, while valuable for identifying trends, does not establish causality, meaning that the link between social media usage and mental health outcomes remains correlational rather than definitive.

Future research should prioritize longitudinal studies, cross-cultural analyses, and experimental designs to better understand causal mechanisms and potential interventions.

Conclusion

This literature review examined 38 studies to investigate the relationship between excessive social media use and its effects on teenagers' mental health. The findings support a strong correlation between social media addiction, depressive symptoms, and sleep disturbances.

Social Media Addiction

Several studies identified excessive social media usage as a behavioral addiction, with mechanisms similar to substance dependence. Neuroscientific research highlights that prolonged engagement leads to dopamine dysregulation, fostering compulsive behaviors. A study by Fiellin et al. [14] found that teenagers who spend more than three hours per day on social media exhibit impaired impulse control, mirroring traits observed in substance-related addictions. Additionally, Alavi et al. [32] emphasized that behavioral addiction follows patterns similar to drug dependency (that is, affecting prefrontal cortex activity and cognitive decision-making).

Depression & Anxiety

Our review furthermore indicated a strong association between excessive social media use and depressive symptoms. A longitudinal study by Abi-Jaoude et al. [37] revealed that teenagers engaging in high-frequency social media interactions noted higher levels of self-comparison, anxiety, and depressive moods. Additionally, cyberbullying and social validation pressures contribute to elevated emotional distress [38]. These findings are consistent with prior research emphasizing that social comparison theory plays a key role in mediating depressive tendencies among adolescents [4].

Sleep Deprivation & Cognitive Impact

Evidence suggests that nighttime social media usage contributes significantly to sleep disturbances, disrupting circadian rhythms. A Pew Research Center survey (2022) found that 58% of teenagers struggle to limit their social media usage before bedtime, leading to delayed sleep onset and reduced sleep quality. Stanford Medicine [34] reports that blue-light exposure from screens inhibits melatonin production, causing chronic sleep debt among adolescents. Furthermore, disrupted sleep cycles correlate with impaired memory retention, decreased academic performance, and heightened stress responses.

The reviewed literature underscores that excessive social media usage manifests as an addictive behavior, exacerbates mental health challenges such as depression and anxiety, and significantly disrupts sleep cycles, leading to long-term cognitive and emotional consequences.

Although social media is currently a major part of teenagers' digital and real lives in means of identity, community, leisure, and communication, excessive usage can lead to many mental and physical health issues. Teenagers should limit the amount of time they spend on social media each day. Some tips for doing so include:

- Consciously recognizing when you have the urge to go on social media.
- Setting reminders to take a break from social media every 5-10 minutes.
- Regularly arranging cell phone breaks.
- Limiting the content you can see on social media.
- Switching to a "dumb phone", like a Nokia, Gabb phone, and/or a flip phone, that only has the ability to text message and call.
- Going on a digital detox at least once per week.
- Getting support from external resources such as a trusted friend, therapist, or support group.

Despite methodological limitations, the cumulative evidence supports a clear trend: teenagers engaging in high-frequency social media use exhibit patterns consistent with addiction, including dopamine dysregulation and compulsive engagement behaviors. Furthermore, social validation mechanisms on platforms like Instagram, TikTok, and Snapchat exacerbate self-esteem concerns, reinforcing negative feedback loops that contribute to depressive symptoms. Sleep deprivation acts as a compounding factor, worsening cognitive function, emotional regulation, and academic performance. To advance research in this domain, future studies should prioritize:

- Longitudinal analyses to assess the long-term neurocognitive consequences of excessive social media use.
- Standardized diagnostic criteria for social media addiction.
- Objective physiological measures (e.g., EEG sleep studies, fMRI dopamine activity).
- Controlled experiments that account for external variables influencing mental health outcomes.

References

1. We Are Social. Digital 2023: Global Overview Report. 2023. Available from: https://wearesocial.com/wp-content/uploads/2023/03/Digital-2023-Global-Overview-Report.pdf
2. DataReportal. Digital 2024: Global Overview Report. 2024. Available from: https://datareportal.com/reports/digital-2024-global-overview-report
3. DataReportal. Digital 2024: The United States of America Report. 2024. Available from: https://datareportal.com/reports/digital-2024-united-states-of-america
4. Vogels EA, Gelles-Watnick R, Massarat N. Teens, social media and technology 2022. Pew Research Center; 2022. Available from: https://www.pewresearch.org/internet/2022/08/10 eens- social-media-and-technology-2022/
5. HHS Office of Population Affairs. America's diverse adolescents. U.S. Department of Health & Human Services; 2019. Available from: https://opa.hhs.gov/adolescent-health/adolescent-health-data/americas-diverse-adolescents
6. Martin F, Wang C, Petty T, Wang W, Wilkins P. Middle school students' social media use. J Educ Technol Syst. 2018;47(1):1-17
7. Bulut D. The association between attention impairments and internet and social media usage among adolescents and young adults with potential consequences: A review of literature. Open J Psychiatry. 2023;13(2):1-10
8. Onwuegbuzie AJ, Frels RK. Methodology of the literature review. Thousand Oaks, CA: Sage Publications; 2016
9. Snyder H. Literature review as a research methodology: An overview and guidelines. J Bus Res. 2019;104:333–9. doi:10.1016/j.jbusres.2019.07.039
10. Goldberg AE. The (in)significance of the addiction debate. Neuroethics. 2020;13(3):311– 24. doi:10.1007/s12152-019-09424-5
11. American Society of Addiction Medicine. What is the definition of addiction? 2019. Available from: https://www.asam.org/quality-care/definition-of-addiction
12. Horseman C, Meyer A. Neurobiology of addiction. Clin Obstet Gynecol. 2019;62(1):118–27. doi:10.1097/GRF.0000000000000416
13. Watson S. Feel-good hormones: How they affect your mind, mood, and body. Harvard Health. 2021. Available from: https://www.health.harvard.edu/mind-and- mood/feel-good-hormones-how- they-affect-your-mind-mood-and-body
14. Fiellin D. How an addicted brain works. Yale Medicine. 2022. Available from: https://www.yalemedicine.org/news/how-an-addicted-brain-works
15. Crocq MA. Historical and cultural aspects of man's relationship with addictive drugs. Dialogues Clin Neurosci. 2007;9(4):355–61. doi:10.31887/DCNS.2007.9.4.macrocq
16. Levinstein E. Morbid craving for morphia: A monograph founded on personal observations. Harrer C, translator. London: Smith, Elder & Co.; 1878
17. Musto DF. Drug abuse research in historical perspective. In: Pathways of Addiction: Opportunities in Drug Abuse Research. Washington, DC: National Academies Press; 1996. Available from: https://www.ncbi.nlm.nih.gov/books/NBK232965/
18. Uhl GR, Koob GF, Cable J. The neurobiology of addiction. Ann N Y Acad Sci. 2019;1451(1):5–19. doi:10.1111/nyas.14129

19. Henden E, Melberg HO, Rogeberg OJ. Addiction: Choice or compulsion? Front Psychiatry. 2013;4:77. doi:10.3389/fpsyt.2013.00077
20. Volkow ND, Warren KR, Ries RK, Fiellin DA, Miller SC, Saitz R. Drug addiction: The neurobiology of behavior gone awry. In: The ASAM Principles of Addiction Medicine. 5th ed. Philadelphia: Wolters Kluwer; 2014. p. 3–18
21. Cleveland Clinic. Addiction: Understanding its effects and treatment. 2023. Available from: https://my.clevelandclinic.org/health/diseases/6407-addiction
22. Armstrong L, Ackermann K, Fuller K, Kelley R, Thomas S, Regan J, et al., editors. Signs & symptoms of addiction (physical & mental). American Addiction Centers; 2024. Available from: https://americanaddictioncenters.org/adult-addiction-treatment-programs/signs
23. Bechara A. Decision making, impulse control, and loss of willpower to resist drugs: A neurocognitive perspective. Nat Neurosci. 2005;8(11):1458–63. doi:10.1038/nn1584
24. Argyriou E, Um M, Carron C, Cyders MA. Age and impulsive behavior in drug addiction: A review of past research and future directions. Pharmacol Biochem Behav. 2018;164:106–17. doi:10.1016/j.pbb.2018.02.007
25. Goodman MD. Addiction: Definition and implications. Br J Addict. 1990;85(11):1403–8. doi:10.1111/j.1360-0443.1990.tb01620.x
26. Panova T, Carbonell X. Is smartphone addiction really an addiction? J Behav Addict. 2018;7(2):252–9. doi:10.1556/2006.7.2018.49
27. Venton BJ, Seipel AT, Phillips PE, Wetsel WC, Gitler D, Greengard P, et al. Cocaine increases dopamine release by mobilization of a synapsin-dependent reserve pool. J Neurosci. 2006;26(12):3206–9. doi:10.1523/JNEUROSCI.5205-05.2006
28. Akshay AF, Sudha S, Ajit S. Social media impact on students' academic performance based on sleeping hours. Int J Recent Technol Eng. 2019;8(4):S.2
29. Watson S. Serotonin: The natural mood booster. Harvard Health. 2023. Available from: https://www.health.harvard.edu/mind-and-mood/serotonin-the-natural-mood-booster
30. LeWine HE, editor. Oxytocin: The love hormone. Harvard Health. 2023. Available from: https://www.health.harvard.edu/mind-and-mood/oxytocin-the-love-hormone
31. Chaudhry SR. Biochemistry of endorphins. StatPearls [Internet]. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470306/
32. Alavi SS, Ferdosi M, Jannatifard F, Eslami M, Alaghemandan H, Setare M. Behavioral addiction versus substance addiction: Correspondence of psychiatric and psychological views. Int J Prev Med. 2012;3(4):290–4
33. Kurniasanti KS, Siste PA, Assandi P, Ismail RI, Nasrun MWS, Wiguna T. Internet addiction: A new addiction? Med J Indones. 2019;28(1):82–91. doi:10.13181/mji.v28i1.2752
34. Richter R. Among teens, sleep deprivation is an epidemic. Stanford Medicine News Center. 2015 Oct 8. Available from: https://med.stanford.edu/news/all-news/2015/10/among- teens-sleep- deprivation-an-epidemic.html
35. Watson S, Cherney K. 11 effects of sleep deprivation on your body. Healthline. 2023. Available from: https://www.healthline.com/health/sleep-deprivation/effects-on- body
36. Torres A, Catena A, Megías A, Maldonado A, Cándido A, Verdejo-García A, et al. Emotional and non-emotional pathways to impulsive behavior and addiction. Front Hum Neurosci. 2013;7:1–11. doi:10.3389/fnhum.2013.00043
37. Shafer L. Social media and teen anxiety. Harvard Graduate School of Education. 2015 Dec 15. Available from: https://www.gse.harvard.edu/ideas/usable-knowledge/17/12/social-media-and- teen-anxiety
38. Abi-Jaoude E, Naylor KT, Pignatiello A. Smartphones, social media use, and youth mental health. CMAJ. 2020;192(6):E136–E141. doi:10.1503/cmaj.190434.
39. Lee H, Kim S, Park J. Oxytocin and maternal behavior: Neuroendocrine mechanisms and clinical implications. J Neuroendocrinol. 2022;34(2):e13124. doi: 10.1111/jne.13124.
40. Albright J. Digital dopamine: The addictive design of social media. Stanford Digital Wellness Report. 2019. Available from: https://digitalwellness.stanford.edu/reports/digital-dopamine
41. Canadian Institute for Health Information. Intentional self-harm among youth in Canada. 2018. Available from: https://www.cihi.ca/en/intentional-self-harm-among-youth-in-canada
42. Twenge JM, Joiner TE, Rogers ML, Martin GN. Increases in depressive symptoms, suicide-related outcomes, and suicide rates among U.S. adolescents after 2010 and links to increased new media screen time. Clin Psychol Sci. 2017;6(1):3-17. doi: 10.1177/2167702617723376.

J Surg Med. 2025;9(10):207-212.
https://doi.org/10.28982/josam.8321

JOSAM

Review
https://jsurgmed.com/

Journal of Surgery and Medicine

e-ISSN: 2602-2079

What are the applications of stem cell therapy for infertility? A literature review

Nawar Al-Khafaji

University of South Wales, Faculty of Life Sciences and Education, Cardiff, UK

ORCID of the author(s)

NAK: https://orcid.org/0009-0007-4583-733X

Abstract

Background/Aim: Stem cell therapy, also known as regenerative medicine, offers great promise in treating a variety of diseases that do not respond to conventional treatments. This systematic literature review aims to critically examine the latest scientific findings on the applications of stem cells in reproductive medicine. It also explores the various types of stem cells discovered to date, highlighting their advantages, disadvantages, and associated ethical considerations.

Methods: Multiple databases, such as PubMed, Google Scholar, grey literature, and the Cochrane Library, were searched for topic-relevant studies within the past 15 years. The search was restricted to the English language. However, literature from all countries was considered, provided it met the inclusion criteria.

Results: The progress of using stem cells in reproductive medicine varied from pre-clinical experiments to clinical stages in varying aspects of male and female infertility-related diseases.

Conclusion: This review highlights the remarkable advancements in the field of reproductive regenerative medicine. Large-scale randomized clinical trials are urgently needed to evaluate the safety and efficacy of stem cell therapies, particularly mesenchymal stem cells (MSCs), which have shown encouraging clinical outcomes. Additionally, MSC-derived extracellular vesicles (EVs) present a promising cell-free therapeutic strategy for infertility, warranting further research to fully explore their potential applications.

Keywords: Stem cells and infertility, reproductive medicine, stem cell therapy applications, subfertility, male infertility, female infertility, types of stem cells, stem cell advantages and disadvantages, clinical use of stem cells in infertility, stem cells and endometriosis, stem cells and non-obstructive azoospermia, stem cells and thin endometrium

Corresponding Author
Nawar Al-Khafaji
University of South Wales, Faculty of Life Sciences and Education, Cardiff, UK
E-mail: nawarj.alkhafaji@yahoo.com

Ethics Committee Approval
This review does not involve any studies with human or animal subjects performed by the author, and therefore, the Faculty Ethics Sub-Group at the University of South Wales granted a low-risk ethical approval for the review process according to the World Medical Association's (WMA) declaration of Helsinki.

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

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

Published
2025 October 28

Introduction

Stem cell therapy, also known as regenerative medicine, offers great promise in treating diseases in the medical field that conventional methods cannot address. Stem cells, the body's raw materials, are the basic building blocks of organs, tissues, blood and the immune system [1, 2]. Under specific conditions, these cells are capable of self-renewal or differentiation into specialized cells and act as an internal repair system in the body to replace lost or damaged tissues [1].

Stem cell therapy has drawn the attention of many researchers over the past decade due to its potential to transform healthcare. Studies of stem cells enhance understanding of disease mechanisms and enable the generation of healthy cells to replace diseased ones. Additionally, stem cells provide platforms for testing the safety and efficacy of new drugs by differentiating them into tissue-specific cells [1, 2].

Infertility affects approximately 15% of couples worldwide [3]. According to WHO [4], around 48 million couples and 186 million individuals experience infertility globally, which severely impacts psychosocial well-being. Causes include male factors (30%), female factors (55%), combined factors (40%), and unexplained cases (25%) [5].

Assisted reproductive technology (ART) eliminates approximately 80% of cases of infertility; however, a significant proportion remains untreated [3]. Therefore, stem cell therapy has been suggested as an alternative, like using patient-specific gametes derived from pluripotent and induced pluripotent stem cells (iPSCs) to overcome the genetic mismatch of donor gametes [6].

Different strains of stem cells possessing the effect of antioxidation, anti-apoptosis, and angiogenesis have been isolated and cultured to regulate reproductive function and immune balance by releasing cytokines as well as exosomes, to ameliorate the reproductive microenvironment [7].

This systematic literature review aims to examine stem cell research conducted on both human and animal models, highlighting the various types of stem cells discovered to date. It assesses the advantages, disadvantages, and ethical considerations associated with each type. Additionally, the review summarizes current applications of stem cell therapy in reproductive medicine, exploring its future potential, safety, and efficacy in both males and females. Moreover, it critically evaluates the existing scientific literature and identifies key areas that warrant further clinical investigation. The review is organized thematically to enable a comprehensive and in-depth analysis of the selected studies.

Questions to be addressed in this review are:

1- What are the applications of stem cell therapy in infertility?
2- What progress has been made in reproductive medicine using stem cells?

Literature Review

Stem cells are undifferentiated cells present in embryos, fetuses, and adults, capable of producing differentiated cells. They originate primarily from early embryonic cells and adult tissues. The zygote, formed by the fusion of an oocyte and spermatozoon, initiates embryonic development. Totipotent cells, such as the zygote and the first two dividing cells, can form any human cell type, including extra-embryonic tissues. Tissue-specific stem cells arise from differentiated organs postnatally and aid in organ repair. Major stem cell types include: embryonic stem cells (ESCs), mesenchymal stem cells (MSCs), spermatogonial stem cells (SSCs), ovarian stem cells (OSCs), and induced-pluripotent stem cells (iPSCs) [3, 8, 9].

Embryonic Stem Cells (ESCs), which are human ESCs (hESCs), are derived mainly from the inner cell mass of pre-implantation blastocysts, express Oct4 and are pluripotent, forming all three germ layers but not extra-embryonic tissues [6, 10]. First observed in mouse blastocysts in 1981 and isolated from humans in 1998, ESCs can differentiate into primordial germ cells, undergo meiosis, and contribute to gamete formation, with hESCs also supporting endometrial repair [3, 7]. ESC-derived extracellular vesicles enhance ovarian function via the PI3K/AKT pathway in premature ovarian failure [7]. Despite their regenerative potential, ethical concerns over embryo destruction, consent, and donor safety, along with risks of immune rejection, limit clinical application [3, 7, 9].

Mesenchymal Stem Cells (MSCs), first isolated from bone marrow in the 1970s, are multipotent stromal cells capable of differentiating into osteocytes, adipocytes, and chondrocytes, while exerting immunoregulatory and trophic effects that support tissue repair [3, 10, 11]. They can be sourced from bone marrow, adipose tissue, umbilical cord, menstrual blood, amniotic fluid, placenta, and dental pulp [3, 10]. MSCs have been applied for ovarian dysfunction and endometrial disorders, promoting angiogenesis, reducing apoptosis and fibrosis, and modulating immune responses [3, 12]. Fetal MSCs exhibit higher proliferation, differentiation, and immunomodulatory capacity than adult MSCs, expressing pluripotency markers and longer telomeres, offering therapeutic advantages [3, 10].

Spermatogonial Stem Cells (SSCs) are pluripotent cells that sustain lifelong spermatogenesis within seminiferous tubules, including spermatogonia proliferation, meiosis, and spermiogenesis, with defects leading to male infertility [7, 3]. Representing a small fraction of testicular cells, SSCs can be isolated using markers such as Stra8 in mice and Thy-1, CD9, and SSEA4 in humans and rats [3, 13]. Their function depends on the Sertoli cells, and co-transplantation with growth factors, such as LIF, FGF, EGF, and GDNF, which can restore spermatogenesis in KITLG-deficient azoospermia [7, 14, 15]. SSCs can transmit genetic information, generating other tissues, and are generally considered ethically acceptable [9, 13].

Ovarian/Oogonial Stem Cells (OSCs) challenge the long-held view that postnatal mammalian ovaries lack germ cell renewal. Mitotically active germline cells have been isolated from adult ovaries in various species [6, 13, 16]. OSC lines from mouse ovarian surface epithelium express MVH, BrdU, telomerase, Oct4, and Nanog, and can generate functional oocytes in sterilized mice, producing GFP-labeled offspring [3, 7, 13, 16]. In humans, rare germ stem cells (GSCs) expressing Ddx4 can form oocyte-like structures in vitro, suggesting potential neo-oogenesis even in women with diminished ovarian reserve [7, 13]. While encouraging, their physiological role in adult ovarian function remains unclear, and in vitro oocyte maturation techniques require further refinement [16].

Induced-Pluripotent Stem Cells (iPSCs) are somatic cells reprogrammed into a pluripotent state using factors such as Oct4, Klf4, Sox2, and c-Myc, resembling ESCs in morphology, marker expression, and differentiation potential [3, 7, 10]. Derived from sources including fibroblasts and cord blood, iPSCs can be differentiated into haploid gamete-like cells expressing germ cell markers like VASA and DAZL [7]. While iPSC-derived germ cells can integrate into gonadal tissue, complete meiosis remains challenging, with regulators such as SOX17 and BLIMP1 guiding primordial germ cell specification [3, 10]. iPSCs bypass ethical issues of embryo destruction and reduce immune rejection but still require careful oversight regarding potential embryo formation and genomic integrity [3, 10, 14]. Although gametogenesis from iPSCs has been achieved in mice, translating these protocols to humans is limited and requires further validation [3, 9, 16].

Stem cell-based therapies offer significant therapeutic potential but are associated with notable risks that need to be managed carefully. These risks can generally be divided into three categories: those that are intrinsic to the cells, those arising out of manufacturing and handling, or those relating to clinical applications [17].

At the cellular level, immune rejection is a problem to be faced, particularly where sources are allogenic. Stem cells can carry pathogenic traits; the wrong cell type can literally be brought forth from an "unintentional" differentiation. Out-of-control proliferation will displace normal physiological processes with harmful cells and thus increase chances for tumor formation. [17].

During manufacturing and handling, contamination from microbes, prions, or residual chemicals remains a persistent challenge. Variability in donor material, processing errors, incomplete removal of undifferentiated cells, and problems in storage or transport can compromise cell quality and safety. Moreover, hidden viruses in donor cells can be reawakened during culture [17].

In clinical application, patients may experience problems, such as graft-versus-host disease, arrhythmias, inappropriate engraftment, etc. Treatments may not work and can be harmful, while some aspects of the damage that results from them may be irreversible [17].

Infertility affects approximately one in six couples worldwide and is defined as the failure to achieve pregnancy after 12 months of unprotected intercourse. While assisted reproductive technologies (ART) resolve around 80% of infertility cases, many challenges remain, motivating research into stem cell therapies [10, 12, 13].

Stem cell therapies are being investigated for female infertility arising from premature ovarian failure (POF), polycystic ovary syndrome (PCOS), Asherman's syndrome (AS), recurrent implantation failure (RIF), endometriosis, and fallopian tube obstruction.

Premature Ovarian Failure (POF) affects about 1% of women under 40 and is characterized by reduced ovarian reserve and low steroid hormones [7, 11, 18, 19]. Current treatments, including hormone replacement and egg donation, are limited, but MSC therapy, particularly from umbilical cord and amniotic membrane, has shown potential in restoring ovarian function, improving hormone levels, and reducing granulosa cell apoptosis [11, 12, 18]. MSC-derived extracellular vesicles (EVs) further support angiogenesis, reduce oxidative stress, and modulate immune responses, with early clinical trials reporting spontaneous pregnancies [20].

Polycystic Ovarian Syndrome (PCOS) affects 5–10% of reproductive-age women and accounts for over 27% of infertility cases [10, 18]. MSC therapy has been shown to reduce ovarian inflammation and fibrosis, and MSC-derived EVs, which deliver miR-323-3p, enhance cumulus cell survival [3, 11].

Asherman's Syndrome (AS), caused by intrauterine adhesions, often results in menstrual irregularities and infertility [18]. Stem cell therapies using various MSC sources have improved endometrial thickness, menstrual volume, and pregnancy rates, with EVs promoting angiogenesis and reducing fibrosis through TGFβ1/Smad2 inhibition and VEGF signaling [3, 18-20].

Recurrent Implantation Failure (RIF) and Thin Endometrium present challenges in IVF, with thin endometrium (<7 mm) linked to higher miscarriage rates [18, 19]. Therapies combining endometrial MSCs (em-MSCs) and platelet-rich plasma (PRP) enhance vascularization, promote differentiation, and improve pregnancy outcomes [12].

Endometriosis affects 10% of reproductive-age women, with pathogenesis involving ectopic endometrial growth, immune dysregulation, and genetic factors [3, 18]. While MSC therapy carries theoretical risks of contributing to disease progression, MSC-derived EVs targeting angiogenesis and inflammation have shown potential in preclinical studies [18].

Fallopian Tube Obstruction impairs fertilization and embryo transport; current treatment is primarily surgical. Animal studies indicate that MSC transplantation or MSC-derived EVs can reduce inflammation and promote tissue repair, with cell-free therapies showing promise via macrophage polarization and NF-κB pathway modulation [11, 21, 31].

Male infertility arises from infections, toxins, radiation, drugs, anatomical defects, and endocrine disorders [11]. Current treatments include surgery, hormone therapy, medications, and ART, such as intracytoplasmic sperm injection (ICSI), but challenges including low success rates and lack of functional gametes remain [18]. Stem cell–based approaches include isolation and transplantation of SSCs, generation of SSCs from BM-MSCs and Ad-MSCs, and differentiation of iPSC-derived germ cells. These approaches may restore fertility in men with normal genetics, although genetic defects cannot be corrected; for example, testicular tissue preservation before puberty is recommended in Klinefelter's Syndrome, yielding about 70% sperm retrieval success [18].

Erectile Dysfunction (ED) affects over half of men older than 40 and is often linked to endothelial dysfunction from diabetes, cardiovascular disease, neurological disorders, or drugs [6, 22]. Conventional treatments, including PDE5 inhibitors, provide temporary relief without addressing underlying tissue dysfunction. Stem cell therapies, including umbilical cord, bone marrow, adipose-derived, and placental matrix stem cells, have shown encouraging improvements in penile blood flow, erection quality, and glycemic control in early clinical studies, though larger randomized trials are required to determine optimal cell type, dose, and safety [22].

Materials and methods

Inclusion Criteria: This study included all published and unpublished articles containing information on types of stem cells in both human and animal models, as well as the application of stem cell therapy for infertility in males and females. Additionally, articles involving infertile couples of reproductive age, regardless of whether the cause of infertility was known or unknown, were included if stem cell therapy was considered a potential treatment option.

Exclusion Criteria: Articles were excluded if they focused on the use of stem cells in medical fields other than reproductive medicine, were published more than 15 years ago, or were not written in English.

Outcome Measures: The primary outcomes included the identification of all stem cell types isolated, cultured, and applied in animal or human models. The study also evaluated the advantages, limitations, and ethical considerations associated with each type of stem cell. Furthermore, a comprehensive summary of current applications of stem cell therapy in reproductive medicine was developed, emphasizing accuracy, quality, and safety. Future perspectives and areas necessitating further research were also delineated.

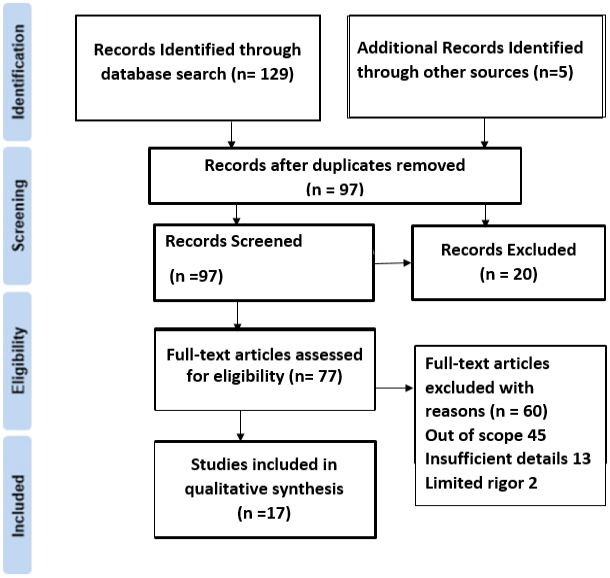
Search Strategy: Multiple databases, including PubMed, Google Scholar, grey literature, and the Cochrane Library, were systematically searched for relevant studies published within the last 15 years. The search was restricted to English-language literature from any country. Keywords used encompassed terms such as stem cells and infertility, reproductive medicine, stem cell therapy applications, subfertility, male infertility, female infertility, types of stem cells, stem cell advantages and disadvantages, clinical use of stem cells in infertility, stem cells and endometriosis, stem cells and non-obstructive azoospermia, and stem cells and thin endometrium [8, 23].

The selected studies underwent critical appraisal to eliminate irrelevant or weak evidence, reduce information overload, and ensure the inclusion of relevant, reliable, and valuable studies while identifying potential biases. As detailed in Table 1, quality assessment employed the Critical Appraisal Skills Programme (CASP) qualitative checklist tool, involving screening of titles, abstracts, and other metadata, followed by full-text article evaluation [15, 24, 25].

Data Analysis: This review followed a thematic analysis process comprising six steps: familiarization, coding, generating themes, reviewing themes, defining and naming themes, and writing up the findings. This approach was crucial in minimizing confirmation bias, which is the tendency to selectively acknowledge information that supports pre-existing beliefs while ignoring contradictory evidence. The results were summarized, with selected data presented in tabular form. Conclusions were drawn through careful interpretation of the findings [8].

Research Method: This study employed a systematic literature review design to identify, select, and critically appraise relevant literature to answer the formulated research questions. Due to its rigorous methodology and reliance on filtered, critically evaluated data, a systematic review is considered the highest level of evidence in the research hierarchy [14, 26]. The systematic review process followed the PRISMA 2020 guidelines, as illustrated by the PRISMA flow diagram (Figure 1) [27, 28]. As the study is qualitative, the grounded theory approach was employed to analyze and categorize the data, allowing for the collection of rich, detailed information on the topic [8, 30].

Figure 1: PRISMA Flow Diagram [28]



Results and Discussion

Most of the characteristics of stem cells used in stem cell-based therapies for infertility are summarized in Table 2.

Worldwide, there are a growing number of human clinical trials investigating stem cell treatments for infertility, reflecting the hopeful results obtained from various animal studies. The application of stem cells in reproductive medicine ranges from preclinical experiments to clinical stages, targeting multiple male and female infertility-related conditions.

This review highlights remarkable ongoing progress in the field of reproductive medicine. It brings attention to the advantages, limitations, and ethical concerns associated with different types of stem cells. Mesenchymal stem cells (MSCs) have received significant attention, as they can be derived from numerous abundant and accessible sources and possess favorable biological properties. These factors include the multipotent differentiation potential, secretory activity, mitochondrial transfer, immunomodulatory and anti-inflammatory properties and their low immunogenicity – especially when dealing with autologous MSCs. Furthermore, MSCs pose minimal ethical or moral concerns, which facilitates their adoption in the field of cellular therapy.

Further clinical evaluations are needed to obtain definitive evidence supporting the effectiveness and safety of stem cell therapy in infertility. MSCs have shown promising clinical results in common male and female infertility disorders, including premature ovarian failure (POF), polycystic ovary syndrome (PCOS), Asherman's syndrome (AS), recurrent implantation failures (RIFs) endometriosis, fallopian tube occlusion, azoospermia as well as erectile dysfunction. In addition, MSC-derived EVs, which release biologically active molecules consisting of nucleic acids, lipids and proteins, are involved in several physiological and pathological processes. Cell-free treatment options using EVs for infertility also appears to be a positive approach, which could have a wide range of applications, but this needs further investigation.

Table 1: Quality assessment by using CASP qualitative checklist tool [15]

Studies	1. Was there a clear statement of the aims of the research	2. Is a qualitative methodology appropriate?	3. Was the research design appropriate to address the aims of the research?	4. Are the study's theoretical underpinnings clear, consistent and conceptually coherent?	5. Was the recruitment strategy appropriate to the aims of the research?	6. Was the data collected in a way that addressed the research issue?	7. Has the relationship between researcher and participants been adequately considered?	8. Have ethical issues been taken into consideration?	9. Was the data analysis sufficiently rigorous?	10. Is there a clear statement of findings?	Score out of 10
1- [19]	Yes	I can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
2-[7]	Yes	I can't tell	Yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	9
3-[9]	Yes	I can't tell	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	8
4-[6]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	8
5-[11]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7
6-[12]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7
7-[10]	No	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
8-[20]	Yes	I can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
9-[16]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7
10-[13]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
11-[29]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7
12-[18]	Yes	I can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
13-[3]	No	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
14-[31]	Yes	I can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
15-[21]	Yes	I can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
16-[22]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7
17-[17]	Yes	I can't tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	7

Table 2: Characteristics of Stem Cells Used in the Treatment of Infertility

Topics	Descriptions	References
ESCs	• ESCs Pluripotent: can differentiate into 3 germ layers (not extraembryonic). • Source: Derived from the inner cell mass of blastocyst/morula; expresses Oct4. • Germline potential: The capacity to form primordial germ cells and gametes (in vitro). • Therapeutic implications: Promote endometrial restoration, hESC-EVs modulate PI3K/AKT, and hopes for POF treatment. • Limitations: Not immune-privileged; ethics restrict clinical utility	[3, 6, 7, 9, 10]
MSCs	• Multilineage: Can give rise to mesodermal cells (bone, adipose tissue and cartilage). • Labelling (ISCT): Plastic-adherent; expression of CD105, CD73 and CD90, lack of expression of CD45, 34 (CD45RA), CD11b or CD14, CD19 or HLA-DR and cultured to chondrogenic differentiation. • Sources: Marrow, adipose tissue, menstrual blood, umbilical cord and matrix amniotic fluid and membrane, placenta/trophoblasts, salivary gland and dental pulp. • Fetal MSCs (FMSCs): Multiply more and differentiate better, display greater telomerase activity and have stronger immune modulating potential than adult MSCs. • Biological functions: Differentiation, secretion of bioactive factors, mitochondrial transfer, balanced immunomodulation, and anti-inflammation. • Ethical: Fewer ethical constraints than ESC and more widely accepted in clinical trials. • Applications: Widely studied testing for preclinical and clinical trials, such as therapies for ovarian dysfunction and endometrial disorder.	[3, 9, 10, 11, 20]
SSCs	• Nature: Pluripotent stem cells that differentiate into spermatogenic cells and undergo self-renewal throughout the life span of a male. • Isolation: Was improved by species markers; SSEA4 and GPR125 were the markers used for human SSCs. • Genetic tools: CRISPR can repair KITLG mutations (supportive cells), but not AZF region mutations (germ cells). • Application: Possible future auto-transplantation, and of promise in both fertility treatment (e.g. pre-pubertal male post chemo/radiotherapy). • Function: Transfer father's genes to his offspring. • Ethics: Not associated with additional substantial ethical requirements.	[3, 7, 9, 13, 16]
OSCs	• Discovery: Identification of germline stem cells (GSCs) in adult ovaries challenged the concept that female germ cells are non-renewable. • Significance: Recovers the idea of neo-oogenesis, offers hope for cancer patients with ovarian insufficiency (i.e., fragile X-associated and otherwise idiopathic POF, iatrogenic POF, age-related infertility). • Challenges: The technical and conceptual challenges in clinical translation are numerous • Ethics: No ethical concerns with its use.	[3, 6, 7, 13, 16]
iPSCs	• Source: Initially derived by inducing mouse fibroblasts with transcription factors; a landmark for cell therapy. • Indications: It may achieve spermatogenesis and oogenesis recovery, even in the presence of chromosomal anomalies. • Pros over ESCs: Adult-derived cells, no embryo, less chance of being controversial, and lower risk of the immune system rejecting them. • Limitations: Informed consent is required; clinical utility under evaluation.	[3, 7, 9, 10, 29]

ART: Assisted Reproductive Technology, **MSCs:** Mesenchymal Stem Cells, **MSC derived EV:** Mesenchymal Stem Cell-derived Extracellular Vesicles, **WHO:** World Health Organization, **iPSCs:** induced Pluripotent Stem Cells, **ESCs:** Embryonic Stem Cells, **SSCs:** Spermatogonial Stem Cells, **OSCs:** Ovarian Stem Cells, **hESCs:** human Embryonic Stem Cells, **ICM:** Inner Cell Mass, **IVF:** In Vitro Fertilisation, **PGCs:** Primordial Germ Cells, **FMSCs:** Foetal Mesenchymal Stem Cells, **VEGF:** Vascular Endothelial Growth Factor, **HGF:** Hepatocyte Growth Factor, **LIF:** Leukaemia Inhibitory Factor, **TGF:** Transforming Growth Factor, **Bcl-2:** B-cell lymphoma 2, **MMP:** Matrix Metalloproteinase, **Thy-1:** Thymocyte Antigen 1, **SSEA4:** Stage-Specific Embryonic Antigen-4, **KITLG:** Membrane-Bound Kit Ligand, **AZF:** Azoospermia Factor, **CRISPR:** Clustered Regularly Interspaced Short Palindromic Repeats, **GSCs:** Germ Stem Cells, **FACS:** Fluorescence-Activated Cell Sorting, **−COOH:** Carboxyl, **PGC-LC:** Primordial Germ Cell-Like Cells, **POF:** Premature Ovarian Failure, **PCOS:** Polycystic Ovary Syndrome, **AS:** Asherman's syndrome, **RIF:** Recurrent Implantation Failure, **IACUC:** Institutional Animal Care and Use Committee, **ESHRE:** European Society of Human Reproduction and Embryology, **FSH:** Follicle Stimulating Hormone, **HIV:** Human Immunodeficiency Virus, **hUC-MSCs:** human Umbilical Cord Mesenchymal Stem Cells, **hAM-MSCs:** human Amniotic Membrane-Derived Mesenchymal SCs, **Ad-MSCs:** Adipose Tissue-Derived MSCs, **hMensSCs:** human Menstrual Stem Cells, **hBM-MSC:** human Bone Marrow MSCs, **IUAs:** Intrauterine Adhesions, **OS:** Oxidative Stress, **PBMCs:** Peripheral Blood Mononuclear Cells, **PRP:** Platelet-Rich Plasma, **em-MSCs:** endometrial MSCs, **ICSI:** Intra-Cytoplasmic Sperm Injection, **KS:** Klinefelter's Syndrome, **ED:** Erectile Dysfunction, **PDE5:** Phosphodiesterase Type-5 inhibitors

Conclusion and Recommendations

Infertility is a global health issue that imposes substantial psychological, social, and economic burdens on affected couples, arising from a wide range of male and female reproductive disorders. Conventional therapies, including hormonal treatments, surgical interventions, and assisted reproductive technologies, offer favorable outcomes but do not address all infertility types, underscoring the need for alternative approaches. Stem cells have considerable potential due to their capacity for self-renewal, differentiation, and secretion of paracrine factors that support tissue repair.

While human clinical trials are increasing and early results are encouraging, no stem cell therapy has yet been approved for routine clinical use. Large, well-designed randomized trials are essential to establish the efficacy and safety of specific stem cell types, particularly MSCs, which have shown the most encouraging outcomes. Additionally, MSC-derived extracellular vesicles represent a potential cell-free therapeutic strategy, warranting further investigation to fully explore their clinical applications in infertility treatment.

Acknowledgements

The author would like to express sincere gratitude to Dr. Janet Evans for her valuable guidance and support throughout this literature review.

References

1. Pruthi S, Allen A, Allen N, Anavekar N, Arora A, Bakkum J, et al. Stem cells: what they are and what they do. Mayo Clinic. 2023.
2. National Stem Cell Foundation. What are stem cells? 2023.
3. Saha S, Roy P, Corbitt C, Kakar S. Application of stem cell therapy for infertility. Cells. 2021;10(7):1613. doi:10.3390/cells10071613.

4. World Health Organization. Infertility. 2022.
5. National Institute for Health and Care Excellence (NICE). Fertility problems: assessment and treatment [CG156]. 2017.
6. Vassena R, Eguizabal C, Heindryckx B, Sermon K, Simon C, Van Pelt A, et al. Stem cells in reproductive medicine: ready for the patient?. Hum Reprod. 2015;30(9):2014-21. doi: org/10.1093/humrep/dev181.
7. Wu J, Xia T, She L, Lin S, Luo X. Stem cell therapies for human infertility: advantages and challenges. Cell Transplant. 2022;31. doi: 10.1177/09636897221083252.
8. Bhandari P. What is qualitative research? Methods and examples. Scribbr. 2020.
9. Wang J, Liu C, Fujino M, Tong G, Zhang Q, Li X, et al. Stem cells as a resource for treatment of infertility-related diseases. Curr Mol Med. 2019;19(8):519-46. doi: 10.2174/1566524019666190709172636.
10. Özdemir A, Tastan A. Stem cell applications in female infertility: a review. J Exp Clin Med. 2023;40(1):122-6. doi: 10.52142/omujecm.40.1.26.
11. Chang Z, Zhu H, Zhou X, Zhang Y, Jiang B, Li S, et al. Mesenchymal stem cells in preclinical infertility cytotherapy: a retrospective review. Stem Cells Int. 2021. doi: org/10.1155/2021/8882368.
12. Zhao Y, Chen S, Su P, Huang F, Shi Y, Shi Q, et al. Using mesenchymal stem cells to treat female infertility: an update on female reproductive diseases. Stem Cells. 2019. doi: org/10.1155/2019/9071720.
13. Volarevic V, Bojic S, Nurkovic J, Volarevic A, Ljujic B, Arsenijevic N et al. Stem cells as new agents for the treatment of infertility: current and future perspectives and challenges. Biomed Res Int. 2014. doi: org/10.1155/2014/507234.
14. Pae C. Why systematic review rather than narrative review? Psychiatry Investig. 2015;12(3):417-9. doi: 10.4306/pi.2015.12.3.417.
15. Long H, French D, Brooks J. Optimising the value of the critical appraisal skills programme (CASP) tool for quality appraisal in qualitative evidence syntheses. Res Methods Med Health Sci. 2020; 1(1): 31-42. doi: org/10.1177/2632084320947559.
16. Ilic D, Telfer E, Ogilvie C, Kolundzic N, Khalaf Y. What can stem cell technology offer to IVF patients? BJOG. 2019; 126(7): 824-7. doi: org/10.1111/1471-0528.15638.
17. Herberts C, Kwa M, Hermsen H. Risk factors in the development of stem cell therapy. J Transl Med. 2011;9(29). doi: org/10.1186/1479-5876-9-29.
18. Qamar A, Hussain T, Rafique M, Bang S, Tanga B, Seong G, et al. The role of stem cells and their derived extracellular vesicles in restoring female and male fertility. Cells. 2021;10(9):2460. doi: org/10.3390/cells10092460
19. Strug M, Aghajanova L. Making more womb: clinical perspectives supporting the development and utilization of mesenchymal stem cell therapy for endometrial regeneration and infertility. J Pers Med. 2021;11(12):1364. doi: org/10.3390/jpm11121364.
20. Rasheed Z, Nordin F, Zaman W, Tan Y, Abd Aziz N. Autologous human mesenchymal stem cell-based therapy in infertility: new strategies and future perspectives. Biology (Basel). 2023;12(1):108. doi: org/10.3390/biology12010108.
21. Zhang C, Liao W, Li W, Liu W, Li M, Xu X, et al. Human umbilical cord mesenchymal stem cells derived extracellular vesicles alleviate salpingitis by promoting M1-to-M2 transformation. Front Physiol. 2023;14. doi: org/10.3389/fphys.2023.1131701.
22. Protogerou V, Chrysikos D, Karampelias V, Spanidis Y, Bisari S,Troupis T. Erectile dysfunction treatment using stem cells: a review. Med (Basel). 2021;8(1):2. doi: 10.3390/medicines8010002.
23. Paré G, Kitsiou S. Methods for literature reviews. In: Lau F, Kuziemsky C, editors. Handbook of eHealth evaluation: an evidence-based approach. Victoria (BC): University of Victoria; 2017.
24. Al-Jundi A, Sakka S. Critical appraisal of clinical research. J Clin Diagn Res. 2017;11(5):JE01-05. doi: 10.7860/JCDR/2017/26047.9942.
25. Morrison K. Dissecting the literature: the importance of critical appraisal. Royal College of Surgeons. 2017.
26. Charles Sturt University Library. Literature review: systematic literature reviews. 2023.
27. University of Guelph-Humber Library Services. Systematic reviews. 2023.
28. Moher D, Liberati A, Tetzlaff J, Altman D, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7). doi: 10.1371/journal.pmed.1000097.
29. Singh V, Kalsan M, Kumar N, Saini A, Chandra R. Induced pluripotent stem cells: applications in regenerative medicine, disease modelling, and drug discovery. Front Cell Dev Biol. 2015;3. doi: org/10.3389/fcell.2015.00002.
30. Pollock A, Berge E. How to do a systematic review. Int J Stroke. 2018;13(2):138-56. doi: 10.1177/1747493017743796.
31. Chen K, Zheng S, Fang F. Endometrial stem cells and their applications in intrauterine adhesion. Cell Transplant. 2023;32:1–9. doi: org/10.1177/09636897231159561.

J Surg Med. 2025;9(10):213-215.
https://doi.org/10.28982/josam.8154

JOSAM

Case report
https://jsurgmed.com/

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Rare case of small bowel inflammatory myofibroblastic tumor

Nemanja Trifunović [1], Nebojsa Mitrović [1, 2], Dejan Stevanović [1, 2], Damir Jašarović [1, 2], Jovana Trifunović [3]

[1] Clinical Hospital Center Zemun, Department of General Surgery, Belgrade, Serbia
[2] University of Belgrade, Faculty of Medicine, Belgrade, Serbia
[3] Clinical Hospital Center Zemun, Oncology hospital, Belgrade, Serbia

ORCID of the author(s)

NT: https://orcid.org/0009-0001-1085-9500
NM: https://orcid.org/0000-0001-8836-3997
DS: https://orcid.org/0000-0001-5623-3901
DJ: https://orcid.org/0000-0003-2527-4860
JT: https://orcid.org/0009-0005-1373-6521

Abstract

The inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal neoplasm with variable biological behavior, which predominantly affects the lungs but can also appear in extrapulmonary sites, including the gastrointestinal tract. When situated in the small intestine, IMT presents substantial diagnostic and therapeutic difficulties. This case emphasizes the complications in diagnosing and surgically managing IMT in an unusual location. A patient, aged 67 with a past record of secondary iron-deficiency anemia, underwent a diagnostic examination due to gastrointestinal symptoms. The esophagogastroduodenoscopy showed a minor hiatal hernia, while a 5 mm hyperemic polyp, confirmed as a tubular adenoma, was identified by colonoscopy. Further MR enterography imaging detected a polypoid tumor approximately 28 mm in the right iliac region, which led to surgical intervention. A lower midline laparotomy revealed an intraluminal tumor in the proximal ileum, 60 cm from the ileocecal valve. A 20 cm segment of the impacted bowel was resected and an end-to-end ileo-ileal anastomosis was successfully achieved. The diagnosis of IMT with an R0 resection was confirmed through histopathological and immunohistochemical analysis. This case underlines the significance of considering IMTs in the differential diagnosis of unexplained gastrointestinal symptoms and highlights the role of imaging and surgical resection in reaching definitive management. Boosting awareness of IMTs in medical practice can lead to earlier recognition and improved patient outcomes.

Keywords: inflammatory myofibroblastic tumor, small intestine neoplasm, chronic secondary anemia, rare gastrointestinal neoplasms

Corresponding Author
Nemanja Trifunović
Clinical Hospital Center Zemun, Department of General Surgery, Ustanička 83, Belgrade, Serbia
E-mail: nemanjaaaaa94@gmail.com

Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

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

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

Published
2025 October 4

Introduction

Inflammatory myofibroblastic tumor (IMT), also referred to as inflammatory pseudotumor or plasma cell granuloma, is a rare mesenchymal neoplasm. It is distinguished by the proliferation of myofibroblastic spindle cells as well as an inflammatory infiltrate consisting of plasma cells and lymphocytes. Brunn first described it in 1939 as a lung tumor, initially believed to be benign with localized growth. However, later variations with local malignancies and rare metastases have been recorded. The World Health Organization (WHO) now classifies IMT as a mesenchymal neoplasm of intermediate malignancy [1].

IMT can occur at any age, with most patients receiving diagnoses before the age of 40. However, IMTs can also develop later in life, even in the eighth decade. IMT has been observed in nearly all body and visceral soft tissue organs. The most common site for IMT is the lungs, but extrathoracic forms have been detected at various other locations, primarily in soft tissues and visceral organs [2]. The small intestine is a rare site for IMT, and cases in this region frequently pose a significant diagnostic and therapeutic challenge.

The etiology of IMT is unclear, with certain factors suggested to be associated with it, such as viral infections (particularly HHV-8), trauma, surgical interventions, and autoimmune mechanisms. The anaplastic lymphoma kinase (ALK) gene is found in 33-67% of cases and is more commonly present in children and young adults [3,4].

How to cite: Trifunović N, Mitrović N, Stevanović D, Jašarović D, Trifunović J. Rare case of small bowel inflammatory myofibroblastic tumor. J Surg Med. 2025;9(10):213-215.

The clinical manifestations of IMT are nonspecific and vary depending on the location of the tumor. For instance, in the gastrointestinal tract, IMT may result in symptoms like abdominal pain, anemia, obstruction, or intussusception, which are attributed to its intraluminal growth. Furthermore, it can present as either acute or chronic gastrointestinal bleeding and may ultimately lead to iron-deficiency anemia [5, 6].

IMTs are typically benign and are usually treated with radical excision, steroids, radiation, and/or chemotherapy [7]. CO_2 laser treatment represents a novel therapeutic option. In the case of small intestine IMT, the recommended treatment is segmental resection with negative margins, carrying a minimal risk of recurrence if the excision is thorough.

Case presentation

A 67-year-old patient has been diagnosed with, and treated for, secondary iron-deficiency anemia within the past year by a gastroenterologist. Upon evaluation, an esophagogastric duodenoscopy (EGD) revealed merely a minor hiatal hernia, absent of any additional pathological findings. A colonoscopy detected a hyperemic polyp, approximately 5 mm in size, situated in the descending colon; it was subsequently removed via electrosurgery.

Histopathology confirmed a tubular adenoma. Further examination revealed no abnormalities in the entire colon and the terminal 30 cm of the ileum. A CT scan of the chest, abdomen, and pelvis also showed no remarkable findings. However, MR enterography revealed a loop of a small bowel in the right iliac region with indications of mechanical obstruction, as well as a polypoid tumor measuring around 28 mm.

Following the diagnostic evaluation, a need for surgical intervention was established to firm up the diagnosis and excise the tumor. Preoperative preparations entailed routine lab tests, a cardiopulmonary assessment, and optimizing the patient's readiness in light of the heightened risks associated with the perioperative period. Informed consent was gathered for the surgery, which delineated potential complications such as infection, hemorrhage, anastomotic leakage, and the possible necessity for additional intervention.

The surgery was conducted under general endotracheal anesthesia, commencing with a lower midline laparotomy for peritoneal access. The abdominal cavity was extensively explored to identify any additional pathology. During the exploration, an intraluminal tumor was discovered in the proximal ileum, roughly 60 cm from the ileocecal valve. The extent of the tumor was confirmed by palpation, and the segment of the small intestine containing the lesion was mobilized.

The resection involved a meticulous dissection of the mesentery supplying the affected segment in order to ensure proper vascular control. Once the ileum was sufficiently mobilized, a 20 cm resection of the affected bowel was carried out (Figure 1, 2). This step was executed with thorough attention to detail, ensuring clear margins for complete tumor removal. Throughout the process, hemostatic control was consistently maintained.

Following resection, an end-to-end ileo-ileal anastomosis was performed. The anastomosis was created using delayed absorbable sutures in a two-layer technique, including an inner continuous mucosal layer and an outer interrupted seromuscular layer. This ensured a tension-free, well-perfused anastomosis. Additionally, the mesenteric defect was sutured to prevent internal herniation. Before closing the abdominal wall, the surgical area was irrigated to remove any debris or contaminants.

The histopathological examination of the resected specimen revealed an IMT located in the submucosa. The tumor was completely removed, thus achieving an R0 resection. Characteristically, IMT is composed of myofibroblastic and fibroblastic spindle cells, supplemented by an inflammatory infiltrate including lymphocytes, plasma cells, and eosinophils. The tumor demonstrated variable cellularity, possessing areas with sparse cellular activity within the hyalinized stroma and other areas showcasing dense myofibroblastic proliferation.

The immunohistochemical analysis of the tumor confirmed the diagnosis, showing positivity for vimentin, smooth muscle actin (SMA), and muscle-specific actin, which is consistent with myofibroblastic differentiation. Further, the tumor also demonstrated positivity for ALK, a feature frequently seen in IMTs. Other markers like desmin, cytokeratins, and S-100 were negative, thus eliminating other differential diagnoses.

The patient had an uneventful postoperative recovery, with bowel function gradually returning. Oral intake was resumed without issues and there were no signs of complications such as infection or anastomotic leakage. The patient was discharged home in stable condition and instructed to follow up regularly with the attending surgeon for monitoring and additional treatment as needed.

Figure 1: Resected small intestine with umbilication of serosa at the site of the intraluminal inflammatory myofibroblastic tumor.

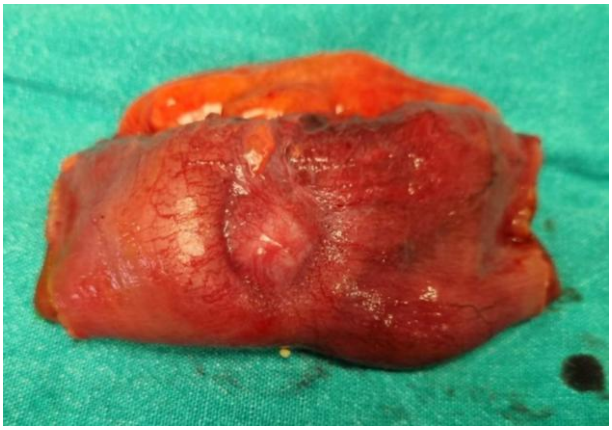
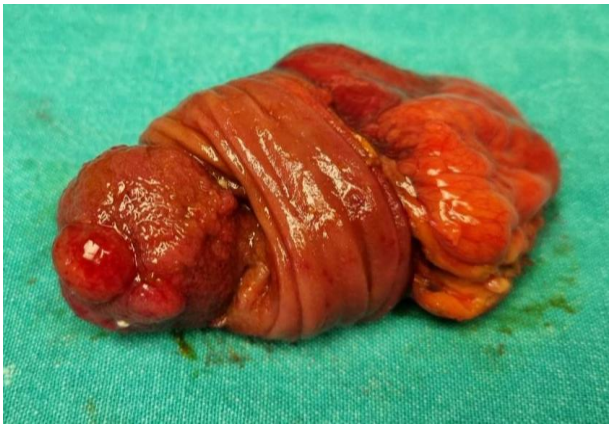


Figure 2: Resected small intestine with intraluminal inflammatory myofibroblastic tumor.



Discussion

IMT represent a rare and heterogeneous group of neoplasms, presenting significant challenges for diagnosis and treatment. Our case report emphasizes key aspects of IMT, including its clinical presentation, surgical approach, and histopathological as well as immunohistochemical diagnosis.

IMTs are typically benign neoplasms that exhibit locally aggressive behavior. These are most commonly found in younger patients, with a peak incidence in children and young adults, but they can occur at any age, including in elderly individuals as demonstrated in our case [1,2]. The clinical presentation of IMT is location-dependent and can include symptoms such as obstruction, a palpable mass, or nonspecific abdominal pain [3]. In the case of this patient, the secondary iron-deficiency anemia is likely attributed to chronic, hidden blood loss induced by the tumor.

The differential diagnosis of small bowel tumors includes gastrointestinal stromal tumors (GISTs), adenocarcinomas, neuroendocrine tumors, and lymphomas. Imaging and histopathological findings are crucial in distinguishing IMTs from these entities. Given the polypoid nature and obstructive symptoms in our patient, considerations included GISTs and adenocarcinomas. These were ruled out through immunohistochemical analysis.

Radiologic assessment plays a key role in detecting IMTs, although the imaging findings are often nonspecific. In this patient, MR enterography revealed a polypoid tumor causing mechanical obstruction. Because of the tumor's location, obstructive symptoms, and the need for a definitive diagnosis, surgical management was prioritized over medical therapy options like corticosteroids or NSAIDs [4,5].

Surgical excision remains the cornerstone of treatment for IMTs, aiming for R0 resection to minimize the risk of recurrence [6]. In our case, an R0 resection was achieved, which is associated with a favorable prognosis. Studies indicate that complete resection leads to excellent survival outcomes, while incomplete excision carries recurrence rates of up to 25–37% [5,7].

Histopathologically, IMTs are characterized by the proliferation of spindle cells amidst an inflammatory background made up of lymphocytes, plasma cells, and eosinophils [3]. The diagnosis is confirmed by the presence of ALK positivity in tumor cells. ALK rearrangements, which occur in roughly 50% of IMTs, are frequently observed in younger patients and act as a crucial diagnostic marker [8].

For unresectable or recurrent IMTs, ALK inhibitors like crizotinib have demonstrated effectiveness in reducing ALK-positive tumors [9,10]. These agents are especially relevant for patients who aren't suitable candidates for surgery. In our case, successful complete resection made additional therapy unnecessary. However, long-term monitoring is critical in identifying potential recurrence.

Conclusion

This case emphasizes the need to consider IMT in the differential diagnosis of unexplained gastrointestinal symptoms, especially in instances of chronic anemia with initial inconclusive findings. Due to the tumor's potential for local aggression and recurrence, prompt imaging and histopathological confirmation are vital for directing definitive management. Surgical resection continues to be the primary treatment, with R0 resection providing the best prognosis. Enhancing clinical awareness of IMT, particularly in atypical locations like the small intestine, can facilitate earlier diagnosis, optimize treatment strategies, and ultimately improve patient outcomes.

References

1. Brunn H. Two interesting benign lung tumors of contradictory histopathology: Remarks on the necessity for maintaining the chest tumor registry. J Thorac Surg. 1939;9(2):119-31. doi:10.1016/S0096-5588(20)32030-4.
2. Rezaii Salim M, Vahedi H, Salimi Z, Froutan H, Sotoudeh M. Inflammatory myofibroblastic tumor of the small bowel: a case report. Middle East J Dig Dis. 2011 Sep;3(2):134-7. PMID: 25197546; PMCID: PMC4154918.
3. Gleason BC, Hornick JL. Inflammatory myofibroblastic tumours: where are we now? J Clin Pathol. 2008 Apr;61(4):428-37. doi: 10.1136/jcp.2007.049387. Epub 2007 Oct 15. PMID: 17938159.
4. Coffin CM, Watterson J, Priest JR, Dehner LP. Extrapulmonary inflammatory myofibroblastic tumor (inflammatory pseudotumor). A clinicopathologic and immunohistochemical study of 84 cases. Am J Surg Pathol. 1995 Aug;19(8):859-72. doi: 10.1097/00000478-199508000-00001. PMID: 7611533.
5. Dishop MK, Warner BW, Dehner LP, Kriss VM, Greenwood MF, Geil JD, et al. Successful treatment of inflammatory myofibroblastic tumor with malignant transformation by surgical resection and chemotherapy. J Pediatr Hematol Oncol. 2003 Feb;25(2):153-8. doi: 10.1097/00043426-200302000-00014. PMID: 12571469.
6. Telugu RB, Prabhu AJ, Kalappurayil NB, Mathai J, Gnanamuthu BR, Manipadam MT. Clinicopathological study of 18 cases of inflammatory myofibroblastic tumors with reference to ALK-1 expression: 5-year experience in a tertiary care center. J Pathol Transl Med. 2017;51(3):255-63. doi: 10.4132/jptm.2017.01.12.
7. Taiymi A, Meryem N, Bouziane M, Zazour A, Kharrasse G, Khannoussi W, et al. Abdominal inflammatory myofibroblastic tumour presenting as a pancreatic mass: A case report. Cureus. 2023 Jun 30;15(6):e41213. doi: 10.7759/cureus.41213. PMID: 37525776; PMCID: PMC10387333.
8. Coffin CM, Hornick JL, Fletcher CDM. Inflammatory myofibroblastic tumor: comparison of clinicopathologic, histologic, and immunohistochemical features including ALK expression in atypical and aggressive cases. Am J Surg Pathol. 2007 May;31(4):509-20. doi: 10.1097/01.pas.0000213393.57322.c7.
9. Siemion K, Reszec-Gielazyn J, Kisluk J, Roszkowiak L, Zak J, Korzynska A. What do we know about inflammatory myofibroblastic tumors? – A systematic review. Adv Med Sci. 2022;67(1):129-38. doi: 10.1016/j.advms.2022.02.002.
10. Butrynski JE, D'Adamo DR, Hornick JL, Dal Cin P, Antonescu CR, Jhanwar SC, et al. Crizotinib in ALK-rearranged inflammatory myofibroblastic tumor. N Engl J Med. 2010 Oct 28;363(18):1727-33. doi: 10.1056/NEJMoa1007056. PMID: 20979472; PMCID: PMC3014292.

J Surg Med. 2025;9(10):216-218.
https://doi.org/10.28982/josam.8135

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Case report
https://jsurgmed.com/

Omental torsion, a rare acute abdominal syndrome: A case report

Tutkun Talih [1], Umut Sercan Eser [1], Kamile Eser [2], Gamze Talih [3]

[1] Department of General Surgery, Erciyes University Medical Faculty, Melikgazi, Kayseri, Turkey
[2] Department of Internal Medicine, Erciyes University Medical Faculty, Melikgazi, Kayseri, Turkey
[3] Department of Anesthesia and Reanimation, Erciyes University Medical Faculty, Melikgazi, Kayseri, Turkey

ORCID of the author(s)

TT: https://orcid.org/0000-0003-3999-6733
USE: https://orcid.org/0009-0000-8140-9892
KE: https://orcid.org/0009-0001-2588-6229
GT: https://orcid.org/0000-0003-4743-9734

Corresponding Author
Tutkun Talih
Department of General Surgery, Erciyes University Medical Faculty, Melikgazi, Kayseri, Turkey
E-mail: tt3882@hotmail.com

Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

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

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

Published
2025 October 4

Abstract

We aimed to present a case of omental torsion, a very rare cause of acute abdomen. The patient, presenting to the emergency clinic with fever, nausea, vomiting, and severe abdominal pain, underwent immediate surgery due to a suspicion of omental torsion based on the physical examination and computed tomography (CT) scan results. It was observed during the nighttime emergency laparotomy for this patient that the omentum was torsioned, interrupting the blood supply to the distal part. This disrupted area was excised using a sealer/divider device. Although rare, omental torsion should be considered in instances of acute abdomen.

Keywords: case report, omental torsion, abdominal pain

Introduction

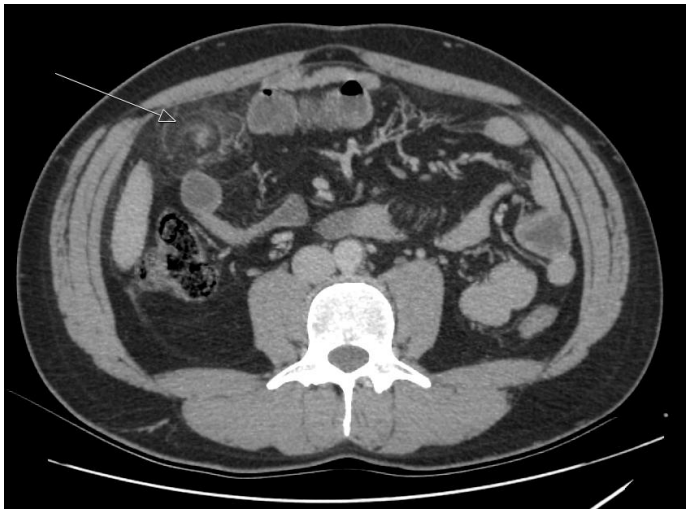
The greater omentum is known to rotate around its long axis [1]. The tissue of the greater omentum may undergo primary torsion or become torsioned secondary to internal or external hernias, tumors, intra-abdominal cysts, and postoperative adhesions [2]. CT scans, as one of the radiological imaging methods, can assist in diagnosing these issues. Acute abdominal symptoms can be indicated by an elevated body temperature, leukocytosis, and an increase in C-reactive Protein (CRP) levels.

How to cite: Talih T, Eser US, Eser K, Talih G. Omental torsion, a rare acute abdominal syndrome: A case report. J Surg Med. 2025;9(10):216-218.

Case presentation

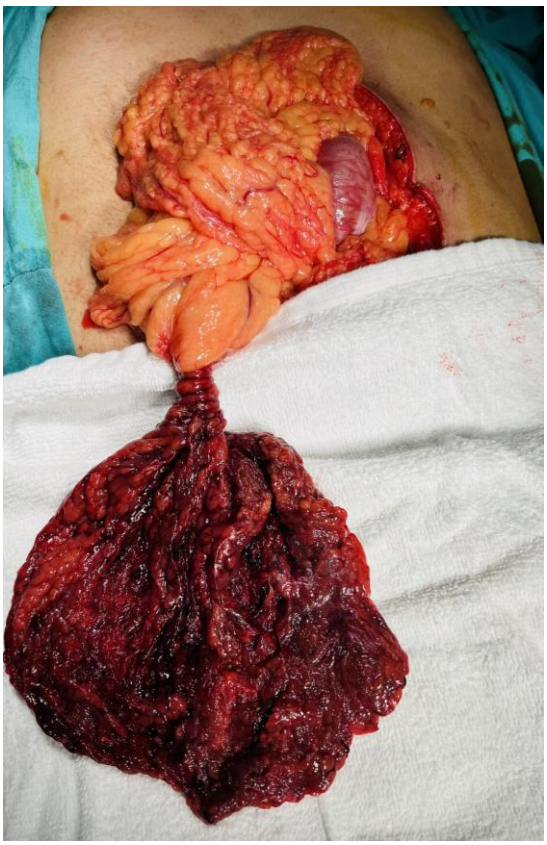
In this case, after receiving informed consent, we reported on a 24-year-old male patient who was admitted to our outpatient clinic with complaints of abdominal pain lasting 72 h. The patient sought help due to persistent abdominal pain, along with the onset of fever and vomiting in the last 24 h. Beyond these symptoms, the patient's medical history was unremarkable. A physical examination revealed sensitivity, defense, and rebound symptoms in the lower right quadrant. Laboratory results showed 17,000 /µL leucocytes and 120 mg/L CRP, while other haemogram and biochemical values were within normal limits. CT imaging indicated omental rotation in the lower right quadrant of the abdominal region (Figure 1), incorrectly described as mesenteric volvulus in the CT report. There was no evidence of acute appendicitis. The laboratory results, taken with the physical exam findings and CT imaging, led to the decision to operate. The patient was hospitalized after consenting to surgery.

Figure 1: Omental rotation CT appearance formed by rotating along the long axle of the greater omentum tissue.



Operative findings revealed an edematous and necrotic omentum that had rotated along its longitudinal axis (Figure 2). The definitive diagnosis was made intra-operatively. No other intra-abdominal pathology was observed. Postoperatively, the patient received treatment as an inpatient. An enteral regimen was initiated 8 h post-operation. The patient was monitored for three days and, showing signs of recovery, was discharged on the third day. Pathological examination of the excised specimen showed "chronic active inflammation and congestion".

Figure 2: Appearance of omental torsion formed by rotating along the long axle of the greater omentum tissue during the operation.



Discussion

Embryologically, the major omentum tissue originates from the dorsal mesogastrium. It comprises four layers that extend between the transverse colon and the greater curvature of the stomach and continues to the front of the small intestines [3]. One end can move freely through the abdomen. According to the type of pathology, omental tissue can undergo primary torsion or torsion due to secondary causes. In the case of primary torsion, the distal tip of the omentum is free. This form of free rotation of the distal omentum tip is also known as unipolar torsion [4]. In one study involving 563 laparoscopic cases, the incidence of omental torsion was found to be a mere 1.1%, making it quite rare [5]. Anatomical variations in primary omentum torsion conditions that cause the omentum to move, such as increased trauma or peristalsis, are predisposing factors for torsion. Obesity also presents a risk factor [6]. Secondary omental torsion occurs as a result of an underlying intra-abdominal pathology, such as cyst adhesion or hernia. Secondary omental torsion is also referred to as bipolar torsion. In the case of secondary torsion, the distal tip is connected to the area causing torsion, depending on the underlying condition [4]. The patient's Body Mass Index (BMI) was measured at 24, which is within normal limits. Additionally, the patient history received was limited, with no mention of trauma. Any secondary causes were excluded according to radiological imaging and operative findings.

Preoperative Ultrasound (US) and CT imaging can assist in diagnosis, helping to ensure a correct diagnosis before surgery. US imaging reveals a focal area with increased echogenicity, making it a useful diagnostic tool for ruling out other acute abdominal conditions [7]. Torsioned omental tissue can be visible as a mass in US imaging [8]. CT imaging is beneficial in distinguishing perforation, diverticulitis, and gallbladder diseases

in acute abdominal cases, with a specific rotating view observable [9]. In our case, CT imaging aided in the differential diagnosis of an acute abdominal condition. US viewing was not the preferred method as it failed to provide objective data. The CT images were reported as mesenteric volvulus, complicating the diagnostic process. Secondary causes like acute appendicitis, acute cholecystitis, intra-abdominal abscess, and diverticulitis were ruled out.

Laparoscopy has become a standard method in managing acute abdominal disease. It is used as both a therapeutic and differential diagnostic tool in selected cases. Nevertheless, a high degree of expertise is necessary for laparoscopy usage in emergency surgical scenarios. Conditions like perforated cancer, fecal peritonitis, abdominal distension, and hemodynamic instability are relatively contraindicated for the laparoscopic method. In recent years, its use in acute abdominal cases has experienced increasing success [10]. In our case, according to the CT report, the definitive diagnosis could not be made. Furthermore, laparoscopy cannot be performed during night hours in our clinic. Given these reasons, differential diagnoses were ruled out by diagnostic laparotomy. Postoperative follow-ups showed a decline in leukocytosis and CRP values after omentectomy. This suggests that the omentectomy had a beneficial impact on the patient's health in this case.

Conclusion

Primary omental torsion is a rare condition, and other diagnoses should be excluded radiologically and during surgery, as acute conditions can mimic the abdominal symptoms in differential diagnoses. It is also important to remember that primary omental torsion alone can account for the cause of an acute surgical abdomen.

References

1. Karayiannakis AJ, Polychronidis A, Chatzigianni E, Simopoulos C. Primary torsion of the greater omentum: report of a case. Surg Today. 2002;32(10):913-5.
2. Borgaonkar V, Deshpande S, Rathod M, Khan I. Primary Omental Torsion Is a Diagnostic Challenge in Acute Abdomen-a Case Report and Literature Review. Indian J Surg. 2013 Aug;75(4):255-7.
3. Theriot JA, Sayat J, Franco S, Buchino JJ. Childhood obesity: a risk factor for omental torsion. Pediatrics. 2003 Dec;112(6 Pt 1):e460.
4. Saad E, Awadelkarim A, Agab M, Babkir A, Yeddi A. Omental Fat Torsion: A Rare Mimicker of a Common Condition. Journal of Investigative Medicine High Impact Case Reports. 2022;10.
5. Aronsky D, Z'graggen K, Banz M, Klaiber C. Abdominal fat tissue necrosis as a cause of acute abdominal pain. Laparoscopic diagnosis and therapy. Surg Endosc. 1997 Jul;11(7):737-40.
6. Breunung N, Strauss P. A diagnostic challenge: primary omental torsion and literature review - a case report. World J Emerg Surg. 2009 Nov 18;4:40.
7. Dias SJT, Gobishangar S, Sureska GM, Vaishnavi T, Priyatharsan K, Theepan JMM. Omental torsion - A mimicker of the acute appendicitis - A case report. Int J Surg Case Rep. 2023 Nov;112:108958.
8. Naffaa LN, Shabb NS, Haddad MC. CT findings of omental torsion and infarction: case report and review of the literature. Clin Imaging. 2003 Mar-Apr;27(2):116-8.
9. Abdennasser el K, Driss B, Abdellatif D, Mehci A, Souad C, Mohamed B. Omental torsion and infarction: CT appearance. Intern Med. 2008;47(1):73-4.
10. Navez B, Navez J. Laparoscopy in the acute abdomen. Best Pract Res Clin Gastroenterol. 2014 Feb;28(1):3-17.

J Surg Med. 2025;9(10):219-221.
https://doi.org/10.28982/josam.8146

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Case report
https://jsurgmed.com/

Deep venous thrombosis after brown recluse spider bite: A rare case report

Reshma Pydi [1], Soumya NFN [1], Sania Thite [1], Jigyasha Pradhan [1], Kaitlyn Hoyt [2], Girishkumar Hanasoge [3]

[1] Department of General Surgery, Bronxcare Health System, Hospital, NY, USA
[2] St. George's University, Grenada, West Indies, Greneda
[3] Department of Vascular Surgery, Bronxcare Health System, Hospital, NY, USA

ORCID of the author(s)

RP: https://orcid.org/0000-0002-6948-773X
SN: https://orcid.org/0009-0001-8444-8536
ST: https://orcid.org/0009-0004-0291-5068
JP: https://orcid.org/0009-0003-7905-8183
KH: https://orcid.org/0009-0007-1639-1308
GH: https://orcid.org/0009-0009-6380-7139

Abstract

Deep vein thrombosis (DVT) is a severe condition marked by the formation of blood clots in the deep veins, usually in the lower limbs. Though DVT is frequently associated with prolonged immobility, trauma, and certain medical conditions, it is exceptionally rare following a brown recluse spider (*Loxosceles reclusa*) bite. Typically, this spider's envenomation causes local necrotic skin reactions, hemolysis, and in serious cases, systemic loxoscelism. In this case report, we present an unusually rare occurrence of DVT developing in a 53-year-old male after a brown recluse spider bit his lower limb. This case underscores the need for vigilance in identifying thromboembolic complications in patients with severe loxoscelism. Clinicians should be aware of the potential systemic effects of spider envenomation and consider early diagnostic and therapeutic interventions to prevent complications, including pulmonary embolism.

Keywords: brown recluse spider bite, deep vein thrombosis, loxoscelism, spider envenomation, brown recluse spider, *Loxosceles reclusa*

Introduction

Brown recluse spiders (*Loxosceles reclusa*) are among the most venomous arachnids in North America [1]. Envenomation from their bites can lead to dermonecrotic arachnidism and systemic loxoscelism, symptoms of which can manifest as hemolysis, thrombocytopenia, renal failure, and in rare cases, thromboembolic events [2]. However, the pathophysiological link between spider envenomation and deep vein thrombosis (DVT) remains unclear, but it may involve venom-induced vascular endothelial damage, inflammatory responses, and platelet aggregation [3,4].

This case report aims to document an unusual occurrence of DVT following a brown recluse spider bite and to explore potential mechanisms involved in this rare complication. The case emphasizes the need for healthcare providers to consider thromboembolic events as potential complications in cases of spider envenomation and to promptly initiate appropriate diagnostic and therapeutic measures.

Corresponding Author
Reshma Pydi
1650 Grand Concourse, Bronx, Department of General Surgery, Bronxcare Health System, Hospital, NY, 10457, USA
E-mail: rajitharajju.reshma@gmail.com

Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

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

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

Published
2025 October 4

How to cite: Reshma P, Soumya N, Sania T, Jigyasha P, Kaitlyn H, Girishkumar H. Deep venous thrombosis after brown recluse spider bite: A rare case report. J Surg Med. 2025;9(10):219-221.

Case presentation

A 53-year-old male arrived at the emergency department (ED) due to progressive pain and swelling in his right lower leg. Two weeks prior, he had been bitten by an insect in his basement, which resulted in painful lesions on his right lower leg and forearm (Figure 1). As time passed, he noted increased leg swelling and discomfort, which led him to seek medical help.

His medical history included hypertension, diabetes mellitus, asthma, a history of knee replacement, and obesity. A physical examination showed an eschar with surrounding erythema at the bite site (Figure 1a) and +2 pitting edema in his right calf.

A modified Wells' score of two suggested a moderate pretest likelihood of DVT, which warranted further imaging. Indeed, a venous duplex ultrasound confirmed DVT in the right common femoral vein (CFV), superficial femoral vein (SFV), popliteal and peroneal veins, along with superficial venous thrombosis in the right greater saphenous vein (GSV) (Figure 2). Results from extensive hypercoagulability testing were unremarkable (Figure 3). Ultimately, the patient was diagnosed with DVT which was provoked by the insect bite. He was started on therapeutic anticoagulation with Lovenox, which was later replaced with direct oral anticoagulants upon his discharge.

Figure 1: a. Erythematous papule with eschar in the center on the right lower extremity b. Healed insect bite on the right upper extremity.

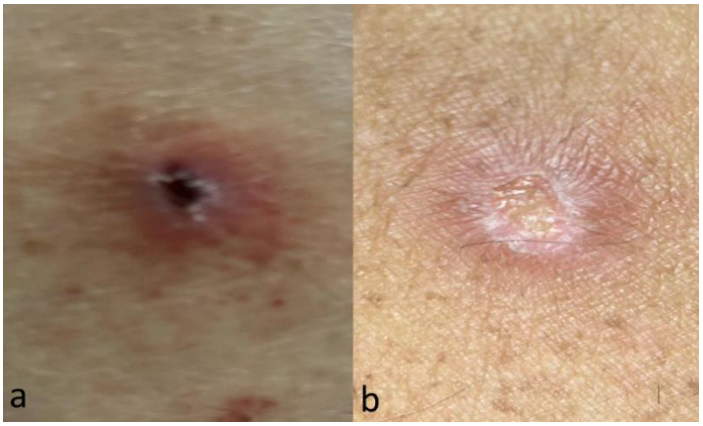


Figure 2: a. Depicting the thrombotic lesion, somewhat echogenic and maybe sub-acute chronicity b. Depicting the dilated and non-compressible Right mid-CFV.

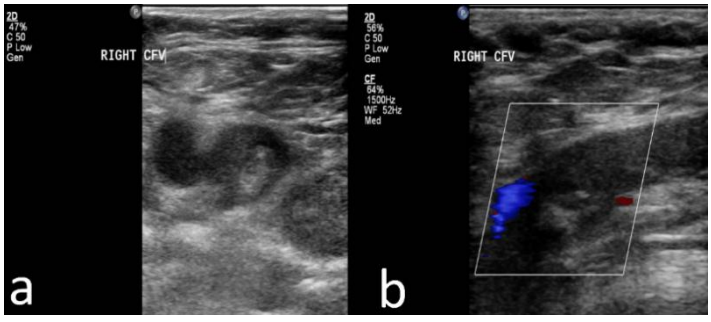


Figure 3: Hypercoagulation workup.

Test	Flag	Value 1	Value 2	Reference
PT		10.6	**10.9 ↓**	10.2
INR		0.87	0.90	0.85
DRVVT Screen	*	33	*	34
Antithrombin III Assay	*	92	*	90
D-Dimer Assay, Plasma	*	**↑ 441**		
Factor V Assay		*	96	
Factor V Leiden Mutation	*	NEGATIVE		
Partial Thromboplastin Time		33.8	31.6	29.8
Protein C Functional Assay	*	127	106	
Protein S Functional Assay	*	93	**↓ 47**	

Discussion

DVT is a multifactorial condition influenced by Virchow's triad: endothelial damage, venous stasis, and hypercoagulability [4]. The temporal link between the brown recluse spider bite and DVT formation suggests a venom-induced prothrombotic state [5].

Phospholipase D, a significant venom component, has been implicated in hemolysis, increased vascular permeability, and platelet aggregation [2]. Additionally, systemic inflammation and immune responses to venom proteins might exacerbate endothelial injury and thrombus formation. Although systemic loxoscelism is a known complication, DVT as a consequence remains exceptionally rare [6].

While this case showcases a potential association between brown recluse envenomation and DVT, other contributing factors should be considered. The patient's obesity and age are recognized risk factors for thromboembolism, but they do not fully explain this extensive DVT in a physically active patient with a history of knee replacement [3]. Previous literature, including a report by Surana et al. [5] on recurrent DVT following a brown recluse spider bite, suggests that spider envenomation might serve as a provoking factor in thromboembolic events. Nevertheless, further research is required to establish causality.

This case underscores the need for clinicians to maintain a high level of suspicion for thromboembolic events in patients presenting with systemic complications of brown recluse envenomation. Early recognition, comprehensive risk assessment, and swift intervention are crucial for maximizing patient outcomes [7].

Conclusion

This case report describes a rare occurrence of DVT developing after a brown recluse spider bite. Loxoscelism is traditionally associated with necrotic skin lesions and systemic toxicity, but this case emphasizes the potential for severe thromboembolic complications. The venom's inflammatory and pro-coagulant effects may aid in thrombus formation. Early recognition, a multidisciplinary approach, and anticoagulation therapy are essential for effective management. More research is needed to better comprehend the pro-coagulant effects of Loxosceles venom and to devise appropriate management strategies for affected patients.

References

1. Swanson DL, Vetter RS. Bites of brown recluse spiders and suspected necrotic arachnidism. N Engl J Med. 2005;352(7):700-7.
2. Chaim OM, Trevisan-Silva D, Chaves-Moreira D, Wille AC, Ferrer VP, Matsubara FH, et al. Brown spider (Loxosceles genus) venom toxins: tools for biological purposes. Toxins (Basel). 2011 Mar;3(3):309-44. doi: 10.3390/toxins3030309.
3. Ali AH, Kang MS, Aldahwi J, Reyes C. P-ANCA vasculitis with diffuse alveolar haemorrhage preceded by a spider bite. BMJ Case Rep. 2020 Jun 17;13(6):e233710. doi: 10.1136/bcr-2019-233710.
4. Cushman M. Epidemiology and risk factors for venous thrombosis. Semin Hematol. 2007;44(2):62-9.
5. Surana A, Anand A, Hazique M, Singh B, Gupta A, Georgy J, et al. Recurrent deep vein thrombosis following brown recluse spider bite complicated by medication noncompliance and residual scar tissue: A rare case report. Clin Case Rep. 2023 Apr 25;11(4):e7263. doi: 10.1002/ccr3.7263.
6. Sams HH, Dunnick CA, Smith ML, King LE Jr. Necrotic arachnidism. J Am Acad Dermatol. 2001 Apr;44(4):561-73; quiz 573-6. doi: 10.1067/mjd.2001.112385.
7. Kirkilesis G, Kakkos SK, Bicknell C, Salim S, Kakavia K. Treatment of distal deep vein thrombosis. Cochrane Database Syst Rev. 2020 Apr 9;4(4):CD013422. doi: 10.1002/14651858.CD013422.pub2.