OPEN ACCESS

ORIGINAL ARTICLE *Volume 14 (Issue 4), 2025*

PAKISTAN JOURNAL OF MEDICINE & DENTISTRY

Effectiveness of Adherence to Procalcitonin- Guided Antibiotic Protocol in Patients with Severe Sepsis

Awais Naeem[1], Aaamir Khan[1], Fahad Naim[1], Uzma Akbar[1], Muhammad Asif[1], Abdul Basi[t1]

[1]*Department of Medicine, MTI-Khyber Teaching Hospital, Peshawar.*

ABSTRACT

Background: The misuse of antibiotic therapies in hospitalized sepsis patients increases hospital length of stay and antimicrobial resistance. Procalcitonin (PCT) is a biomarker for bacterial infections that can guide doctors in their decisions about whether to continue antibiotic therapy. The study aimed to compare hospital length of stay and duration of antibiotic therapy in patients managed with PCT decision protocols against comparable patients managed with standard care without PCT.

Methods: A randomized controlled trial was conducted in the Department of Medicine, MTI/Khyber Teaching Hospital, Peshawar, over six months from 1st December 2023 to 30th June 2024. A total of 104 patients with severe sepsis were reviewed and randomized into two equal groups using a non-probability consecutive sampling technique. PCT-guided antibiotic therapy was given to Group A patients while Group B patients received standard treatment without PCT. Patients were followed to discharge. Outcomes assessed were hospital length of stay and duration of antibiotic therapy. Data was analysed using SPSS version 25, with a $p \leq 0.05$ considered statistically significant.

Results: The mean length of hospital stay was shorter in the PCT-guided group (14.2 ± 4.6 days) than the standard group (18.1 ± 5.3 days; p = 0.0001). The mean length of antibiotic therapy was also reduced in Group A (7.9 ± 2.3 days) versus Group B (11.6 ± 3.1 days; p = 0.0001).

Conclusion: PCT-guided antibiotic protocol significantly reduces antibiotic exposure in addition to hospital stay for patients who present with severe sepsis. As a result, this treatment fostered antimicrobial stewardship and positively impacted clinical outcomes

Keywords: Procalcitonin, Drug Resistance, Microbial, Length of Stay.
***Corresponding Author:** Fahad Naim,
Email: awasinaeem06@gmail.com

How to cite: Naeem A, Khan A, Naim F, Akbar U, Asif M, Basit A. Effectiveness of Adherence to Procalcitonin-Guided Antibiotic Protocol in Patients with Severe Sepsis. Pak J Med Dent. 2025 September ;14(4): A-B. Doi: https://doi.org/10.36283/ziun-pjmd14-4/059.

Received: Tue, April 22, 2025 **Accepted:** Sun, September 28, 2025**. Published:** Mon, September 29, 2025

INTRODUCTION

Sepsis is a life-threatening condition associated with a dysregulated host response to infection, leading to multi-organ dysfunction and death [1, 2]. Severe sepsis is a more serious condition, and both conditions pose a substantial burden to health systems around the world; complications arise due to high mortality rates, prolonged hospital lengths of stay, and the consumption of healthcare resources [3]. The primary therapeutic focus should be on timely and appropriate cases of antimicrobial therapy, source control, and supportive care [4]. Excessive duration and unnecessary prescription of antibiotics are important factors in exacerbating the emergence of antimicrobial-resistant pathogens, costs to healthcare systems, and the adverse effects of drugs [5].

Individually, in recent years, Procalcitonin (PCT) - a precursor of the hormone calcitonin - has been explored as a biomarker for the diagnosis, prognosis, and management of antibiotic therapy for bacterial infections, such as sepsis[6, 7]. Procalcitonin is particularly advantageous, as it rises rapidly in systemic bacterial infections, and undergoes a rapid decline when the resolution of the infection occurs (CRP takes longer to resolve) [8, 9]. Procalcitonin offers clinicians guidance in terms of real-time updates on the patient's status of infection and treatment response[10]. PCT-guided protocols have also shown promise for allowing clinicians to treat septic patients with the lowest possible duration of antibiotic therapy[11]. These examples demonstrate that PCT-guided protocols can reduce total exposure to antibiotics without compromising patient outcomes as currently measured[12].

There is growing evidence to support the role of procalcitonin (PCT) to guide antibiotic (Ab) therapy, and whether guideline adherence by providers could influence variability encountered with antibiotic stewardship based on the use of PCT guidelines[13, 14]. With clinical judgment exercised alongside no standard protocols, variations will emerge as to when and how, antibiotics are initiated and/or stopped; this variation will affect the variability of improvement that will be seen with clinical outcomes. An understanding of the clinical implications of how strict adherence to using PCT-guided protocols impacts severe sepsis will help in antibiotic stewardship and patient care improvement.

Sepsis management has historically included the overuse of antibiotics, seeking to reduce mortality rates, and can occasionally inadvertently contribute to antibiotic resistance and complications like Clostridium difficile infections[14]. Procalcitonin-guided protocols are a basis for evidence-based approaches to optimize the use of antibiotics. However, the protocols' adherence in the real world is variable and could also affect their clinical effectiveness. Exploring and analyzing patient outcomes of those in whom evidence-based guidelines have been strictly adhered to versus those in whom guidelines were not used could provide useful information on their practical application and utility

of future guidelines. The purpose of this study was to examine the effectiveness of adherence to procalcitonin-guided antibiotic (AB) protocols in severe sepsis patients.

METHODS

This randomized controlled trial took place at the Department of Medicine, Khyber Teaching Hospital, MTI, Peshawar, over six months from 1st December 2023 to 30th June 2024. Ethical approval was obtained from the Institutional Review Board (IRB) of the Khyber Teaching Hospital, Peshawar (Approval No: 733/DME/KMC; Dated:16th November 2023)

Using a non-probability consecutive sampling technique, 104 patients in total were recruited, with 52 patients assigned to each group. The sample size was calculated using the WHO sample size formula, based on the assumption that the anticipated mean hospital stays in patients receiving procalcitonin (PCT)-guided antibiotic therapy would be 16.38 ± 5.87 days, compared to 19.68 ± 6.03 days in those receiving standard non-PCT-guided antibiotic therapy. The study was powered at 80% with a 95% confidence level[15].

Patients aged 18 to 60 years of both genders who were diagnosed with severe sepsis, as defined by standard criteria, were eligible for inclusion. Patients who were immunocompromised, had received antibiotics within the preceding two weeks, or had severe cardiopulmonary compromise were excluded. After obtaining approval from the hospital's research review board, eligible patients admitted to the indoor medical wards were enrolled. Informed consent was obtained from each participant. Baseline demographic and clinical data were collected, including age, gender, BMI, education, profession, socioeconomic status, residence, and duration of illness.

Patients were randomized into two equal groups using blocked randomization. Group A received PCT-guided antibiotic therapy, while Group B received standard antibiotic treatment without PCT guidance. The PCT-guided protocol involved initiating antibiotics based on clinical judgment, followed by daily PCT measurements from days 1 to 3, and then every other day from day 4 onward. Antibiotics were discontinued when the PCT level dropped below 0.50 ng/mL or decreased to ≤10% of the peak value. Patients were followed until discharge from the hospital. The primary outcomes assessed were length of hospital stay and duration of antibiotic treatment. The length of hospital stay was defined as the total number of calendar days the patient remained admitted. The duration of antibiotic treatment was calculated by dividing the total number of doses by the number of daily doses. In cases of combination therapy, the duration of the antibiotic administered for the longest period was considered, without summing concurrently administered antibiotics.

Sepsis was diagnosed when at least two of the following criteria were met: temperature >38°C or <36°C, heart rate >90/min, respiratory rate >20/min or $PaCO_2$ <32 mm Hg, and leukocyte count >12×10⁹/L or <4×10⁹/L or >10% immature neutrophils. Severe sepsis was defined as sepsis with evidence of organ dysfunction, such as a rise in serum creatinine by >0.5 mg/dL, serum bilirubin >2 mg/dL, or altered mental status. Data were recorded on a structured proforma by the principal investigator.

Statistical analysis was conducted using IBM SPSS version 25. Continuous variables such as age, BMI, disease duration, hospital stay, and antibiotic duration were summarized using mean ± standard deviation. Categorical variables such as gender, education, occupation, socioeconomic status, and residence were expressed as frequencies and percentages. Stratification was done for potential confounders, including age, gender, BMI, education, profession, socioeconomic status, residence, disease duration, and infection source. Both groups will be compared for length of hospital stay and length of antibiotic treatment by using the Independent Sample t-test. Length of hospital stay and antibiotic treatment were stratified by age, gender, BMI, disease duration, and source of infection. Post-stratification Independent Sample t-test was applied. P value ≤0.05 will be considered statistically significant.

RESULTS

The trial had 104 patients with severe sepsis who were randomly assigned to one of two groups: Group A (PCT-guided therapy, n = 52) or Group B (Standard care, n = 52). The individuals' initial clinical and demographic traits were similar in the two groups. Patients in Group A were 45.6 ± 11.2 years old on average, whereas those in Group B were 46.3 ± 10.8 years old (p = 0.746). Similarly, there was no significant difference in the mean BMI between Group A and Group B, which was 25.4 ± 3.6 kg/m² and 25.8 ± 3.3 kg/m² (p = 0.556). Group A and Group B had similar mean durations of illness before hospitalization, with Group A's mean being 4.2 ± 0.9 days and Group B's being 4.4 ± 0.8 days (p = 0.233).

Table 1: Baseline Characteristics of Study Participants (n = 104)

Variable	Group A (PCT-guided) n=52	Group B (Standard) n=52	p-value
Age (years)	45.6 ± 11.2	46.3 ± 10.8	0.746
BMI (kg/m²)	25.4 ± 3.6	25.8 ± 3.3	0.556
Disease duration (days)	4.2 ± 0.9	4.4 ± 0.8	0.233
Gender			
Male	28 (53.8%)	30 (57.7%)	0.692
Female	24 (46.2%)	22 (42.3%)	
Literacy			
Educated	30 (57.7%)	27 (51.9%)	0.554
Uneducated	22 (42.3%)	25 (48.1%)	
Occupation			
Employed	24 (46.2%)	26 (50.0%)	0.694
Unemployed	28 (53.8%)	26 (50.0%)	
Socioeconomic Status			
Low	33 (63.5%)	31 (59.6%)	0.686
High	19 (36.5%)	21 (40.4%)	
Residence			
Urban	29 (55.8%)	28 (53.8%)	0.843
Rural	23 (44.2%)	24 (46.2%)	

The Independent Sample T-test and the Chi-square test were used, and the p-value was statistically significant if ≤0.05.

Regarding the distribution of patients by gender, Group A had 53.8% more male patients than Group B, which had 57.7% more patients (p = 0.692). With 57.7% of patients in Group A and 51.9% in Group B being educated, the groups' literacy levels were comparable (p = 0.554). Given that 50.0% of patients in Group B and 46.2% of patients in Group A were employed, there was no discernible difference in employment status (p = 0.694). In terms of socioeconomic level, 59.6% of patients in the standard therapy group came from a low-income background, whereas 63.5% of patients in the

PCT-guided group did so (p = 0.686). 55.8% of participants in Group A and 53.8% of participants in Group B reported living in an urban area (p = 0.843). traits of the two groups, suggesting that the randomization process was successful and that the groups were comparable before the intervention, **Table 1**.

Table 2: Comparison of Outcomes Between Study Groups (n=104)

Outcome	**Group A** (PCT-guided) **n=52**	**Group B** (Standard) **n=52**	**p-value**
Length of hospital stay (days)	14.2 ± 4.6	18.1 ± 5.3	0.0001
Duration of antibiotic therapy (days)	7.9 ± 2.3	11.6 ± 3.1	0.0001

An Independent Sample T-test was used, and p≤ 0.05 is considered significant.

Compared to patients in the usual therapy group, those in the PCT-guided group had noticeably better results. Group A had a significantly shorter average hospital stay (14.2 ± 4.6 days) than Group B (18.1 ± 5.3 days), and the difference was statistically significant (p = 0.0001). Similarly, the PCT-guided group's antibiotic therapy duration was shorter than that of the standard therapy group, with a mean of 7.9 ± 2.3 days compared to 11.6 ± 3.1 days (p = 0.0001). According to these results, patients with severe sepsis can successfully decrease their hospital stay and antibiotic exposure by following a procalcitonin-guided antibiotic strategy, **Table 2**.

Stratification was performed to assess whether the beneficial effects of procalcitonin-guided therapy on hospital stay and antibiotic duration were consistent across key demographic and clinical subgroups. The reduction in both outcomes remained statistically significant in all stratified categories. When stratified by age, patients aged ≤50 years in the PCT-guided group had a significantly shorter hospital stay (13.8 ± 4.2 vs. 17.3 ± 5.1 days; $p = 0.002$) and antibiotic duration (7.6 ± 2.1 vs. 10.9 ± 2.8 days; $p = 0.001$) compared to the standard group. Similar results were observed in patients >50 years, with a hospital stay of 15.1 ± 4.1 vs. 19.0 ± 5.0 days ($p = 0.001$) and antibiotic duration of 8.4 ± 2.1 vs. 12.0 ± 3.0 days ($p = 0.0001$).

Table 3: Comparison of Length of Hospital Stay and Antibiotic Duration by the Potential Confounding Variables

Variable	Category	Outcome	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value*
Age	**≤50 years**	**Hospital Stay (days)**	13.8 ± 4.2	17.3 ± 5.1	0.002
		Antibiotic Duration (days)	7.6 ± 2.1	10.9 ± 2.8	0.001
	>50 years	**Hospital Stay (days)**	15.1 ± 4.1	19.0 ± 5.0	0.001
		Antibiotic Duration (days)	8.4 ± 2.1	12.0 ± 3.0	0.0001
Gender	**Male**	**Hospital Stay**	13.9 ± 4.4	18.0 ± 5.2	0.001
		Antibiotic Duration	7.8 ± 2.4	11.4 ± 3.0	0.001
	Female	**Hospital Stay**	14.5 ± 4.5	18.3 ± 5.5	0.002
		Antibiotic Duration	8.0 ± 2.2	11.8 ± 3.2	0.001
BMI	**Normal**	**Hospital Stay**	13.6 ± 4.1	17.5 ± 4.9	0.004
		Antibiotic Duration	7.4 ± 2.0	10.8 ± 2.9	0.001
	Overweight	**Hospital Stay**	14.7 ± 4.5	18.7 ± 5.4	0.003
		Antibiotic Duration	8.1 ± 2.5	12.0 ± 3.2	0.001
Disease Duration	**≤5 days**	**Hospital Stay**	13.8 ± 4.3	17.5 ± 5.1	0.004
		Antibiotic Duration	7.6 ± 2.1	11.0 ± 3.0	0.001
	>5 days	**Hospital Stay**	15.0 ± 4.6	19.0 ± 5.3	0.002
		Antibiotic Duration	8.5 ± 2.5	12.3 ± 3.1	0.001
	Respiratory	**Hospital Stay**	14.0 ± 4.4	18.1 ± 5.1	0.002

Source of Infection		**Antibiotic Duration**	7.9 ± 2.3	11.5 ± 3.0	0.001
	Urinary Tract	**Hospital Stay**	14.5 ± 4.7	18.5 ± 5.4	0.003
		Antibiotic Duration	8.2 ± 2.4	12.0 ± 3.1	0.001
	Abdominal	**Hospital Stay**	14.8 ± 4.8	18.8 ± 5.5	0.004
		Antibiotic Duration	8.3 ± 2.2	12.1 ± 3.0	0.001

The Independent Sample T-test was used to compare Group A and Group B, and a p-value ≤ 0.05 is considered significant.

Stratification by gender showed a consistent trend. Among males, the PCT group had significantly shorter hospital stays (13.9 ± 4.4 vs. 18.0 ± 5.2 days; $p = 0.001$) and antibiotic durations (7.8 ± 2.4 vs. 11.4 ± 3.0 days; $p = 0.001$). A similar pattern was seen in females. In both normal and overweight BMI categories, the PCT-guided group experienced significantly reduced hospital stays and antibiotic durations (all $p < 0.01$). This trend persisted regardless of disease duration, with patients having both ≤5 days and >5 days of symptoms benefiting from shorter treatment durations in the PCT group. When analyzed by source of infection, the PCT-guided group consistently showed reductions in hospital stay and antibiotic duration across respiratory, urinary tract, and abdominal infections, with all comparisons reaching statistical significance ($p < 0.005$) **Table 3**.

DISCUSSION

The duration of antibiotic medication and length of hospital stay were the main outcomes of this study, which looked at the effects of adhering to a procalcitonin (PCT)-guided antibiotic strategy in a cohort of patients who had severe sepsis. The findings demonstrated that, when compared to the standard care group, patients treated with a procalcitonin-guided approach experienced significantly shorter hospital stays and shorter antibiotic durations. These findings were consistent across other stratified variables, including age, gender, BMI, education, length of illness, and source of infection, suggesting that any effects of procalcitonin-guided therapy were strong and broadly applicable.

Our findings are very comparable to those shown by other studies which assessed the effects of a PCT-guided antibiotic cessation approach in ICU patients [16, 17]. This result is in line with our finding of a 3.7-day reduction in duration of antibiotics between groups (11.6 days versus 7.9 days). Another study by Siriwardena et al. (2022) reported fewer days of antibiotic use and fewer deaths at 28 days

in patients who had procalcitonin guidance, further validating the clinical use of PCT in septic patients[18].

Several studies showed that PCT-guided protocols are associated with a reduction in antibiotic duration of about 2.4 days and a shorter hospital stay in some studies[19, 20, 21]. In our study, the hospital length of stay was 3.9 days shorter in the PCT group (14.2 vs 18.1 days), thus affirming the utility of PCT not only in optimizing antibiotic use but also in contributing to the reduction of costs and resource burden for the healthcare system.

Importantly, the consistency of our findings across subgroups adds strength to the argument for using PCT-guided algorithms in routine clinical practice. For example, both younger (≤50 years) and older (>50 years) patients showed significantly improved outcomes with PCT-guided care. Likewise, reductions were observed in patients with both short (≤5 days) and longer (>5 days) disease durations, and in all infection types (respiratory, urinary, abdominal). This aligns with the findings of several studies that reported in their multicenter trial that the benefits of PCT guidance were consistent regardless of infection source or site of care (ICU vs. general wards)[22, 23]. Another recent trial supported our findings by reporting significantly lower antibiotic duration in the PCT group, demonstrating similar effectiveness of the protocol in a non-Western population, which is particularly relevant to our setting in Pakistan[24, 25].

In terms of practical implementation, our study supports the feasibility and effectiveness of integrating a PCT-guided approach in a resource-limited tertiary care hospital. The statistical significance observed in our results ($p < 0.001$ for both primary outcomes) underscores not only clinical relevance but also the potential to enhance antibiotic stewardship programs in low- and middle-income countries (LMICs). Considering the rising threat of antimicrobial resistance (AMR) in such settings, the timely use of biomarkers like PCT could play a vital role in rationalizing antibiotic use without compromising patient outcomes.

Despite the compelling findings, our study has certain limitations. First, while randomization ensured comparable groups, it was conducted in a single center, potentially limiting generalizability. Second, we did not assess long-term outcomes such as 28-day mortality or reinfection rates, which are relevant endpoints in severe sepsis. Additionally, although PCT-guided therapy led to shorter treatment duration, the cost-effectiveness analysis of implementing serial PCT testing was beyond the scope of this study and warrants further exploration.

Overall, our findings are consistent with and reinforce previous research supporting PCT-guided antibiotic therapy as an effective, evidence-based strategy in the management of severe sepsis. The

observed reductions in both antibiotic duration and hospital stay highlight its potential to improve clinical outcomes while combating the overuse of antibiotics. These results advocate for wider adoption of PCT-guided protocols, particularly in resource-constrained healthcare systems facing increasing antimicrobial resistance.

CONCLUSION

The present study found that adherence to a procalcitonin-guided antibiotic protocol in patients with severe sepsis significantly reduced both the length of hospital stay and the duration of antibiotic therapy compared to standard care. These effects were consistent across multiple patient subgroups, reinforcing the reliability of the intervention. The findings support the clinical utility of PCT in optimizing antibiotic use, minimizing unnecessary exposure, and potentially reducing healthcare costs. Incorporating PCT-guided protocols into routine practice could be a valuable step toward improving sepsis management and combating antimicrobial resistance, particularly in resource-limited healthcare settings.

LIST OF ABBREVIATIONS

None

ACKNOWLEDGEMENT

The authors would like to thank the staff of the Department of Medicine, MTI/Khyber Teaching Hospital, Peshawar, for their support during data collection. We are also grateful to all the patients who participated in this study.

FUNDING

None

CONFLICT OF INTEREST

No conflict of interest.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Review Board (IRB) of the Khyber Teaching Hospital, Peshawar (Approval No: 733/DME/KMC; Dated:16th November 2023).

AUTHORS' CONTRIBUTIONS

All authors contributed equally as per ICMJE.

REFERENCES

1. Wang W, Liu CF. Sepsis heterogeneity. World J Pediatr. 2023 Oct;19(10):919-927. doi: 10.1007/s12519-023-00689-8. Epub 2023 Feb 3. PMID: 36735197.

2. Zhu CL, Wang Y, Liu Q, Li HR, Yu CM, Li P, Deng XM, Wang JF. Dysregulation of neutrophil death in sepsis. Front Immunol. 2022 Aug 18;13:963955. doi: 10.3389/fimmu.2022.963955. PMID: 36059483; PMCID: PMC9434116.

3. La Via L, Sangiorgio G, Stefani S, Marino A, Nunnari G, Cocuzza S, La Mantia I, Cacopardo B, Stracquadanio S, Spampinato S, Lavalle S, Maniaci A. The Global Burden of Sepsis and Septic Shock. Epidemiologia (Basel). 2024 Jul 25;5(3):456-478. doi: 10.3390/epidemiologia5030032. PMID: 39189251; PMCID: PMC11348270.

4. De Waele JJ. Importance of timely and adequate source control in sepsis and septic shock. J Intensive Med. 2024 Feb 27;4(3):281-286. doi: 10.1016/j.jointm.2024.01.002. PMID: 39035625; PMCID: PMC11258501.

5. Ahmed SK, Hussein S, Qurbani K, Ibrahim RH, Fareeq A, Mahmood KA, Mohamed MG. Antimicrobial resistance: Impacts, challenges, and future prospects. Journal of Medicine, Surgery, and Public Health. 2024 Apr 1;2:100081, https://doi.org/10.1016/j.glmedi.2024.100081.

6. Xu HG, Tian M, Pan SY. Clinical utility of procalcitonin and its association with pathogenic microorganisms. Crit Rev Clin Lab Sci. 2022 Mar;59(2):93-111. doi: 10.1080/10408363.2021.1988047. Epub 2021 Oct 18. PMID: 34663176.

7. Biswas S, Rani F, Haque S, Suman D, Dixit RK, Biswas S. Procalcitonin: A revolutionary biomarker in the diagnosis and management of infections. Int J Life Sci Biotechnol Pharm Res. 2025 Feb;14(2):93. doi:10.69605/ijlbpr_14.2.2025.93.

8. Gornik I, Lapić I, Franić H, Radulović B, Miklić L, Rogić D. Unnecessary repetitions of C-reactive protein and leukocyte count at the emergency department observation unit contribute to higher hospital admission rates. Diagnosis (Berl). 2024 Sep 17;12(1):108-114. doi: 10.1515/dx-2024-0139. PMID: 39279324.

9. Llor C. C-reactive protein point-of-care testing to guide antibiotic prescribing for respiratory tract infections. Expert Rev Respir Med. 2025 Aug;19(8):863-877. doi: 10.1080/17476348.2025.2510378. Epub 2025 May 23. PMID: 40401764.

10. Perrella A, Giuliani A, De Palma M, Castriconi M, Molino C, Vennarecci G, Antropoli C, Esposito C, Calise F, Frangiosa A; Infection in Surgery Study Group AORN A. Cardarelli. C-reactive protein but not procalcitonin may predict antibiotic response and outcome in infections following major abdominal surgery. Updates Surg. 2022 Apr;74(2):765-771. doi: 10.1007/s13304-021-01172-7. Epub 2021 Oct 26. PMID: 34699035; PMCID: PMC8546392.

11. Essmann L, Wirz Y, Gregoriano C, Schuetz P. One biomarker does not fit all: tailoring anti-infective therapy through utilization of procalcitonin and other specific biomarkers. Expert Rev Mol Diagn. 2023 Jul-Dec;23(9):739-752. doi: 10.1080/14737159.2023.2242782. Epub 2023 Jul 31. PMID: 37505928.

12. Schuetz P. How to best use procalcitonin to diagnose infections and manage antibiotic treatment. Clin Chem Lab Med. 2022 Nov 2;61(5):822-828. doi: 10.1515/cclm-2022-1072. PMID: 36317790.

13. Papp M, Kiss N, Baka M, Trásy D, Zubek L, Fehérvári P, Harnos A, Turan C, Hegyi P, Molnár Z. Procalcitonin-guided antibiotic therapy may shorten length of treatment and may improve survival-a systematic review and meta-analysis. Crit Care. 2023 Oct 13;27(1):394. doi: 10.1186/s13054-023-04677-2. PMID: 37833778; PMCID: PMC10576288.

14. Kourbeti I, Kamiliou A, Samarkos M. Antibiotic Stewardship in Surgical Departments. Antibiotics (Basel). 2024 Apr 4;13(4):329. doi: 10.3390/antibiotics13040329. PMID: 38667005; PMCID: PMC11047567.

15. Hohn A, Balfer N, Heising B, Hertel S, Wiemer JC, Hochreiter M, Schröder S. Adherence to a procalcitonin-guided antibiotic treatment protocol in patients with severe sepsis and septic shock. Ann Intensive Care. 2018 Jun 4;8(1):68. doi: 10.1186/s13613-018-0415-5. PMID: 29869120; PMCID: PMC5986690.

16. Duijkers R, Prins HJ, Kross M, Snijders D, van den Berg JWK, Werkman GM, van der Veen N, Schoorl M, Bonten MJM, van Werkhoven CH, Boersma WG. Biomarker guided antibiotic stewardship in community acquired pneumonia: A randomized controlled trial. PLoS One. 2024 Aug 20;19(8):e0307193. doi: 10.1371/journal.pone.0307193. PMID: 39163362; PMCID: PMC11335096.

17. Gutiérrez-Pizarraya A, León-García MDC, De Juan-Idígoras R, Garnacho-Montero J. Clinical impact of procalcitonin-based algorithms for duration of antibiotic treatment in critically ill adult patients with sepsis: a meta-analysis of randomized clinical trials. Expert Rev Anti Infect Ther. 2022 Jan;20(1):103-112. doi: 10.1080/14787210.2021.1932462. Epub 2021 Jun 4. PMID: 34027785.

18. Siriwardena AK, Jegatheeswaran S, Mason JM; PROCAP investigators. A procalcitonin-based algorithm to guide antibiotic use in patients with acute pancreatitis (PROCAP): a single-centre, patient-blinded, randomised controlled trial. Lancet Gastroenterol Hepatol. 2022 Oct;7(10):913-921. doi: 10.1016/S2468-1253(22)00212-6. Epub 2022 Jul 19. PMID: 35863358.

19. Siriwardena AK, Jegatheeswaran S, Mason JM; PROCAP investigators. A procalcitonin-based algorithm to guide antibiotic use in patients with acute pancreatitis (PROCAP): a single-centre, patient-blinded, randomised controlled trial. Lancet Gastroenterol Hepatol. 2022 Oct;7(10):913-921. doi: 10.1016/S2468-1253(22)00212-6. Epub 2022 Jul 19. PMID: 35863358.

20. Heilmann E, Gregoriano C, Annane D, Reinhart K, Bouadma L, Wolff M et al. Duration of antibiotic treatment using procalcitonin-guided treatment algorithms in older patients: a patient-level meta-analysis from randomized controlled trials. Age Ageing. 2021 Sep 11;50(5):1546-1556. doi: 10.1093/ageing/afab078. PMID: 33993243; PMCID: PMC8437072.

21. Heilmann E, Gregoriano C, Annane D, Reinhart K, Bouadma L, Wolff M, Chastre J, Luyt CE, Tubach F, Branche AR, Briel M. Duration of antibiotic treatment using procalcitonin-guided treatment algorithms in older patients: a patient-level meta-analysis from randomized controlled trials. Age and ageing. 2021 Sep;50(5):1546-56. doi: 10.1093/ageing/afab078. PMID: 33993243; PMCID: PMC8437072.

22. Chambliss AB, Patel K, Colón-Franco JM, Hayden J, Katz SE, Minejima E, Woodworth A. AACC Guidance Document on the Clinical Use of Procalcitonin. J Appl Lab Med. 2023 May 4;8(3):598-634. doi: 10.1093/jalm/jfad007. PMID: 37140163.

23. Park DW, Choi JY, Kim CJ, Kim JH, Kim HB, Lee DG. Implementation of Procalcitonin in Antibiotic Stewardship: Derivation of a Consensus Algorithm for Procalcitonin Use in Clinical Practice. Infect Chemother. 2022 Dec;54(4):621-636. doi: 10.3947/ic.2022.0170. PMID: 36596678; PMCID: PMC9840958.

24. 24. Gavazzi G, Drevet S, Debray M, Bosson JL, Tidadini F, Paccalin M, de Wazieres B, Celarier T, Bonnefoy M, Vitrat V. Procalcitonin to reduce exposure to antibiotics and individualise

treatment in hospitalised old patients with pneumonia: a randomised study. BMC Geriatr. 2022 Dec 14;22(1):965. doi: 10.1186/s12877-022-03658-4. Erratum in: BMC Geriatr. 2023 Mar 30;23(1):189. doi: 10.1186/s12877-023-03818-0. PMID: 36517740; PMCID: PMC9748380.

25. Elnajdy D, El-Dahiyat F. Antibiotics duration guided by biomarkers in hospitalized adult patients; a systematic review and meta-analysis. Infect Dis (Lond). 2022 Jun;54(6):387-402. doi: 10.1080/23744235.2022.2037701. Epub 2022 Feb 17. PMID: 35175169.