Research Article / Araştırma Makalesi

The Role of Machine Learning Algorithms in Sepsis Diagnosis: A Retrospective Overview using Bibliometric Analysis

Sepsis Teşhisinde Makine Öğrenmesi Algoritmalarının Rolü: Bibliyometrik Analiz Kullanarak Retrospektif Genel Bakış

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Abstract: Machine learning has great potential to extract meaningful information from large data sets and build powerful predictive models for disease diagnosis. The aim of this study is to conduct a comprehensive review of the role of machine learning algorithms in sepsis diagnosis. The research was conducted using the bibliometric analysis method. Within the scope of the research, an advanced search query was created in the Web of Science (WoS) Core Collection database and WoS index Science Citation Index Expanded (SCI-Exp), publication type article, publication language English, open access publications published between 2000 and 2024 were included. In the WoS database, 277 publications were accessed using an advanced search query created with the relevant keywords on 05.07.2024. After excluding 87 non-English publications that did not include sepsis and machine learning, 190 publications were analyzed. In the treemap obtained in bibliometric analysis, the first five keywords include sepsis, machine learning, intensive care units, mortality, and artificial intelligence, respectively. China led in publication count, whereas the USA boasted the most cited publications. "Frontiers in Medicine" featured the highest number of articles, while "Critical Care Medicine" contained the most cited ones. According to the analysis of articles published, the use of artificial intelligence and machine learning in sepsis diagnosis has significant potential, especially in intensive care units. These technologies show promise in early diagnosis, disease classification, and prognosis prediction. Expanding research collaborations and a growing publication focus on key themes suggest continued growth in this research area.
Keywords: Sepsis, Machine Learning, Intensive Care Units, Mortality, Artificial Intelligence, Bibliometric Analysis.

Özet: Makine öğrenmesi, büyük veri setlerinden anlamlı bilgiler çıkarma ve hastalık teşhisi için güçlü tahmin modelleri oluşturma konusunda büyük bir potansiyele sahiptir. Bu çalışmanın amacı, makine öğrenmesi algoritmalarının sepsis teşhisindeki rolüne ilişkin kapsamlı bir incelemesini gerçekleştirmektir. Araştırma bibliyometrik analiz yöntemi ile gerçekleştirilmiştir. Araştırma kapsamında Web of Science (WoS) Core Collection veri tabanında gelişmiş arama sorgusu oluşturularak 2000-2024 yılları arasında yayınlanan WoS dizini Science Citation Index Expanded (SCI-Exp), yayın türü makale, yayın dili ingilizce, açık erişimli yayınlar dahil edildi. WoS veri tabanında 05.07.2024 tarihinde ilgili anahtar kelimelerle oluşturulan gelişmiş arama sorgusu kullanılarak 277 yayına ulaşıldı. Sepsis ve makine öğrenmesini içermeyen, ingilizce olmayan 87 yayın dışlanarak 190 yayının analizi yapılmıştır. Bibliyometrik analiz sonucunda elde edilen kelime haritasında ilk beş anahtar kelime sırasıyla sepsis, makine öğrenmesi, yoğun bakım üniteleri, mortalite ve yapay zekâ yer almaktadır. En çok yayına sahip olan ülke Çin, en çok atıf alan ülke Amerika iken, dergiler arasında en çok makaleye sahip olan “Frontiers in Medicine”, en çok atıf alan yayının olduğu dergi “Critical Care Medicine” oldu. 2000-2024 yılları arasında yayınlanan makalelerin analizine göre, sepsis teşhisinde yapay zekâ ve makine öğrenmesi kullanımı, özellikle yoğun bakım ünitelerinde önemli bir potansiyele sahiptir. Bu teknolojilerin erken teşhis, hastalık sınıflandırması ve prognoz tahmininde etkili bir şekilde kullanılabileceğini ortaya koymaktadır. Araştırma iş birliği ağlarının yoğunlaşması ve belirlenen anahtar kelimeler etrafında yoğunlaşan yayınların artması, bu alandaki araştırma eğilimlerinin gelecekte daha da büyüyeceğini işaret etmektedir.
Anahtar Kelimeler: Sepsis, Makine Öğrenmesi, Yoğun Bakım Üniteleri, Mortalite, Yapay Zekâ, Bibliyometrik Analiz.

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1. Introduction

Sepsis is a serious condition set apart by an immune response in which the body harmfully attacks its own tissues (1). It has important effects on millions of people annually, thus making it a significant health issue; therefore, asserting its need for early detection. Diagnosis of sepsis is mainly based on symptoms at the clinical level and on laboratory tests; however, these techniques are not able to provide satisfactory accuracy (2).

Machine learning (ML) can significantly transform how problems are addressed in the medical profession (3), with the detection of sepsis being only one area that stands to benefit from this technology. ML algorithms make diagnosis faster and more accurate by their nature of being able to learn and build models from large datasets. Applying these developing technologies was considered one more substantial step forward in the fight against sepsis.

Recent studies have confirmed the feasibility of using ML algorithms to achieve an accurate diagnosis of sepsis. Nemati et al.'s (2018) study, a machine learning model outperformed all traditional methods in recognizing early sepsis in ICUs (4). Scicluna et al.'s (2017) study, in which they classified sepsis patients based on blood genomic endotypes, demonstrated how personalized medicine approaches can play a critical role in sepsis diagnosis and treatment (5). Desautels et al. proved that training a machine learning model on a large volume of data concerning patients could significantly increase the accuracy of predictions related to sepsis (6).

This study offers a bibliometric review focused on evaluating the current trends and research trajectories in the use of machine learning for sepsis diagnosis. A bibliometric analysis approach was adopted to systematically examine scientific publications regarding the application of machine learning in diagnosing sepsis, with an emphasis on both qualitative and quantitative aspects. The study aims to highlight the potential of artificial intelligence and machine learning technologies in enabling the timely identification and management of sepsis.

2. Materials and Methods

2.1. Research mapping

The data were retrieved from the Web of Science database on July 5, 2024. The Web of Science Core Collection was selected for this study because of its extensive resources and comprehensive coverage in the field of health.

Publications were accessed using the following advanced search query on topic searches (TS).

TS=("sepsis associated thrombocytopenia" OR "sepsis related thrombocytopenia" OR "thrombocytopenia" OR "sepsis" OR "septic shock") AND ("machine learning" OR "artificial intelligence" OR "AI" OR "random forest" OR "artificial neural networks" OR "neural networks" OR "NN" OR "gradient boosting" OR "XGboost" OR "bayesian") AND ("intensive care unit" OR "ICU" OR "critical care" OR "critical illness") AND ("classification" OR "diagnosis" OR "recognition" OR "prognosis" OR "prediction").

Web of Science Index: Science Citation Index Expanded, open access publications with document type "article" were included in the study.

Using the search query in the Web of Science database, a total of 277 publications were accessed. Publications that did not meet certain criteria were excluded from the study: (1) early access and proceedings papers, (2) publications not related to "sepsis" and "machine learning", and (3) publications not in English. Out of the initial 277 publications, 87 were excluded, resulting in a final dataset of 190 publications for analysis (Figure 1).

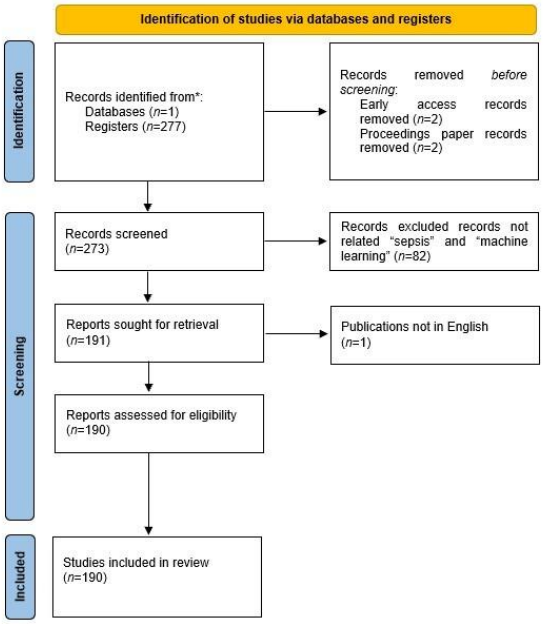

Figure 1. A flow diagram for bibliometric analysis of publications on sepsis and machine learning algorithms in WoS database

2.2. Quantitative Analysis

The 190 publications were organized into two distinct files: a BibTeX file for the Bibliometrix package (version 4.3.0) of the RStudio (version 2024.04.2+764), R programming language (version 4.4.1) and a .txt file for the VOSviewer software (Manual for VOSviewer version 1.6.20) (7,8). Both files encompass comprehensive records and cited references pertaining to the publications. VOSviewer serves as a robust tool for visualizing the interrelationships between scientific publications. Conversely, Bibliometrix is a bibliometric analysis package in R, enabling detailed analyses when working with extensive datasets. By employing both software tools collaboratively, a multidimensional analysis of studies on sepsis and machine learning was conducted. Analyses focusing on authors, keywords, journals, and countries were executed using Bibliometrix and VOSviewer, accompanied by the creation of data visualizations (7). Moreover, Google Trends data, which demonstrate numerical trends based on user searches on Google, were employed to illustrate the distribution of machine learning applications in disease diagnosis using Excel.

3. Results

3.1. Distribution of searches for machine learning for disease diagnosis

According to the Google trends popularity index graph, which is based on the searches made by users worldwide, the use of machine learning in disease diagnosis between 2004 and July 2024, while there were no searches in 2016 and before, searches started in 2017, and the number of searches has increased every year since 2022 (Figure 2).

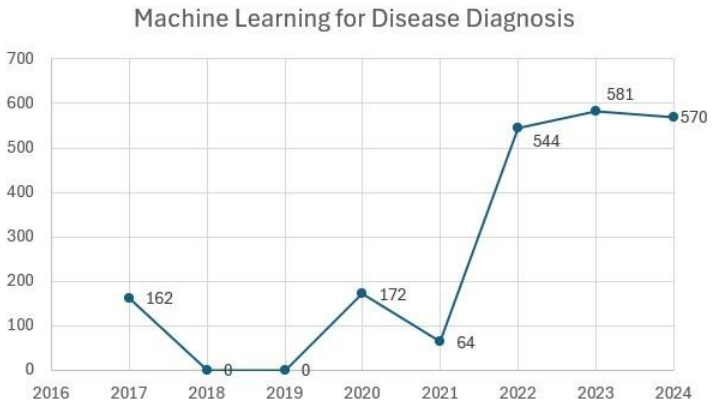

Figure 2. Google trends popularity index on the use of machine learning algorithms in disease diagnosis

3.2. Distribution of annual scientific production

The annual scientific production graph shows that 190 publications were published between 2005 and July 2024. Notably, there were only 16 publications before 2019, but there was a significant increase in the number of publications, with 174 published between 2019 and July 2024 (Figure 3).

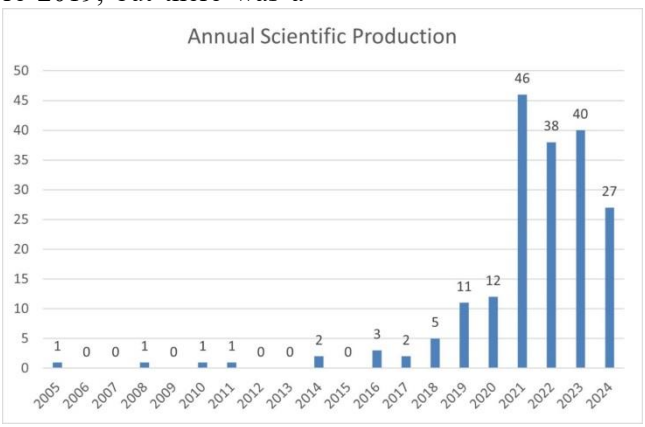

Figure 3. Annual scientific production graph for the use of machine learning algorithms in sepsis diagnosis

3.3. Distribution of Authors and Keywords

Using VOSviewer, 1054 authors with at least one publication and one citation were identified out of a total of 1243 authors. When creating the table of the most relevant authors with Bibliometrix, Chen et al. and Zhang et al. were found to have the most publications, each with 6 articles. The author with the most citations was Nemati S et al., with 500 citations (Table 1).

With VOSviewer, a total of 415 keywords that the authors used at least once were identified. The most frequently used keywords were "sepsis" (90 times), "machine learning" (75 times), "intensive care units" (25 times), "mortality" (22 times), and "artificial intelligence" (18 times) (Figure 4). Figure 5 shows the first 40 keywords used by the authors, analyzed through multiple correspondence analysis and presented in a map as 2 clusters. In Figure 5, the first cluster covers 30.31% and the second cluster covers approximately 16.86%. Keywords that are more similar are represented closer together on the map (Figure 5).

Table 1. Analysis of the most cited and relevant authors in machine learning algorithms publications in sepsis diagnosis

Most cited authors			Most relevant authors		
Rank	**Author**	**Total Citations**	**Rank**	**Author**	**Articles**
1	Nemati Shamim	500	1	Chen	6
2	Calvert Jacob	435	2	Zhang Shen	6
3	Chettipally Uli	435	3	Hua Tianfeng	4
4	Das Ritankar	435	4	Liu	4
5	Jay Melissa	435	5	Nemati Shamim	4
6	Kerem Yaniv	435	6	Shashikumar Supreeth	4
7	Shieh Lisa	435	7	Wardi Gabriel	4
8	Shimabukuro David	435	8	Yang Min	4
9	Holder Andre	424			
10	Buchman Timothy	403			

Figure 4. The distribution of author keywords used in machine learning algorithms publications in sepsis diagnosis

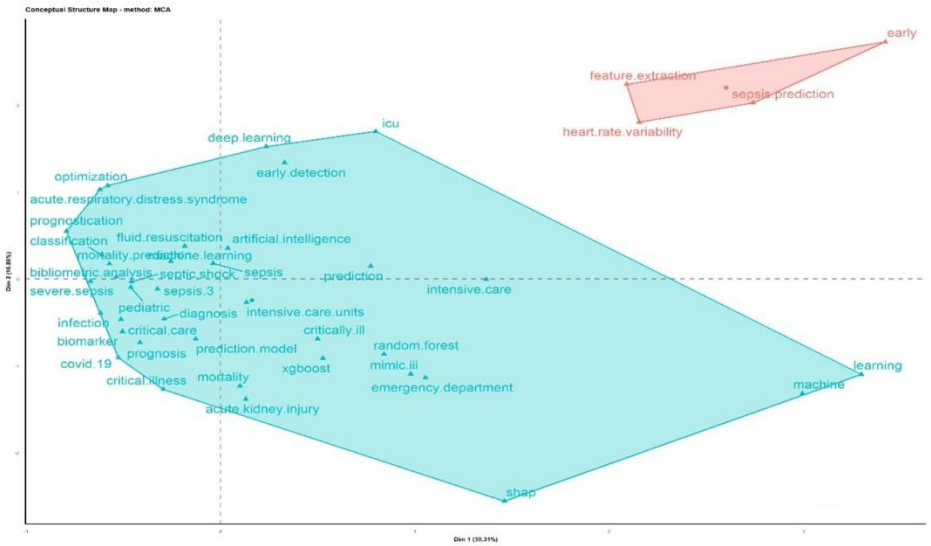

Figure 5. Factorial map of the distribution of author keywords used in machine learning algorithms publications in sepsis diagnosis

Dim 1: Dimension 1, Dim 2: Dimension 2, icu: intensive care unit, MCA: Multiple Correspondence Analysis, mimic iii: The Medical Information Mart for Intensive Care III, sepsis 3: The Third International Consensus Definitions for Sepsis and Septic Shock, shap: Shapley Additive Explanations, XGboost: Extreme Gradient Boosting

3.4 Distribution of sources

The article by Nemati et al. (2018), titled "An Interpretable Machine Learning Model for Accurate Prediction of Sepsis in the ICU", published in Critical Care Medicine, was the most cited article with 394 citations (Table 2). Using VOSviewer, 79 journals with at least one document and one citation among the sources were identified. The journals with the most publications are "Frontiers in Medicine" (16 publications), "Scientific Reports" (12 publications), "PLOS ONE" (11 publications), "International Journal of Medical Informatics" (6 publications), "BMC Medical Informatics and Decision Making" (5 publications), "BMC Infectious Diseases" (5 publications), "Critical Care" (5 publications), and "Frontiers in Immunology" (5 publications) (Table 3).

Table 2. Examining of the most cited scientific journals according to publications on machine learning algorithms in sepsis diagnosis

Rank	Author Surname-Name, Year, Journal Name	Title	Total Citations
1	Nemati S et al., 2018, Critical Care Medicine (4)	An Interpretable Machine Learning Model for Accurate Prediction of Sepsis in the ICU	394
2	Scicluna BP et al., 2017, Lancet Respiratory Medicine (5)	Classification of patients with sepsis according to blood genomic endotype: a prospective cohort study	308
3	Desautels T et al., 2016, JMIR Medical Informatics (6)	Prediction of Sepsis in the Intensive Care Unit with Minimal Electronic Health Record Data: A Machine Learning Approach	255
4	Mao Q et al., 2018, BMJ Open (9)	Multicenter validation of a sepsis prediction algorithm using only vital sign data in the emergency department, general ward and ICU	180
5	Bihorac A et al., 2019, Annals of Surgery (10)	MySurgeryRisk: Development and Validation of a Machine-learning Risk Algorithm for Major Complications and Death After Surgery	166
6	Hou N et al., 2020, Journal of Translational Medicine (11)	Predicting 30-days mortality for MIMIC-III patients with sepsis-3: a machine learning approach using XGboost	151
7	Giannini HM et al., 2019, Critical Care Medicine (12)	A Machine Learning Algorithm to Predict Severe Sepsis and Septic Shock: Development, Implementation, and Impact on Clinical Practice	131
8	Sutherland A et al., 2011, Critical Care (13)	Development and validation of a novel molecular biomarker diagnostic test for the early detection of sepsis	117
9	Mani S et al., 2014, Journal of the American Medical Informatics Association (14)	Medical decision support using machine learning for early detection of late-onset neonatal sepsis	109
10	Kaji DA et al., 2019, Plos One (15)	An attention based deep learning model of clinical events in the intensive care unit	94

ICU: Intensive Care Unit, MIMIC III: The Medical Information Mart for Intensive Care III, Sepsis-3: The Third International Consensus Definitions for Sepsis and Septic Shock, XGboost: Extreme Gradient Boosting

The journals with the most citations are "Critical Care Medicine" (540 citations), "Lancet Respiratory Medicine" (308 citations), "Critical Care" (284 citations), "JMIR Medical Informatics" (284 citations), and "PLOS ONE" (274 citations) (Table 3).

Table 3. Examining scientific journals that include publications investigating the role of machine learning algorithms in sepsis diagnosis according to the number of citations they received

Most cited journal name			Most relevant journal name		
Rank	**Journal name**	**Total Citations**	**Rank**	**Journal name**	**Articles**
1	Critical Care Medicine	540	1	Frontiers in Medicine	16
2	Lancet Respiratory Medicine	308	2	Scientific Reports	12
3	Critical Care	284	3	Plos One	11
4	JMIR Medical Informatics	284	4	International Journal of Medical Informatics	6
5	Plos One	274	5	BMC Infectious Diseases	5
6	Scientific Reports	196	6	BMC Medical Informatics and Decision Making	5
7	Frontiers in Medicine	191	7	Critical Care	5
8	BMJ Open	187	8	Frontiers in Immunology	5
9	Annals of Surgery	166			
10	Journal of Translational Medicine	162			

BMC: BioMed Central, BMJ: British Medical Journal, JMIR: Journal of Medical Internet Research, Plos: Public Library of Science

3.5. Distribution of Countries and Institutions

Among the countries, the ones with the most publications are China (84 publications), the USA (36 publications), and Germany, Italy, Korea, the Netherlands, and England (each with 6 publications) (Table 4). According to VOSviewer output, in terms of citations, the countries with the highest numbers are the USA (1,843 citations), China (870 citations), the Netherlands (357 citations), Australia (184 citations), and England (177 citations).

Table 4. Distribution of publications on machine learning algorithms in sepsis diagnosis according to authors' countries

Rank	Country	Articles
1	China	84
2	United States of America	36
3	Germany	6
4	Italy	6
5	Korea	6
6	Netherlands	6
7	United Kingdom	6
8	Canada	4
9	France	4

Using Bibliometrix, in institution analysis, the institutions with the highest number of publications were identified as Central South University (43 publications), Anhui Medical University (26 publications), Jinan University (22 publications), University of California San Diego (20 publications), and Emory University (19 publications) (Figure 6). Figure 7 presents a network visualization of 397 institutions out of 465 institutions with at least one document and one citation in institution citation analysis.

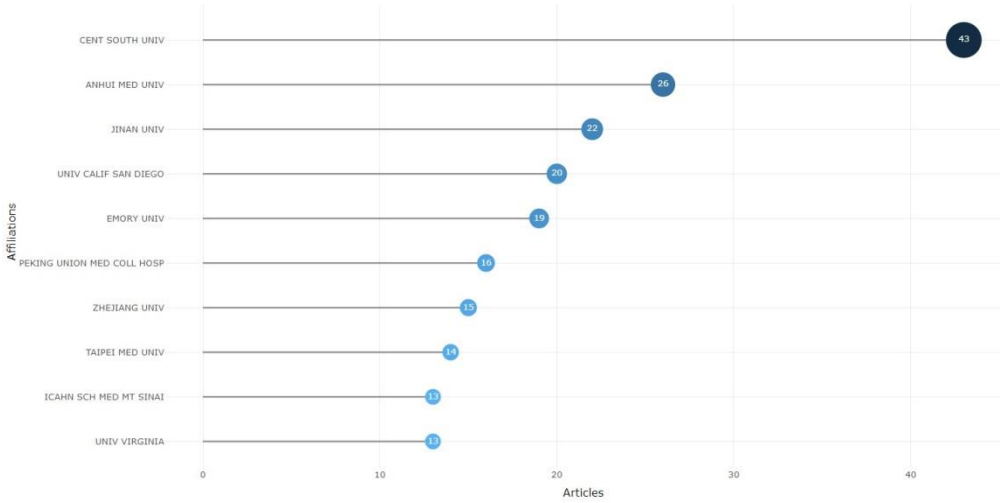

Figure 6. Distribution of publications on machine learning algorithms in sepsis diagnosis by institutions

CALIF: California, COLL: college, HOSP: hospital, MED: medical or medicine, MT: mount, SCH: school, UNIV: university

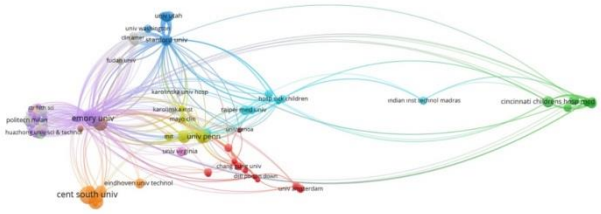

Figure 7. Inter-institutional citation network for publications on machine learning algorithms in sepsis diagnosis

hosp: hospital, med: medical or medicine, univ: university

4. Discussion

Sepsis diagnosis has undergone a significant transformation with the advent of ML technologies (16, 17, 18, 19). Current methods of diagnosing sepsis are usually based on clinical symptoms and laboratory tests. These do not adequately reflect the complex nature of the disease. Clinical symptoms such as procalcitonin and lactate are often elevated in infections other than sepsis, making early diagnosis difficult (20,22,23). Laboratory tests are used in the diagnosis of sepsis, but the results of these tests usually take time and may not be sufficient to make a definitive diagnosis due to low sensitivity and specificity (21). Therefore, current methods cannot provide satisfactory accuracy in the early stages of sepsis, which can lead to delayed therapeutic intervention. The recent increase in publications on the use of machine learning in sepsis diagnosis shows that these challenges emphasize the need for advanced technologies such as machine learning that can provide faster and more accurate diagnosis. According to the results, China has the highest number of scientific publications, while the most cited publications belong to the USA. As China is a country that invests heavily in artificial intelligence technologies,

it conducts many scientific studies. However, in the field of medicine, the USA has been the country with the highest number of citations due to its strong academic structure and leading position.

This bibliometric analysis highlights key trends, influential studies, and emerging research themes that shape the current and future perspectives of this critical interdisciplinary field. Our analysis reveals a significant increase in the volume of publications on machine learning applications in sepsis diagnosis over the past three years. This increase reflects the broader trend of adopting artificial intelligence and data-driven methodologies to improve clinical decision-making in healthcare. Increasing dataset sizes and advances in computational power have enabled the development of sophisticated ML algorithms capable of discovering subtle patterns in large amounts of biomedical data. Considerable research has pioneered various ML techniques, such as random forests (RF), neural networks (NN), support vector machines (SVM), and XGboost as an ensemble method, each bringing unique strengths to the diagnostic process (24,25,26).

These methodologies have been developed to improve accuracy, early detection, and prognostic prediction in sepsis diagnosis, where timely intervention is crucial. The influential articles widely cited in our analysis often have descriptions of novel algorithmic approaches or the integration of ML with electronic health records (EHRs), which have been important in advancing practical applications.

Several emerging themes identified in the bibliometric analysis point to future research directions. The interpretability of ML models is a critical area for clinicians to trust and use effectively in clinical settings. Therefore, explainable artificial intelligence (XAI) methods are increasingly gaining traction. Furthermore, the integration of multimodal data including genomic, proteomic, and imaging data is expected to increase the robustness of diagnostic algorithms. Collaborative research across disciplines such as computer science, medicine, and bioinformatics has accelerated innovation in this field. The interdisciplinary nature of this research is evident in the diversity of connections and the wide range of journals publishing related work. Another important trend is the emphasis on prospective validation and real-world application studies, which are increasingly prioritized to move from theoretical models to clinically applicable solutions.

This bibliometric study focused exclusively on Science Citation Index Expanded indexed open access articles in English from the Web of Science database. Limitations of the study include the relatively small number of publications on machine learning in sepsis diagnosis and the retrospective nature of many included publications.

5. Conclusion

This bibliometric analysis has allowed to provide an overview of the current literature on the use of machine learning in sepsis diagnosis and shows the status and potential of scientific studies in the fields of medicine and biostatistics related to the research topic.

Through the analyses conducted in this study, it has been observed that the application of machine learning in sepsis diagnosis has shown rapid growth in recent years, having been investigated in approximately 37 countries. This feature reveals that it is a vibrant and rapidly developing field that provides significant contributions from various disciplines. There are currently no studies indexed in SCI Expanded from Türkiye on this subject. In our future research, we plan to evaluate the performance of machine learning algorithms in the diagnosis of sepsis or sepsis associated thrombocytopenia using data obtained from two centers in Türkiye and contribute to the literature.

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Ethics

Ethics Committee Approval: This study was conducted on electronic bibliometric data obtained from the WoS database and did not include any patient data, an ethics committee or institutional review approval was not required.
Informed Consent: This study did not require informed consent.
Authorship Contributions: Concept: EO, BE. Design: EO, BE. Supervision: BE. Resources: EO, BE. Materials: EO, BE. Data Collection and/or Processing: EO, BE Analysis and/or Interpretation: EO, BE. Literature Search: EO, BE. Writing Manuscript: EO, BE. Critical Review: BE.
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