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Review Article

Predictive Value of Infection Related Critical Illness Scores on the Risk of Death in Infected Patients: A Systematic Review and Meta-Analysis

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Abstract

Background: This article aimed to compare the value of infection related critical illness scores in predicting the risk of death in infected patients, and evaluate the predictive accuracy of three scoring indicators: SOFA score, APACHE II score, and NEWS score.

Methods: Through the established retrieval strategy, the relevant literature from January 2013 to December 2023 were searched on platforms such as CNKI, Wanfang, PubMed, Embase, and Cochrane Library, eight relevant literature were included for meta-analysis. Literature screening and data extraction were conducted according to predetermined standards, using a fixed effects model for data analysis.

Results: Among the 8 included literature (References (5-12)), the ratio of mortality to survival and 95% confidence interval for SOFA scores were 1.33 and (0.98, 1.75), respectively; The APACHE II score is 2.24 and (1.58, 2.97); The NEWS score is 1.64 and (1.45, 1.85). All three scoring indicators had significant value in predicting the risk of death in infected patients. In addition, comparing the AUC of the three scoring indicators, the SOFA score had the highest AUC, followed by the APACHE II score, and showed significant differences compared to the NEWS score, with $P<0.001$ and $P<0.05$ respectively.

Conclusion: The SOFA score has higher accuracy and predictive value in predicting the condition and risk of death of infected patients. However, further attention needs to be paid to the selection of scoring methods to comprehensively consider the clinical situation and research objectives. The results of this study are helpful in guiding the evaluation and prediction of infected patients in clinical practice, and providing a basis for optimizing treatment strategies.

Keywords: Infection; Death; Risk prediction; Critical illness score; Meta-analysis

Introduction

Infection is a serious health problem worldwide, which can lead to serious complications and death (1). In the process of managing infected patients, timely assessment of their condition and risk of death is crucial in order to take appropriate treatment and care measures (2). Infection-related critical illness scoring indicators (IRCISI)

are commonly used tools to assess the severity of infection in patients and predict the risk of death.
We aimed to compare the value of IRCISI in Infected Patients Mortality Risk Prediction (IPMRP), and focuses on evaluating the accuracy and predictive ability of three scoring indicators: SOFA score, APACHE II score, and NEWS score. The SOFA score is an indicator for evaluating multiple organ dysfunction (3), the APACHE II score is a comprehensive tool for evaluating clinical indicators in patients (4), and the NEWS score is an indicator for evaluating acute life-threatening conditions (5).
To achieve this goal, this paper has carried out a systematic document retrieval and included relevant research that meets specific standards. By applying the meta-analysis method, the data included in the literature was integrated and analyzed to compare the performance of different scoring indicators in IPMRP.
The results of this study are of great significance for guiding the evaluation and prediction of infected patients in clinical practice. By comparing the accuracy and predictive ability of different scoring indicators, the most suitable scoring tool can be selected for monitoring the condition and risk assessment of infected patients, thereby optimizing treatment strategies and improving patient prognosis. In addition, the results of this study also provide reference and basis for further research on the application of IRCISI.

Methods

Inclusion and Exclusion Criteria

This study needed to clarify the inclusion and exclusion criteria for infected patients to ensure consistency and comparability of the study subjects.
Inclusive criteria: ① Infection diagnosis: Patients must meet the infection criteria defined in the CDC Infectious Diseases Diagnosis Guidelines; ② Severity: The included infected patients should be critically ill patients with severe infections or infection related conditions. The definition of severe infection usually involves clinical manifestations such as infection combined with organ dysfunction or abnormal blood circulation; ③ Age range: Research can include infected patients in different age ranges, such as adults, children, or a specific age group of patients; ④ Research from January 2013 to December 2023; ⑤ Subjects: The study included samples from patients with severe infections. ⑥ Scoring system: Research must involve one of the three IRCISIs: SOFA score, APACHE II score, and NEWS score. ⑦ Outcome: The study reported the predicted risk of death for infected patients. ⑧ Study design: Observational study, Cohort study, Case–control study or Prospective cohort study. ⑨ Literature types: original research, systematic evaluation, meta-analysis, etc.
Exclusive criteria: ① Non infected patients: Patients who did not meet the infection definition criteria or have not reported an accurate infection diagnosis need to be excluded; ② Non severe infection patients: Patients who do not meet the definition criteria for severe infection or only include mild or moderate infections need to be excluded; ③ Specific diseases or pathological conditions: Based on the research purpose, certain specific infectious related diseases or pathological conditions can be excluded to ensure the consistency of the research subjects. For example, patients with specific Organ system infection or certain pathogen infection. ④ Incomplete or inaccessible data: Studies with significant deficiencies or unavailability in the extraction and analysis of required data are excluded.

IRCISI

Sequential Organ Failure Assessment (SOFA): It is used to evaluate the degree of organ function damage in patients with septic shock and severe infection. It considers six indicators: cardiovascular, respiratory, liver, coagulation, kidney, and nervous system. The scores of each system range from 0 to 4 points, and are divided according to the severity of organ dysfunction. The total score is 0-24 points. The higher the score, the more severe the organ dysfunction.

Acute Physiology and Chronic Health Evaluation II (APACHE II Score): It is used to evaluate the severity and prognosis of severe patients. It includes cardiovascular, respiratory, nervous system, kidney, liver, pancreas, metabolism and Hematology. Physiological indicators are scored according to different numerical ranges (ranging from 0 to 4 points), with a total score of 0-71 points. The higher the score, the more serious the condition and the higher the risk of death.

National Early Warning Score (NEWS score): It is used to monitor changes in vital signs of patients and detect potentially dangerous situations in the early stages. It includes indicators such as respiratory rate, blood oxygen saturation, body temperature, systolic blood pressure, heart rate, and state of consciousness. Each indicator is scored according to the numerical change (0 to 3 points), and the scores are added together to obtain a total score, which ranges from 0 to 20 points. The higher the score, the higher the risk of the disease. Usually, a score ≥ 5 requires emergency evaluation. These scoring systems are widely used in clinical practice, helping doctors assess the severity of patients' diseases, predict prognosis, and guide treatment decisions.

Document retrieval strategy

Choose comprehensive databases that cover a wide range of medical and related literature, such as PubMed, Embase, Cochrane Library, etc. Considering that the research may involve Chinese literature, it is necessary to choose Chinese databases such as CNKI (China National Knowledge Infrastructure), Wanfang (Wanfang Data), HowNet (VIP Network), etc. to ensure the comprehensiveness of search results. Based on the research topic, identify core keywords such as "infection", "critical illness score", "risk of death prediction", etc. Considering that different authors may express the same concept differently, using synonyms and synonyms can expand the search scope, such as extending "critical illness score" to "severity of illness score", "severity index", etc; Replace 'risk of death' with 'mortality', 'mortality rate', etc. According to the specific needs of the research, specific disease names (such as "sepsis", "pneumonia") or specific scoring system names (such as "APACHE II", "SOFA") can also be added to obtain more accurate results. Combine keywords into search statements using Boolean operators (AND, OR, NOT) to improve the accuracy and comprehensiveness of the search. For example, use "infection AND (critical illness score or severity of illness score) AND (risk of death or mortality)" to simultaneously search for literature containing infection and severity scores as well as death risk related content.

Literature screening and data extraction

In the full text reading stage, researchers carefully read the included literature and extract relevant data from it. Data extraction includes basic information of literature (such as author, year, and journal), research design, sample size, comparison of scoring indicators, and prediction of mortality risk. Researchers use standardized data extraction tables or tools to ensure the accuracy and consistency of the data. After the data extraction is completed, researchers need to merge and analyze the included literature. This includes comparing and comprehensively analyzing the predictive value of death risk for different scoring indicators, such as using meta-analysis methods to summarize and synthesize the results of various studies.

Quality Evaluation

Quality Assessment of Diagnostic Accuracy Studies (QUADAS) is a tool used to evaluate the quality of diagnostic accuracy research. It includes 14 evaluation projects aimed at evaluating whether research designs, methods, and reports have bias and uncertainty (6). The QUADAS score evaluates the quality and reliability of diagnostic accuracy research by evaluating 14 items such as clarity of research objectives and selection of research subjects, and assigning scores based on the quality level of each item. A higher QUADAS score indicates higher research quality and more reliable results.

Statistical Methods

RevMan5.3 software was used for meta-analysis, and the counting data is represented as %. Comparison between groups using $\chi 2$-test or Fisher's method. The measurement data conforming to Normal distribution is expressed in ($x \pm s$). The independent sample *t*-test was used for comparison between the two groups, which was used to compare whether there is significant difference between the mean values of two independent Sample mean. In the above statistical analysis, the statistical significance is generally limited to $P<0.05$, that is, when the *P*-value was less than 0.05, the results are considered statistically significant and there is a significant difference. This setting can help researchers determine whether the results are solely due to random factors.

Results

Document retrieval results

The retrieval strategy that has been developed secretly was used for retrieval, and a total of 536 articles were detected on platforms such as CNKI and Wanfang. After removing duplicates, 280 related articles were included. The titles and abstracts of 280 literature were read for preliminary screening. Finally, 8 relevant literatures (References (5-12)) were included, and the specific process is shown in Fig. 1.

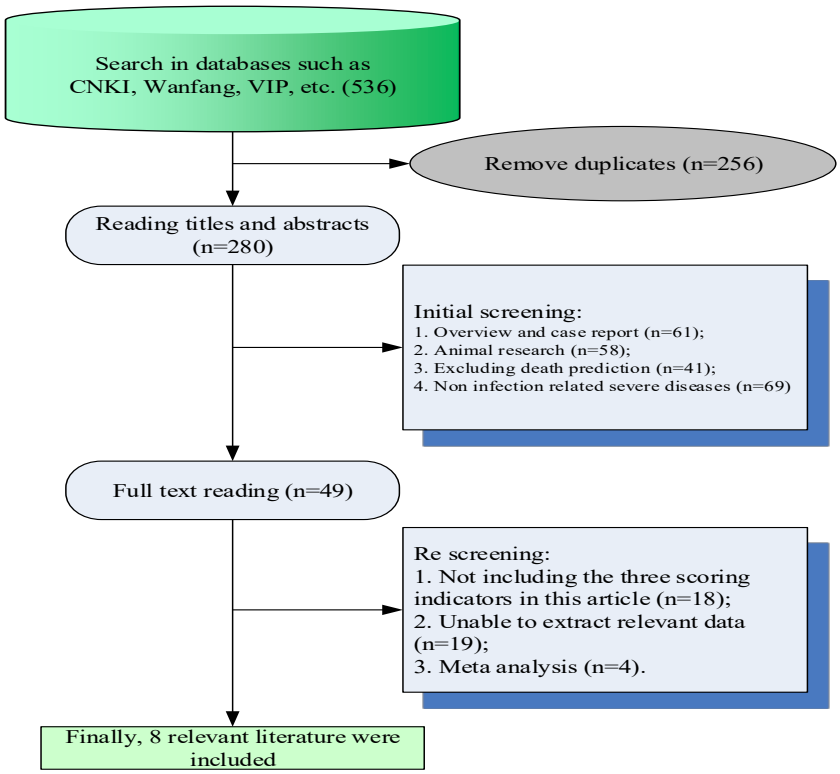


Fig. 1: Literature inclusion process

Among the 8 included literature References (5-12), References (5, 10, 12) included SOFA scores, References (5, 7, 8, 10, 11) included APACHE II scores, and References (5, 6, 7, 9) included NEWS scores. The included literature can directly or indirectly calculate the sensitivity and specificity of the risk of death in critically ill patients with infection. The basic clinical characteristics are detailed in Table 1. In addition, the QUADAS scores of the studies included in this article were all above 10, indicating high quality (Fig. 2).

Table 1: Basic characteristics of included studies

Included study	Country	Death group(D)	Survival group(S)	Scoring tool
Reference (5) Wang XT2021	China	145	483	APACHEII SOFA NEWS
Reference (6) Stark A2021	U.K.	36	176	NEWS
Reference (7) Kenealy RJ2022	China	161	572	NEWS APACHEII
Reference (8) Calderon R I2022	China	29	71	APACHEII
Reference (9) Sader HS2021	China	68	1116	NEWS
Reference (10) Liu KS2021	China	76	213	APACHEII SOFA
Reference (11) Julienne J2023	China	24	73	APACHEII
Reference (12) Macnicoll F2021	USA	42	142	SOFA

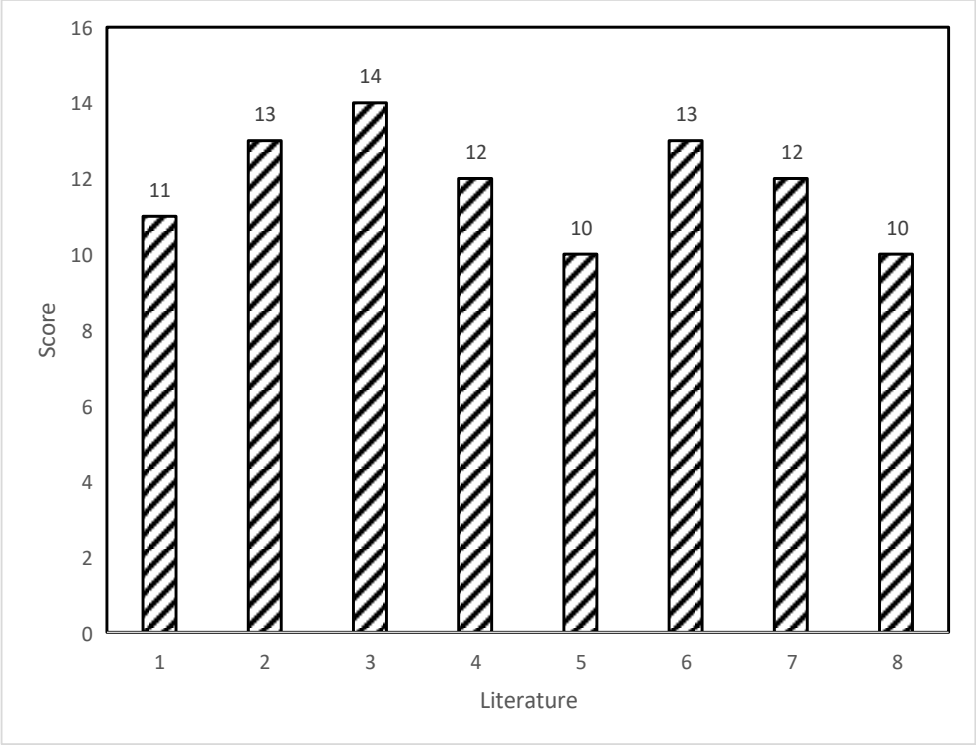


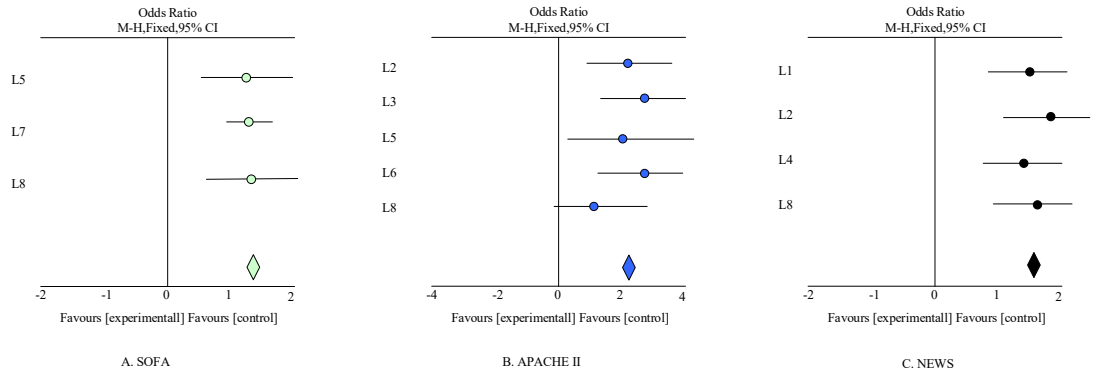
Fig. 2: Quality of Literature Inclusion QUADAS Score

The Value of Three Scoring Indicators for IPMRP

In Table 2 and Fig. 3, in the included studies (3-5 literature) reported differences in SOFA scores, APACHE II scores, and NEWS scores between the survival group (S) and the death group (D), respectively. Heterogeneity tests were consistent with $P>0.1$ and I2<50%, and fixed effects models were used for analysis. The comprehensive results showed that all three scoring indicators in the S were significantly lower than those in the control group(C) ($P<0.001$).

Table 2: Analysis results of three scoring indicators on the fixed effect model of IPMRP value

SOFA Score			
	D	S	OR
Summary (95% CI)	263	838	1.33(0.98,1.75)
Heterogeneity test	Chi2=5.17	Df=3(*P*=0.42)	I2=11%
Total effect test	Z=22.41(*P*<0.001)		
APACHE II Score			
	D	S	OR
Summary (95% CI)	435	1412	2.24(1.58,2.97)
Heterogeneity test	Chi2=5.12	Df=5(*P*=0.28)	I2=8%
Total effect test	Z=10.89(*P*<0.001)		
NEWS Score			
	D	S	OR
Summary (95% CI)	410	2347	1.64(1.45,1.85)
Heterogeneity test	Chi2=4.39	Df=4(*P*=0.36)	I2=9%
Total effect test	Z=24.91(*P*<0.001)		



Note: "L" refers to "Literature".

Fig. 3: Meta-Analysis Results

Comparative Analysis of the Value of Three Scoring Indicators for IPMRP

Comparing the sensitivity, specificity, and AUC of the three diagnostic indicators, the results are shown in Table 3. The SOFA score had the highest AUC, which was $P<0.001$ compared to the NEWS score. At the same time, the APACHE II score has the highest AUC compared to the

NEWS score, which is $P<0.05$. However, there was no significant difference between the AUC and APACHE II scores of SOFA scores.

Table 3: Comparison of three diagnostic indicators

Scoring tool	SOFA score	APACHE II score	NEWS score
Sensitivity (%)	72.6±0.17	80.5±5.05	64.8±3.37
Specificity (%)	88.4±0.26	74.2±3.01	77.5±4.26
Positive predictive value (%)	91.0±1.32	78.6±3.62	81.2±2.43
Negative predictive value (%)	70.3±1.51	75.2±3.84	61.4±4.58
Positive likelihood ratio	6.259±0.127	3.120±0.261	2.880±0.324
Negative likelihood ratio	0.310±0.001	0.320±0.038	0.454±0.005
Youden index	0.610±0.036	0.547±0.020	0.423±0.010
AUC	0.826±0.025*	0.815±0.053#	0.748±0.028

Note: *Indicates that the SOFA score is $P<0.001$ compared to the NEWS score; # indicates that the APACHE II score is $P<0.05$ compared to the NEWS score

Publication bias analysis

In Fig. 4, the observed funnel plot literature exhibits a symmetrical distribution, and the estimated effects and accuracy of small sample studies are relatively high, indicating that there is no publication bias in the literature included in this study.

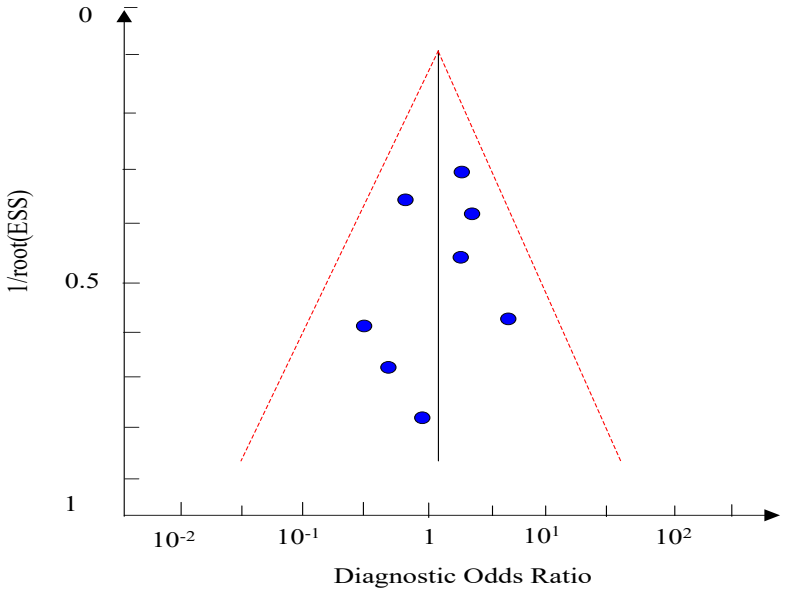


Fig. 4: Funnel diagram of literature inclusion

Discussion

Infection is an important public health issue on a global scale, which is common in medical institutions and communities, and poses a serious threat to the lives and health of patients (7). The risk assessment of death in infected patients is of great significance for determining treatment

plans, optimizing clinical management, and improving prognosis.

Infected patients refer to patients with infectious diseases caused by pathogens (such as bacteria, viruses, fungi, parasites, etc.). Infection refers to the process in which pathogens invade the body and reproduce, leading to abnormal physiological or pathological reactions (8). The risk of death for infected patients depends on various factors, including the type of infection, the severity of the infection, the patient's immune status, and the timeliness of early diagnosis and treatment. Some types of infection may lead to higher risk of death, especially serious infectious diseases such as sepsis, severe pneumonia, meningitis, etc. (9).

In addition, patients with low immune function (such as AIDS patients, organ transplant recipients, chemotherapy patients, etc.) usually face a higher risk of death. The severity of infection can also affect the risk of death, for example, patients with severe complications such as septic shock and multiple organ dysfunction syndrome (MODS) have a higher risk of death (10). Early diagnosis and timely treatment are crucial for reducing the risk of death in infected patients. Early diagnosis can help doctors take timely treatment measures to prevent infection progression and complications (11). Appropriate antibiotics, Antiviral drug or other anti-infection treatments can effectively control infection and improve the survival chances of patients.

However, the assessment and prediction of mortality risk is a complex process that requires comprehensive consideration of multiple factors. In clinical practice, assessing the risk of death in infected patients usually relies on scoring tools and indicators (12). Currently, commonly used IRCISIs include SOFA score, APACHE II score, and NEWS score (13).

The results of this study showed that SOFA score, APACHE II score and NEWS score are all of great value in predicting the risk of death in patients with infection. Lin Lan (14) pointed out in a meta-analysis that SOFA has moderate sensitivity and specificity for predicting death in patients with sepsis, the systemic inflammatory response syndrome (SIRS) score has the highest sensitivity, and NEWS has the strongest specificity for predicting death in patients with sepsis. This study and Lin Lan's meta-analysis both recognize the importance of SOFA, APACHE II and NEWS scores in predicting the risk of death in patients with infection, and show certain differences in sensitivity and specificity. The main difference is that Lin Lan emphasized the advantages of SIRS score in sensitivity and the high specificity of NEWS, while this study did not involve SIRS and focused on SOFA, APACHE II and NEWS.

Overall, the conclusions of the two are consistent, and both believe that each scoring system is helpful for clinical decision-making, but the scope of this study is wider and not limited to patients with sepsis infection. Therefore, for the common hospital infection, the results of this study have more general value.

SOFA score is a commonly used scoring tool for evaluating organ dysfunction in critically ill patients, including infected patients (15). SOFA score covers multiple Organ system, including respiratory system, circulatory system, liver function, coagulation function, kidney function, etc., which can comprehensively assess the organ function status of patients. Meanwhile, the physiological indicators used in SOFA scoring (such as arterial oxygen partial pressure, platelet count, creatinine level, etc.) are usually routine clinical monitoring items, easy to obtain and calculate, and have high practicality. This meta-analysis included three studies in the morning that mentioned SOFA scores. According to the analysis results, the summarized number of D patients is 263, and the number of S patients is 838. The calculated risk of death (OR) is 1.33, and the 95% confidence interval is (0.98, 1.75). Heterogeneity testing shows that, $\chi 2=5.17$, degree of freedom (DF)=3, $P= 0.42$, $I^2=11\%$. The Z-value of the total effect test is 22.41, $P<0.001$, indicating that compared to infected patient D, S's SOFA score is lower than D. The use of SOFA score for IPMRP has significant value.

The APACHE II score covers multiple physiological parameters, including age, chronic disease status, physiological indicators (such as heart rate,

body temperature, arterial oxygen partial pressure, etc.), and can comprehensively evaluate the patient's condition and organ functional status (16). The APACHE II scoring system has strict scoring standards and unified calculation methods, making comparisons and data analysis between different medical institutions and clinical studies more reliable and feasible. In addition, the APACHE II scoring system clarifies the scoring items and calculation methods, allowing for high consistency and repeatability in the scoring results between different doctors and the same doctor at different times. This meta-analysis included a total of 5 studies that mentioned the APACHE II score. The number of D patients was 435, the number of S patients was 1412, the OR was 2.24, and the 95% confidence interval was (1.58, 2.97). The heterogeneity test results show that, $\chi 2=5.12$, DF=5, p=0.28, $I^2=8\%$, Z=10.89, $P<0.001$. This indicates that compared to the death group of infected patients, the APACHE II score in the survival group is lower, and using the APACHE II score for IPMRP is valuable.

The NEWS scoring system adopts a simple scoring system that includes common physiological indicators such as respiratory rate, blood pressure, body temperature, etc. It is easy to understand and use, and is suitable for various medical environments and clinical staff (17). The NEWS score has been widely applied and recommended by multiple guidelines and institutions as a basis for evaluating changes in patient conditions and triggering emergency interventions, with good practicality and operability. There are a total of 4 studies on the NEWS score in this meta-analysis, among which there are 410 patients with D and 2347 patients with S, with OR=1.64 and a 95% confidence interval of (1.45, 1.85). $\chi 2=4.39$, DF=4, $P=0.36$, $I^2=9\%$, Z=24.91, $P<0.001$. The data indicates that compared to infected patients with D, S has a lower NEWS score, and using the NEWS score for IPMRP is valuable.

In terms of the comparison of the three scoring methods, in this study, the SOFA score had the highest positive likelihood ratio (6.259) and the lowest negative likelihood ratio (0.310), while the APACHE II score and NEWS score performed relatively low on these two indicators. In addition, SOFA score has the highest Youden's J statistic (0.610) and AUC value (0.826), APACHE II score is the last of these two indicators, while NEWS score is lower. The AUC of SOFA score is the highest, and $P<0.001$ compared to NEWS score; The AUC of APACHE II score compared to NEWS score was $P<0.05$; There is no significant difference between the AUC and APACHE II scores of SOFA scores.

The SOFA score showed high sensitivity, specificity, positive predictive value, and negative predictive value in this study. High sensitivity means that the SOFA score can accurately identify the proportion of patients with severe infections, while high specificity means that patients with non-severe infections can be excluded (18). At the same time, the SOFA score has high positive and negative predictive values, which means that when the score result is positive or negative, the accuracy of predicting the actual situation of the patient is higher. SOFA score is an index to comprehensively evaluate the functions of multiple Organ system, including respiratory system, circulatory system, liver function, blood coagulation function, kidney function, etc. In contrast, the APACHE II score and NEWS score have less consideration for multiple organ function (19). The SOFA score can provide a more comprehensive assessment of the patient's organ function status and provide a more comprehensive assessment of the condition. Meanwhile, SOFA scores can be continuously monitored and evaluated based on the patient's condition at different time points after admission (20). It can reflect the dynamic changes in the condition of infected patients, providing more accurate prediction and monitoring capabilities. In contrast, APACHE II and NEWS scores are more commonly used for evaluation at admission or specific time points, and cannot provide continuous monitoring and dynamic evaluation. In addition, SOFA scoring is relatively simple, just measure and record the indicators of different Organ system of patients, and then calculate the scoring (21). Compared with APACHE II and NEWS

scores, SOFA scores are more convenient to operate and calculate, reducing the complexity of measurement and calculation, and reducing usage costs and workload.

These findings have significant implications for clinical doctors and medical teams in the treatment and management of infected patients. Accurately assessing the condition of infected patients and predicting their risk of death can help doctors develop more reasonable treatment plans, provide more accurate monitoring and care, and thus improve the prognosis and survival rate of patients. Especially the SOFA score shows higher reliability and accuracy in this regard, so it should be valued and applied in clinical practice. However, there are also some limitations to this study. Firstly, the number of included literatures is limited, and there may be potential publication bias and preference. Secondly, there is a certain degree of heterogeneity in the research, which may affect the stability and generalization of the results. Therefore, further large-scale, multicenter studies are still needed to validate and strengthen the conclusions of this study.

Conclusion

This article focuses on evaluating the value of SOFA score, APACHE II score, and NEWS score in IPMRP through a comparative meta-analysis of IRCISI. The SOFA score shows high accuracy and predictive value in predicting the condition and risk of death of infected patients. In contrast, the APACHE II score and NEWS score also have certain predictive ability, but their predictive effect is slightly inferior to the SOFA score. The results of this study provide an important reference basis for IPMRP, emphasizing the importance of SOFA scoring in this field. This has guiding significance for improving the treatment and management of infected patients, and provides direction for further research and clinical practice. It is hoped that these results can provide useful references for the medical community and clinical practitioners, thereby improving the prognosis and survival rate of infected patients and contributing to their health and well-being.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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