

Meta-analysis of the diagnostic value of procalcitonin in adult burn sepsis

Zhao Chen^{1,A–C,E}, Nurlan Turxun^{1,B–D}, Fangyan Ning^{2,A,E,F}

¹ Department of Burns, People's Hospital of Xinjiang Uygur Autonomous Region, China

² Intensive Care Unit, People's Hospital of Xinjiang, Uygur Autonomous Region, China

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;

D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online)

Adv Clin Exp Med. 2021;30(4):455–463

Address for correspondence

Zhao Chen

E-mail: mn35241@126.com

Funding sources

None declared

Conflict of interest

None declared

Received on June 2, 2020

Reviewed on September 1, 2020

Accepted on December 17, 2020

Published online on April 28, 2021

Abstract

Sepsis is one of the main causes of death in burn patients, and many studies have suggested that procalcitonin (PCT) is a biomarker for the early diagnosis of sepsis, but the results are controversial. The aim of this study was to evaluate the diagnostic value of serum PCT in adult burn sepsis by conducting a meta-analysis of published studies. The PubMed, Embase, Web of Science, CNKI and China Wanfang databases were searched, and studies on PCT as a marker for the diagnosis of adult burn sepsis from the establishment of the database, to February 1, 2020 were screened. The data were analyzed using Stata v. 15.0 software. A total of 10 studies and 704 patients were included. The combined sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR) and diagnostic odds ratio (DOR) were 0.67 (95% CI: 0.48–0.81), 0.87 (95% CI: 0.72–0.95), 5.20 (95% CI: 2.49–10.84), 0.38 (95% CI: 0.24–0.61) and 13.70 (95% CI: 5.72–32.82), respectively. The area under the summary receiver operating characteristic curve (SROC) was 0.85 (95% CI: 0.82–0.88), and the diagnostic threshold was the main source of heterogeneity. Results demonstrate that serum PCT may be used as a useful biomarker for the early diagnosis of burn sepsis in adults, and may be combined with other diagnostic indexes to further improve the sensitivity and specificity.

Key words: sepsis, burn, procalcitonin, meta-analysis

Cite as

Chen Z, Turxun N, Ning F. Meta-analysis of the diagnostic value of procalcitonin in adult burn sepsis. *Adv Clin Exp Med.* 2021;30(4):455–463. doi:10.17219/acem/131755

DOI

10.17219/acem/131755

Copyright

Copyright by Author(s)

This is an article distributed under the terms of the Creative Commons Attribution 3.0 Unported (CC BY 3.0) (<https://creativecommons.org/licenses/by/3.0/>)

Background

Burns are common injuries in life and war. Although there are many strategies for the prevention and treatment of infection in burns, burn sepsis is still one of the common causes of death in patients with severe burns.¹ Burns, especially severe burns, can lead to extensive damage to the skin tissue, the body's first defense barrier, resulting in serious damage to the body's internal homeostasis, a decrease in immunity, and a large volume of necrotic wound tissue. These changes provide good conditions for the growth and reproduction of bacteria. Therefore, infection in patients with severe burns is difficult to avoid.^{2,3} Septic shock and multiple organ failure can develop rapidly from burn sepsis, which can lead to death.⁴ Therefore, early detection of high-risk groups prone to burn sepsis, early diagnosis, and prediction of the prognosis of burn sepsis are key to reducing the mortality of patients with this condition. Bacterial blood culture is an important aspect of clinical etiological detection and diagnosis of burn sepsis, however blood culture does not enable a rapid diagnosis of burn sepsis, as it may take 3 days or more to produce a result. The use of prophylactic antibiotics in severe burn patients leads to a low positive rate of blood culture, which leads to a delay in the diagnosis of burn sepsis and an increase in antibiotic resistance.⁵ Patients with severe burns often have similar symptoms to infection, such as increased respiratory rate, increased heart rate, and an obvious increase of white blood cells. The commonly used clinical indicators such as blood pressure, heart rate, respiratory rate, white blood cells, neutrophils, liver, and kidney function have low specificity and sensitivity in the diagnosis of burn sepsis, and these indexes cannot accurately estimate the prognosis of burn sepsis patients. Therefore, it is necessary to identify a rapidly detectable indicator, with high specificity and sensitivity, to enable the early prediction, diagnosis, and prognosis of burn sepsis. Such an indicator would facilitate timely treatment measures, guide the use of antibiotics, and increase the survival rate of patients with burn sepsis.

In recent years, various studies have shown that serum procalcitonin (PCT) plays an important role in the diagnosis of sepsis.^{6,7} Serum PCT is a non-hormone active glycoprotein composed of 116 amino acids, which is a propeptide of calcitonin (CT).⁸ The content of serum PCT in the blood of healthy people is very low, generally less than 0.1 ng/mL.⁹ It has been shown that the release of serum PCT is closely related to the release of endotoxins and inflammatory mediators.¹⁰ Serum PCT level has been demonstrated to be increased in differing degrees of bacterial and fungal infections, burns, trauma, surgery, and other conditions, but the increase in patients with systemic bacterial infection was the most significant.^{11,12} The level of serum PCT in patients with systemic bacterial infection increased rapidly in 6–8 h and reached a peak at about

24 h. The level of serum PCT can change from low to high with severity of infection, i.e., local infection, sepsis, severe sepsis, septic shock. The level of serum PCT can always be at a high level or can increase continuously with persistent infection or aggravation of infection, so there is a significant correlation between serum PCT level and the severity of infection.¹¹

Objectives

At present, there is still a debate regarding the significance of PCT in burn sepsis, so this study uses the method of meta-analysis to comprehensively analyze the relationship between serum PCT level and the diagnosis of sepsis in adult burn patients, to provide medical evidence for its diagnostic value.

Materials and methods

Literature search

PubMed, Embase, Web of Science, CNKI, China Wanfang, and other databases were searched for literature related to PCT and burn sepsis, published from the establishment of each database, to February 1, 2020. The key words used were: PCT, sepsis, burn, diagnosis. The search language was limited to Chinese and English. A detailed study flow chart is shown in Fig. 1, as per PRISMA guidelines.

Inclusion and exclusion criteria

Inclusion criteria: 1) the purpose of the study was to evaluate and explore the value of PCT in the diagnosis of sepsis in burn patients over 18 years old; 2) they can directly obtain four-grid data or provide sufficient information to construct four-grid data; 3) sepsis was diagnosed using accurate definition criteria: according to the American Society of Chest Physicians (ACCP)/Society of Critical Care Medicine (SCCM) meeting definition or the American Burn Association (ABA) meeting definition; 4) there were comparative data on clinical diagnosis and blood culture results. The literature was screened independently by 2 researchers according to the inclusion criteria, and the data were extracted according to a designed data extraction table. Finally, the data extraction was cross-compared, and if any differences were solved through discussion and negotiation.

Exclusion criteria: 1) poor experimental design or implementation of the study, unable to extract accurate data to construct a 2 × 2 four-grid table; 2) the subjects included children; 3) the Quality Assessment Of Diagnostic Accuracy Studies (QUADAS) score was less than 10.



PRISMA 2009 Flow Diagram

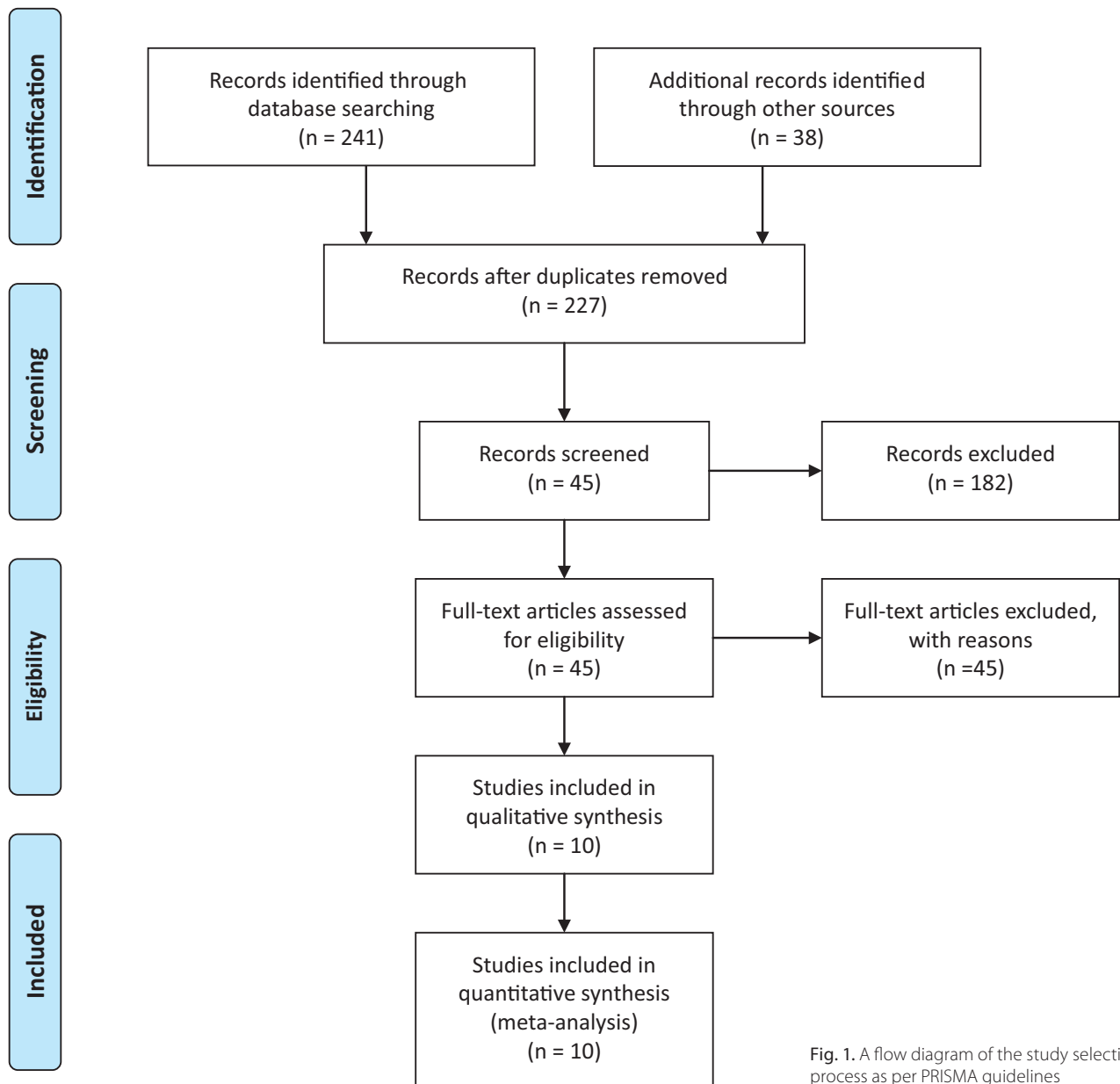


Fig. 1. A flow diagram of the study selection process as per PRISMA guidelines

Data extraction

Literature extraction: first author, publication time, country, experimental design, sample number of patients, age, burn area, critical value of PCT, sensitivity/specificity, and other indicators for the diagnosis of burn sepsis were extracted. When we observed a significant difference between the data reported in the study and the calculated data, we contacted the first or last author of the individual study by email to request clarification of the original data for the patient group.

Document quality evaluation

The QUADAS tool¹³ was used for quality assessment, which included 14 items covering multiple dimensions of research quality. The QUADAS score was the sum of the 14 items. The scores for each item were discussed by two researchers. The highest available QUADAS score was 14, and to ensure the quality of the study, all included projects scored greater than 70% of the maximum QUADAS score (QUADAS score ≥ 10).

Statistical analyses

Stata v. 15.0 software was used to analyze the data. Cochran Q and Higgins' I^2 statistics were used to test the heterogeneity between the studies. The diagnostic threshold effect was evaluated by the receiver operating curve (ROC) and the Spearman's correlation coefficient was used to determine sensitivity and specificity. The typical shoulder-arm representation in ROC space and a strong positive correlation between the logarithm of sensitivity and the logarithm of 1-specificity were used to indicate the existence of the threshold effect. The bivariate mixed-effect regression model was used, combined with 95% confidence interval (CI), to calculate the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR) and diagnostic odds ratio (DOR) aggregate statistics, and to draw the corresponding forest plot. Deeks' test was used to detect publication bias, and finally; sensitivity analysis was carried out. The area under the summary receiver operating curve (SROC), (AUC) was obtained. The AUC value varies from 0.5 to 1.0, with a value close to 0.5 indicating poor diagnostic performance, and AUC value close to 1.0 indicating good diagnostic performance. Where there was heterogeneity, meta-regression was used to analyze the source.

Results

Literature retrieval and quality evaluation

When retrieving statistics related to vital signs and blood samples collected at a specific time point, according to the diagnostic criteria of sepsis, each time point was defined as either sepsis or non-sepsis, and divided into a sepsis group and non-sepsis group accordingly. Initially, 227 articles were retrieved through keywords and all titles and abstracts were reviewed, resulting in exclusion of 182 articles. Full text and data integrity were then reviewed,

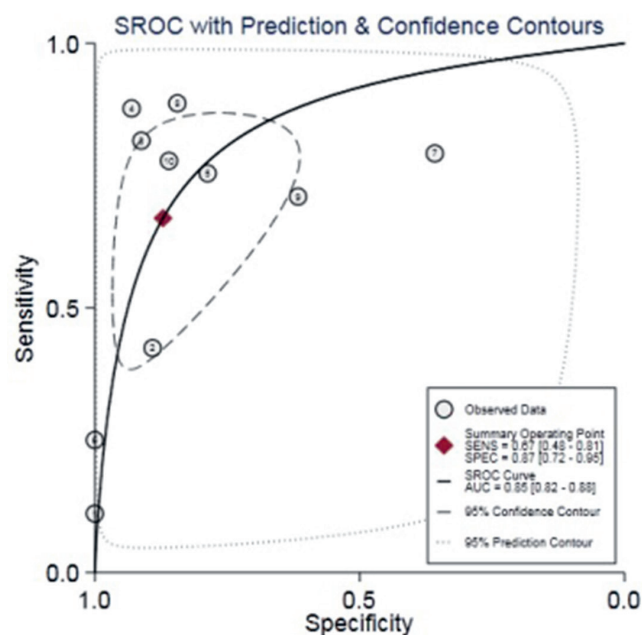


Fig. 2. SROC curve for the accuracy of PCT in the diagnosis of adult burn sepsis

and a further 35 were excluded. Finally, 10 studies met all the inclusion criteria^{14–23}, with a total of 704 patients, and 6062 time points. The information on the screening flow chart is shown in Fig. 1, which was prepared as per PRISMA guidelines.²⁴ The basic characteristics and quality score of the included literature are shown in Table 1.

The results of diagnostic accuracy analysis showed that significant heterogeneity was observed in the studies of sensitivity ($p = 0.00$, $I^2 = 93.40$), specificity ($p = 0.00$, $I^2 = 98.66\%$), PLR ($p = 0.00$, $I^2 = 97.13\%$), and DOR ($p = 0.00$, $I^2 = 100.0\%$). There was no obvious threshold effect in the current meta-analysis because the ROC curve was not a typical “shoulder-arm” pattern (Fig. 2). The Spearman correlation coefficient between the logarithm of sensitivity and the logarithm of 1-specificity was -0.2857 , and the difference was not statistically significant. Overall, the diagnostic accuracy

Table 1. Characters of included studies

First author	Year	Country	Design	PCT cut-off	Age [years]	TBSA [%] burned	Time points	Sample size	TP	FP	FN	TN	QUADAS score
Heimburg et al. ¹⁵	1998	Germany	PS	3	37.3 (18–65)	51 (20–91)	27	27	2	0	16	9	10
Bargues et al. ¹⁴	2007	France	PS	0.534	40 ± 14	40 ± 17	359	25	39	29	53	237	11
Lavrentieva et al. ¹⁶	2007	Greece	PS	1.5	45.6 ± 20.1	41.4 ± 22	934	43	93	72	21	748	13
Lavrentieva et al. ¹⁷	2012	Greece	PS	1.5	48.2 ± 18.3	38.8 ± 18	145	145	64	5	9	67	13
Cakir et al. ¹⁸	2013	Turkey	PS	0.759	40 ± 17	36.1 ± 23.4	611	37	181	79	59	292	11
Seoane et al. ²⁰	2014	Spain	RS	1.7	52.5 ± 17.2	37.6 ± 22.9	34	34	4	0	12	18	10
Paratz et al. ¹⁹	2014	Australia	PS	1.4	40.16 (18–60)	40.1 ± 16.0	344	54	38	190	10	106	11
Mokline et al. ²¹	2015	Tunisia	PS	0.69	37 ± 17	23 ± 17	121	121	39	12	5	65	11
Cabral et al. ²²	2017	Portugal	RS	0.5	40.8 ± 79.0	16.0–38.8	3419	150	463	1062	189	1705	12
Zhou M et al. ²³	2020	China	PS	4.05	30.93–54.31	40.6–53.7	68	68	14	7	4	43	10

TP – true positive; FP – false positive; FN – false negative; TN – true negative; QUADAS – Quality Assessment Of Diagnostic Accuracy Studies; PS – prospective; RS – retrospective; TBSA – total body surface area; PCT – procalcitonin.

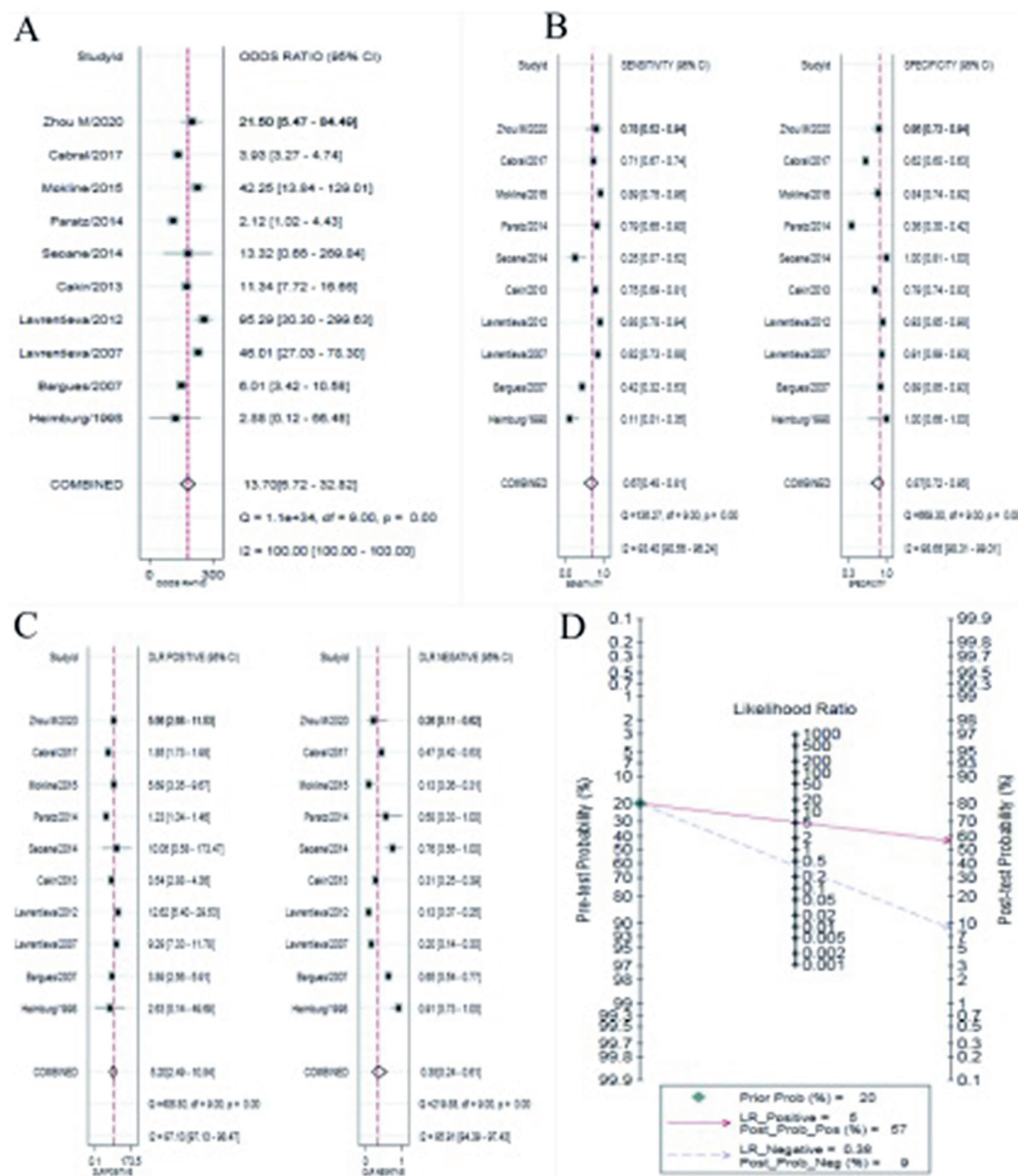


Fig. 3. Forest plot of PCT in the diagnosis of adult burn sepsis

A – DOR; B – sensitivity and specificity; C – PLR and NLR; D – Fagan's nomogram.

of PCT in adult burn sepsis was: combined sensitivity = 0.67 (95% CI: 0.48–0.81), combined specificity = 0.87 (95% CI: 0.72–0.95), PLR = 5.20 (95% CI: 2.49–10.84), NLR = 0.38 (95% CI: 0.24–0.61), DOR = 13.70 (95% CI: 5.72–32.82). The forest plot of DOR is shown in Fig. 3A, the sensitivity and

specificity of the forest plot are shown in Fig. 3B, and the forest plot of PLR and NLR are shown in Fig. 3C. The SROC is shown in Fig. 2 (AUC = 0.85, 95% CI: 0.82–0.88). Fagan's nomogram result showed that when the pre-test probability ratio was 20%, the post-test probability of PLR was 57% and

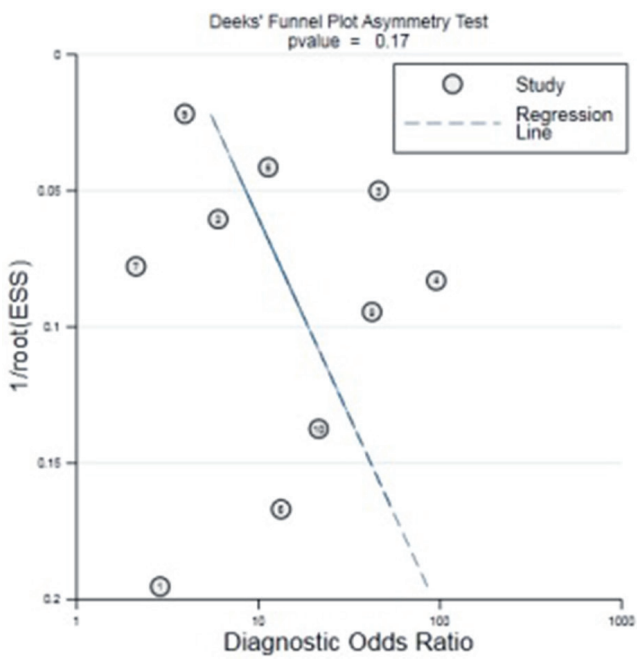


Fig. 4. Funnel plot of PCT in the diagnosis of adult burn sepsis

the post-test probability of NLR was 9% (Fig. 3D). This shows that PCT has a good diagnostic performance for adult burn sepsis. The Deeks' funnel plot in Fig. 4 shows that the p-value was 0.61, which can be considered as a lack of publication bias. The results of the meta-regression analysis are shown in Table 2, which shows that the ethnicity of the study population and experimental design did not affect the source of heterogeneity, and the diagnostic threshold was the main source of heterogeneity.

Sensitivity analysis

The result of the sensitivity analysis is shown in Fig. 5. Goodness-of-fit and bivariate normal analysis (Fig. 5A,B) show that the bivariate mixed-effect model was robust for meta-analysis. Also, through sensitivity analysis (Fig. 5C) and outlier detection (Fig. 5D), a study that deviated from the others was identified, that may affect the robustness of meta-analysis. After excluding this study, in the overall analysis with or without outliers, there was no significant change in sensitivity (0.67 vs 0.73), specificity (0.87 vs 0.84), PLR (5.20 vs 4.60), NLR (0.38 vs 0.32), DOR (13.70 vs 14.00) and AUC (0.85 vs 0.85), indicating that the meta-analysis of diagnostic value in this study was robust.

Discussion

Burns are tissue injuries caused by thermal, chemical, electrical, or radiation factors, which can damage the physiological barriers of the body surface of burn patients. When an extensive area of this physiological barrier is destroyed, the resulting large wound becomes a suitable medium for the growth of bacteria, and as the body surface has the temperature and humidity suitable for the reproduction and growth of bacteria, the proliferation of bacteria is promoted within the wound. The immune function of the patient after burns is impaired and maladjusted, and the anti-infection ability of the whole body is low. Therefore, burn patients have a higher incidence of sepsis. Severe sepsis and septic shock are common causes of death in burn patients, accounting for 30% of hospital mortality.²⁵

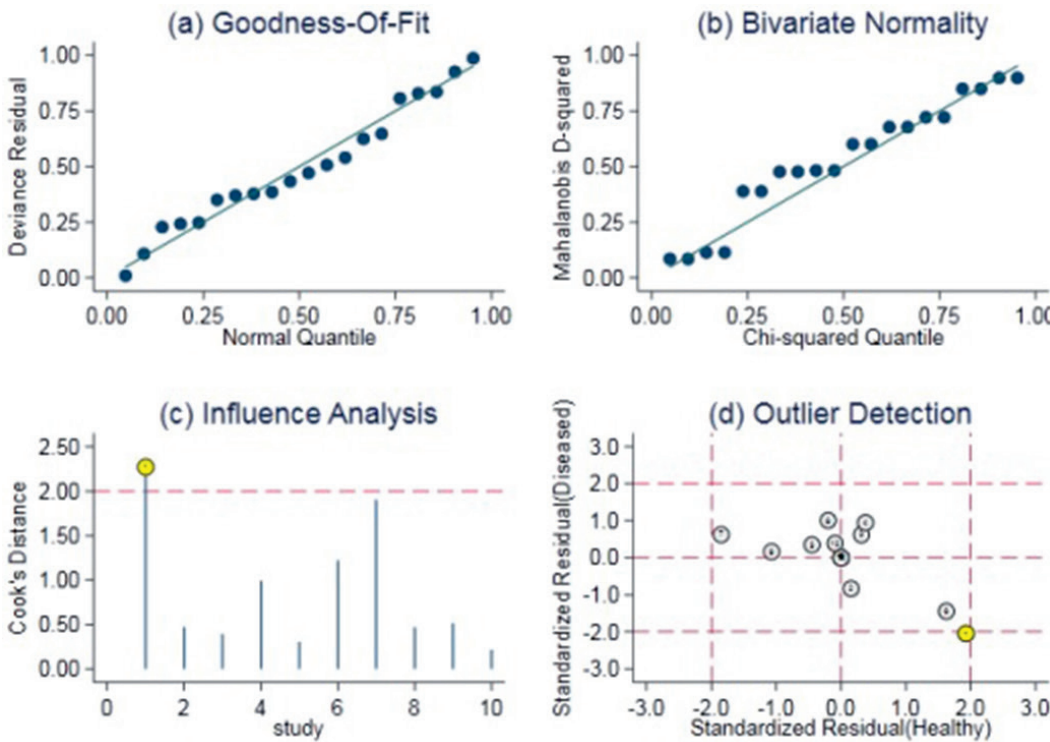


Fig. 5. The results of sensitivity analysis

Table 2. Results of meta-regression analysis

Parameter	Category	Studies	Sen (95% CI)	p-value for Sen	Spe (95% CI)	p-value for Spe
Ethnicity	Non-Caucasian	2	0.85 (0.64–1.00)	0.22	0.86 (0.62–1.00)	0.94
	Caucasian	8	0.62 (0.43–0.81)		0.88 (0.76–0.99)	
Design	RS	2	0.48 (0.07–0.89)	0.29	0.88 (0.65–1.00)	0.65
	PS	8	0.71 (0.55–0.88)		0.87 (0.75–0.98)	
PCT cut-off	>1.5 ng/mL	3	0.35 (0.09–0.62)	0.02	0.97 (0.90–1.00)	0.04
	≤1.5 ng/mL	7	0.77 (0.65–0.89)		0.80 (0.67–0.93)	

Sen – sensitivity; Spe – specificity; PS – prospective; RS – retrospective; PCT – procalcitonin.

Although interventions for the treatment of sepsis have been improving, such as anti-infective treatment and efforts to follow the development of supportive methods such as immunotherapy from the surviving sepsis guidelines, prognosis remains not optimistic for patients with sepsis.²⁶ Burn sepsis is a severe systemic inflammatory response syndrome (SIRS) reaction caused by a bacterial infection, which occurs and develops rapidly. When the course of burn sepsis progresses to septic shock or multiple organ dysfunction syndrome (MODS), there are no clear, effective, and specific treatment measures, and this condition carries a poor prognosis and high mortality. Early diagnosis of sepsis and appropriate treatment can reduce the mortality of burn sepsis.²⁷ Therefore, the early diagnosis of sepsis in burn patients becomes particularly critical, and there is an urgent need for more effective markers for early diagnosis. Mann et al.²⁸ in 2011 and Ren et al.²⁹ in 2015 systematically reviewed the relationship of PCT and the diagnostic value of burn sepsis, until then there was little systematic analysis on the topic. Therefore, we carried out a meta-analysis to comprehensively evaluate the diagnostic value of PCT in adult burn sepsis.

The date of literature retrieval included in this study was from the establishment of each relevant database to February 1, 2020. A total of 10 studies, 704 patients, and 6062 time points were included. There were strict inclusion and exclusion criteria for the included literature. To ensure the quality of the literature, each paper was scored by QUADAS, and studies with a score of less than 10 were not included. In the data collection, we carefully read the original literature, and through the sensitivity and specificity reported in the original literature, and other values, obtained four-grid table data. In this process, we found that some of the study designs were not rigorous enough to extract accurate data from the original data, and such papers were also excluded. To more accurately evaluate the role of PCT in the diagnosis of adult burn sepsis, this study also imposed a strict age limit, with all subjects being over 18 years old, which reduced the heterogeneity to some extent. Besides patient age, there are many

factors that may affect the heterogeneity of the diagnostic value of PCT, such as detection method, burn severity etc. Therefore, this study conducted a meta-analysis including ethnicity of the study, experimental design and diagnostic threshold to analyze the source of heterogeneity. The results of this study showed that the AUC was 0.85, and combined sensitivity and specificity of SROC were 0.67 and 0.87 respectively. In terms of sensitivity, the ability of serum PCT to detect sepsis in adult burn patients was weaker, and the ability to detect non-sepsis in adult burn patients was stronger. The PLR was 5.20 and the NLR was 0.38. Where the likelihood ratio is more than 1, it means that the result of the diagnostic test is related to the disease; and where the likelihood ratio is less than 1, it means that the result of the diagnostic test is not related to the disease. In our results, the PLR was 5.20, which means that sepsis patients with positive diagnostic tests were 5.20 times more likely to develop sepsis than non-sepsis patients with positive diagnostic tests. The results of the likelihood ratio showed that serum PCT could be used to distinguish adult burn patients with sepsis from those without sepsis. DOR combines the results of sensitivity and specificity, which is an ideal independent index. When the lower limit of 95% CI of its value is more than 1, the difference is considered statistically significant, and the larger the value is, the more obvious the diagnostic effect is. In our study, DOR = 13.70 (95% CI: 5.72–32.82), therefore this showed that serum PCT had good accuracy in the diagnosis of adult burn sepsis. The analysis of publication bias showed that there was no obvious publication bias in this study. The results of the sensitivity analysis showed that the results of this study were robust.

The diagnostic criteria of sepsis are defined by the ACCP/SCCM, but in patients with burn sepsis, there is a higher incidence of local bacterial colonization and more obvious SIRS, which will affect the diagnosis of burn sepsis. The ABA meeting in 2007 proposed new diagnostic criteria for SIRS and sepsis in burn patients, which were more suitable for this group of patients.^{29,30} Meta-regression analysis showed that the main source

of heterogeneity may be the threshold of PCT, and was not related to race or experimental design. The criteria of Bargues et al.¹⁴ for the diagnosis of sepsis were based on the ACCP/SCCM consensus, in which the proportion of respiratory system infection and wound infection was higher, which tend to mislead or exaggerate the diagnosis of sepsis, combined with the relatively conservative diagnostic threshold of 0.534 ng/mL. There was reason to suspect that the subjects were patients with mild to moderate infection rather than severe burns, so it was recommended to adopt the ABA sepsis criteria in future studies to avoid exaggerating the diagnosis of sepsis.

The results of this study suggest that PCT may not be the most ideal biomarker for early diagnosis of burn sepsis in adult patients. In fact, an ideal biomarker may not exist, due to the complex pathophysiological processes in sepsis that cannot be described by a single biomarker. However, it may be a useful and promising biomarker of sepsis in burn patients. In practical application, PCT may be combined with other biomarkers to aid in the early diagnosis of burn sepsis, which may achieve higher diagnostic accuracy.

Limitations

Of course, inevitably, this study had some limitations:

1. There were relatively few studies included, and only 10 articles met the criteria. We aimed to collect all studies that met the requirements, but some of them were of low quality or the data was not accurate, which were therefore excluded from our study.

2. There is a certain heterogeneity in the study. Although we have carried out meta-regression according to the diagnostic threshold, ethnicity and experimental design, and come to the conclusion that the diagnostic threshold has the greatest influence on the heterogeneity, it is still inevitable that there is still a certain heterogeneity, which may be caused by different ages or burn areas, but cannot be further stratified. As a result, it is impossible for us to conduct further research on it.


3. This study only considers published studies in Chinese and English, which may mean important data obtained from unpublished studies and studies written in other languages was excluded.

Conclusions

Procalcitonin is useful in the diagnosis of burn sepsis in adult burn patients. This index can be used in early diagnosis of adult burn sepsis. At the same time, it is necessary to combine PCT with other diagnostic indexes to further improve the diagnostic sensitivity and specificity of burn sepsis. Sepsis leads to a complex inflammatory response, and clinicians should understand the diagnostic efficiency and limitations of PCT and other inflammatory indicators.

Combination of a variety of inflammatory indicators for comprehensive evaluation is often more reliable than relying solely on one diagnostic threshold.

ORCID iDs

Zhao Chen  <https://orcid.org/0000-0003-3239-8642>
Nurlan Turxun  <https://orcid.org/0000-0003-1476-4629>
Fangyan Ning  <https://orcid.org/0000-0002-8569-8385>

References

- Nitzschke S, Offodile AC, Cauley RP, et al. Long term mortality in critically ill burn survivors. *Burns*. 2017;43(6):1155–1162. doi:10.1016/j.burns.2017.05.010
- Calvano TP, Hospenthal DR, Renz EM, Wolf SE, Murray CK. Central nervous system infections in patients with severe burns. *Burns*. 2010; 36(5):688–691. doi:10.1016/j.burns.2009.08.004
- Yoon J, Kym D, Hur J, et al. Comparative usefulness of sepsis-3, burn sepsis, and conventional sepsis criteria in patients with major burns. *Crit Care Med*. 2018;46(7):e656–e662. doi:10.1097/CCM.00000000000003144
- Belba MK, Petrela EY, Belba AG. Epidemiology and outcome analysis of sepsis and organ dysfunction/failure after burns. *Burns*. 2017; 43(6):1335–1347. doi:10.1016/j.burns.2017.02.017
- Hidalgo F, Mas D, Rubio M, Garcia-Hierro P. Infections in critically ill burn patients. *Med Intensiva*. 2016;40(3):179–185. doi:10.1016/j.medint.2016.02.001
- Rao L, Song Z, Yu X, et al. Progranulin as a novel biomarker in diagnosis of early-onset neonatal sepsis. *Cytokine*. 2020;128:155000. doi:10.1016/j.cyto.2020.155000
- Solé-Ribalta A, Bobillo-Pérez S, Valls A, et al. Diagnostic and prognostic value of procalcitonin and mid-regional pro-adrenomedullin in septic paediatric patients. *Eur J Pediatr*. 2020;179(7):1089–1096. doi:10.1007/s00431-020-03587-7
- Sakr Y, Sponholz C, Tuche F, Brunkhorst F, Reinhart K. The role of procalcitonin in febrile neutropenic patients: Review of the literature. *Infection*. 2008;36(5):396–407. doi:10.1007/s15010-008-7374-y
- Ozmen M, Oktay E, Tarhan EF, Aslan O, Oflazoglu U, Koseoglu MH. Serum procalcitonin levels in patients with ankylosing spondylitis. *Int J Rheum Dis*. 2016;19(5):500–505. doi:10.1111/1756-185X.12386
- Nakae H, Inaba H, Endo S. Usefulness of procalcitonin in Pseudomonas burn wound sepsis model. *Tohoku J Exp Med*. 1999;188(3):271–273. doi:10.1620/tjem.188.271
- Wirz Y, Meier MA, Bouadma L, et al. Effect of procalcitonin-guided antibiotic treatment on clinical outcomes in intensive care unit patients with infection and sepsis patients: A patient-level meta-analysis of randomized trials. *Crit Care*. 2018;22(1):191. doi:10.1186/s13054-018-2125-7
- Schneider HG, Lam QT. Procalcitonin for the clinical laboratory: A review. *Pathology*. 2007;39(4):383–390. doi:10.1080/00313020701444564
- Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: A tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol*. 2003;3:25. doi:10.1186/1471-2288-3-25
- Bargues L, Chancerelle Y, Catineau J, Jault P, Carsin H. Evaluation of serum procalcitonin concentration in the ICU following severe burn. *Burns*. 2007;33(7):864. doi:10.1016/j.burns.2006.10.401
- Heimburg DV, Stieghorst W, Khorram-Sefat R, Pallua N. Procalcitonin – a sepsis parameter in severe burn injuries. *Burns*. 1998;24(8):750. doi:10.1016/s0305-4179(98)00109-0
- Lavrentieva A, Kontakiotis T, Lazaridis L, et al. Inflammatory markers in patients with severe burn injury. What is the best indicator of sepsis? *Burns*. 2007;33(2):189–194. doi:10.1016/j.burns.2006.07.001
- Lavrentieva A, Papadopoulou S, Kioumis J, Kaimakamis E, Bitzani M. PCT as a diagnostic and prognostic tool in burn patients. Whether time course has a role in monitoring sepsis treatment. *Burns*. 2012; 38(3):363. doi:10.1016/j.burns.2011.08.021
- Cakir Madenci Ö, Yakupoğlu S, Benzonana N, Yücel N, Akbaba D, Orçun Kaptanağası A. Evaluation of soluble CD14 subtype (presepsin) in burn sepsis. *Burns*. 2014;40(4):664–669. doi:10.1016/j.burns.2013.08.024

19. Paratz JD, Lipman J, Boots RJ, Muller MJ, Paterson DL. A new marker of sepsis post burn injury? *Crit Care Med*. 2014;42(9):2029–2036. doi:10.1097/CCM.0000000000000400
20. Seoane L, Pérttega S, Galeiras R, Astola I, Bouza T. Procalcitonin in the burn unit and the diagnosis of infection. *Burns*. 2014;40(2):223–229. doi:10.1016/j.burns.2013.11.018
21. Mokline A, Garsallah L, Rahmani I, et al. Procalcitonin: A diagnostic and prognostic biomarker of sepsis in burned patients. *Ann Burns Fire Disasters*. 2015;28(2):116–120. PMID: 27252609
22. Cabral L, Afreixo V, Santos F, Almeida L, Paiva JA. Procalcitonin for the early diagnosis of sepsis in burn patients: A retrospective study. *Burns*. 2017;43(7):1427–1434. doi:10.1016/j.burns.2017.03.026
23. Zhou M, Wang XC, Guo L, Chen H, Huang DP, Wang LJ. Value of soluble myeloid cell trigger receptor-1, CD64 and procalcitonin in diagnosis of burn patients complicated with sepsis. *Chin J Nosocomiol*. 2020;30:216–219.
24. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed1000097
25. Levy MM, Dellinger RP, Townsend SR, et al. The Surviving Sepsis Campaign: Results of an international guideline-based performance improvement program targeting severe sepsis. *Intensive Care Med*. 2010;36(2):222–231. doi:10.1007/s00134-009-1738-3
26. Veach RA, Liu Y, Zienkiewicz J, et al. Survival, bacterial clearance and thrombocytopenia are improved in polymicrobial sepsis by targeting nuclear transport shuttles. *PLOS ONE* 2017;12:e179468. <https://doi.org/10.1371/journal.pone.0179468>
27. Wineberg D, Moore R, Kruger D. Procalcitonin and bacterial sepsis in burn patients in south africa. *J Surg Res*. 2020;246:490–498. doi:10.1016/j.jss.2019.09.040
28. Mann EA, Wood GL, Wade CE. Use of procalcitonin for the detection of sepsis in the critically ill burn patient: A systematic review of the literature. *Burns*. 2011;37(4):549–558. doi:10.1016/j.burns.2010.04.013
29. Ren H, Li Y, Han C, Hu H. Serum procalcitonin as a diagnostic biomarker for sepsis in burned patients: A meta-analysis. *Burns*. 2015;41(3):502–509. doi:10.1016/j.burns.2014.08.019
30. Vandijck DM, Brusselsaers N, Blot SI. Inflammatory markers in patients with severe burn injury: What is the best indicator of sepsis? *Burns*. 2007;33(7):940. doi:10.1016/j.burns.2007.02.003