A Retrospective Study of Procalcitonin Utilization in Clinical Practice

Tanner Norris MD, Matthew Yurkewicz DO, Patrick Jenkins MD,
Beth Hicks MD, Dmitriy Scherbak DO

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Introduction

- Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin and is upregulated in response to products of bacterial infection (LPS and tumor necrosis factor-α) It is not affected by viral infection.[1]

- First proposed in 1993 by Assicot et al., PCT was identified as a surrogate of active bacterial infection in the context of sepsis. It was found that children with severe bacterial infections had significantly elevated PCT values which declined promptly with antibiotic therapy.

- Under normal physiological conditions the level of circulating PCT is relatively low (≤0.1 ng/mL), while an elevation in serum PCT is associated with a potential bacterial infection.[3,4]

- PCT has therefore been identified as a surrogate biomarker to differentiate bacterial infections from viral infections and noninfectious systemic inflammatory diseases.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Introduction

- PCT levels have specifically been studied as a marker for initiation, de-escalation and discontinuation of antibiotics in the settings of lower respiratory infections and septic shock.[5–9]

- A 2018 meta-analysis (>4,000 patients) on the use of PCT-guided protocol in patients with suspected or confirmed LRTI found a reduction in the duration of antibiotic use (mean duration -2.15 days) with a trend toward reduced mortality (without meeting statistical significance).[17]

- However, several studies suggest outside of study protocols PCT levels have limited impact on prescribers' behavior, and the results of previous clinical trials may not be generalizable outside of study populations.[16,29,33–36]
  - The largest study looked at 1,656 patients presenting with LRTI. Despite providing graded recommendations based on PCT values, there was **no appreciable difference** in antibiotic-days between the study group and the control.[16]

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Introduction

- One limitation of these studies is that they do not specify providers' response when receiving PCT results – whether antibiotic regimens are escalated or de-escalated with positive or negative results.

- So, the question we pose is: Do clinicians alter their antibiotic prescribing patterns based on PCT lab values in real-world practice?

- We conducted a retrospective review of data from HCA's Continental division (11 hospitals in the rocky mountain and mid-west region of the U.S.) to evaluate the real-world clinical responses to PCT values in the setting of both LRTI's and sepsis.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Methods

- Retrospective cohort study
  - The institutional review board (IRB) overseeing all hospitals determined the protocol was exempt from IRB oversight.

- Data obtained from 11 facilities comprising the Continental Division of Hospital Corporation of America (HCA) using a de-identified data repository compiled for internal use by the HCA Continental Division.

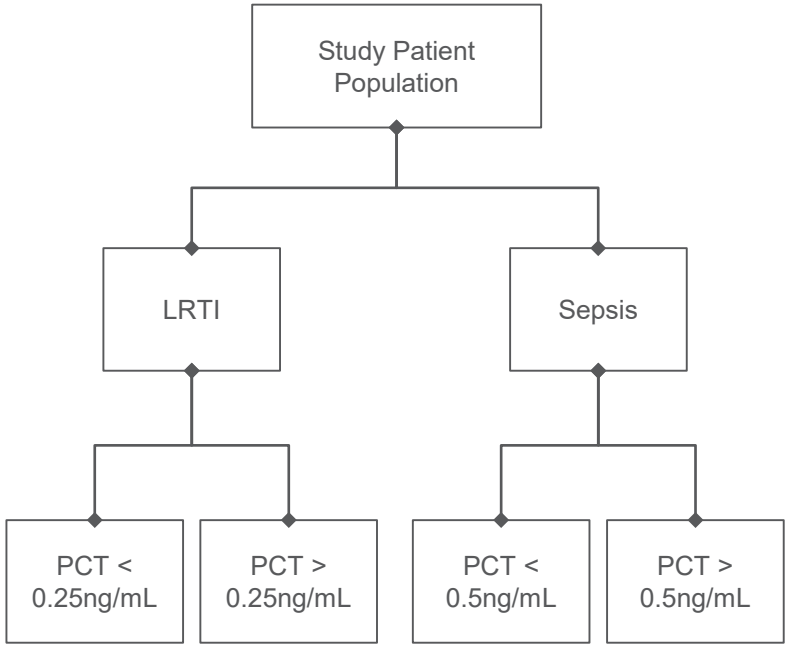
- Inclusion criteria:
  - Patients admitted from January 1, 2018 through August 30, 2019 across HCA Continental Division hospitals who had a PCT level tested during hospitalization
  - ICD-10 codes pertaining to sepsis, or any lower respiratory tract infection
- Exclusion criteria:
  - Current pregnancy, patients over 89 years of age or under 18, and at-risk individuals (those admitted from or discharged to prisons, jails, or law enforcement custody).

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Methods

- The patients selected for analysis were grouped to diagnoses of LRTI or sepsis.
  - LRTI: ICD-10 codes including, bacterial/viral PNA, COPD exacerbation, acute bronchitis, or lung abscesses.
  - Patients with diagnoses of both sepsis and LRTI were analyzed as part of the LRTI group.

- For the two groups, patients were further categorized according to PCT values in relation to defined cutoffs pertaining to high likelihood of bacterial infection in LRTI (0.25ng/mL) and sepsis (0.5ng/mL).



This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Methods

- We aimed to measure provider response following a PCT test, this was done first by calculating an antibiotic coverage score:

- Antibiotics were each assigned a point value of 1-3, corresponding to spectrum of microbial coverage (higher scores correlating to broader coverage)
  - Ex) ampicillin was assigned a score of 1, while piperacillin/tazobactam was assigned a score of 3
  - Multiple antibiotics ordered for a given patient were tabulated as a sum.

- Data were then analyzed to assess for change in antibiotic coverage score within 24 hours of PCT results being available.
  - An increase in score = escalation
  - A change from 0 to a positive value = initiation
  - Equivalent scores were considered as either non-initiation of antibiotics (if 0) or continuation of equivalent coverage.
  - A decrease in score = de-escalation
  - A change from a non-zero score to a score of 0 = discontinuation

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Results

- Initial data extraction yielded 36,423 patients. After applying the exclusion criteria, 8,223 patients were included in the final analysis (Fig. 1).
  - 49.12% of patients had an ICD-10 code pertaining to LRTI
  - 50.88% of patients had an ICD-10 code for sepsis with no ICD-10 associated with LRTI.

- PCT tests:
  - 74.89% of patients had a single PCT level drawn
  - 16.32% of patients had two tests
  - 8.79% of patients had three or more (Table 1).

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Results

- LRTI Group
- 4039 (49.12%) patients
  - Positive procalcitonin (PCT > 0.25ng/mL)
  - Negative procalcitonin (PCT < 0.25ng/mL)

- Positive PCT (1,414 patients, 35.0%):
  - 461 (32.6%) underwent de-escalation, discontinuation, or non-initiation of antibiotics within 24 hours
  - 953 (67.4%) had initiation, escalation, or equivalent coverage

- Negative PCT (2,625 patients, 65.0%):
  - 1,250 (47.62%) underwent de-escalation, discontinuation, or non-initiation of antibiotics within 24 hours
  - 1,375 (52.38%) had initiation, escalation, or equivalent coverage (Table 2).

- Sepsis Group
- 4,184 (50.88%) patients
  - Positive procalcitonin (PCT > 0.5ng/mL)
  - Negative procalcitonin (PCT < 0.5ng/mL)

- Positive PCT (2,032 patients, 48.57%):
  - 691 (34.01%) underwent de-escalation, discontinuation, or non-initiation of antibiotics within 24 hours
  - 1,341 (65.99%) had initiation, escalation, or equivalent coverage

- Negative PCT (2,152 patients, 51.43%):
  - 788 (36.62%) underwent de-escalation, discontinuation, or non-initiation of antibiotics within 24 hours
  - 1,364 (63.38%) had initiation, escalation, or equivalent coverage(Table 2).

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Figures

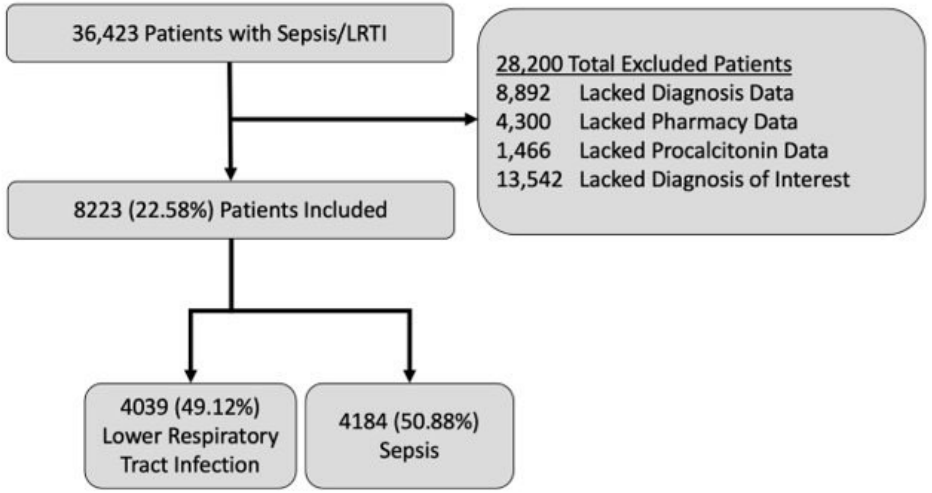


Figure 1: Population flow chart.

Table 1: Number of procalcitonin tests ordered in analyzed patients.

Number of Tests	Number of Patients	Percent of Patients	Cumulative Number of Patients
1	6,158	74.89%	8,223
2	1,342	16.32%	2,065
3+	723	8.79%	723

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Figures

Table 2: Determination of antibiotic regimen in response to procalcitonin results

Lower RTI/Upper RTI/Viral RTI (procalcitonin cut off at 0.25)		
Response	Procalcitonin elevated	Procalcitonin Not elevated
Antibiotics Initiated	306 (21.64%)	321 (12.23%)
Antibiotics Escalated	185 (13.08%)	263 (10.02%)
Antibiotics Unchanged	462 (32.67%)	791 (30.13%)
Antibiotics Not Initiated	122 (8.63%)	372 (14.17%)
Antibiotics De-Escalated	250 (17.68%)	490 (18.67%)
Antibiotics Discontinued	89 (6.29%)	388 (14.78%)
Sepsis (except lower RTI sepsis) (procalcitonin cut off at 0.50)		
Response	Procalcitonin elevated	Procalcitonin Not elevated
Antibiotics Initiated	137 (6.74%)	148 (6.88%)
Antibiotics Escalated	413 (20.32%)	348 (16.17%)
Antibiotics Unchanged	791 (38.93%)	868 (40.33%)
Antibiotics Not Initiated	25 (1.23%)	55 (2.56%)
Antibiotics De-Escalated	614 (30.22%)	587 (27.28%)
Antibiotics Discontinued	52 (2.56%)	146 (6.78%)

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Figures

Table 3: Categorization of antibiotic prescribing behavior according to procalcitonin values

Lower RTI/Upper RTI/Viral RTI (procalcitonin cut off at 0.25)			
	Procalcitonin elevated	Procalcitonin Not elevated	All
Anticipated Provider Response	953 (67.4%)	1250 (47.62%)	2203 (54.54%)
Unanticipated Provider Response	461 (32.6%)	1375 (52.38%)	1836 (45.46%)
All	1414 (100%)	2625 (100%)	4039 (100%)
Sepsis (except lower RTI sepsis) (procalcitonin cut off at 0.50)			
	Procalcitonin elevated	Procalcitonin Not elevated	All
Anticipated Provider Response	1341 (65.99%)	788 (36.62%)	2129 (50.88%)
Unanticipated Provider Response	691 (34.01%)	1364 (63.38%)	2055 (49.12%)
All	2032 (100%)	2152 (100%)	4184 (100%)

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Discussion

- In the majority of patients (75%) a single PCT was ordered.
- Our data for PCT negative LRTI found less than half (47.62%) of patients had the anticipated de-escalation, discontinuation, or non-initiation of antibiotics.
- Our data for sepsis showed an even smaller minority (36.62%) of patients whose PCT values were negative with the anticipated clinical response (Table 3).
- Half of patients in the LRTI group and two thirds of patients in the sepsis group saw unanticipated initiation, escalation, or continuation of their antibiotic regimen.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Discussion

- In our patient population, PCT results had limited influence on the decision to escalate or deescalate antibiotic use. This is consistent with a number of previous studies which demonstrated that PCT values have a relatively low impact on prescriber behavior outside of study protocols.[16,29,33–35]

- Although prospective trials show benefits to PCT use in the setting of a strict protocol, it seems in real world practice providers do not strictly adhere to PCT protocols.[4,6,12–17] Our findings highlight the lack of practical clinical utility of PCT testing.

- Further, the studies demonstrating benefit were nonuniform in their protocol, with no protocol clearly superior to another. In addition, PCT is estimated at having only 65-70% accuracy in differentiating bacterial versus viral infection.[40]

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Limitations

- For our study, recommended cutoffs for LRTI and sepsis were 0.25ng/mL and 0.5ng/mL respectively. The cutoffs found in the literature are varied – ranging anywhere from 0.25ng/mL to 1ng/mL.[13,14,17,19–27,37–39] It is possible some providers used cutoffs that deviated from our protocol.
  - To counter this, normal values as well as recommended course of treatment for abnormal values were included with the test result. In addition, physician education was provided during the studied time frame.

- Antibiotic scoring system was based on provider consensus without a standardized protocol (determined as a consensus by the authors).

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Conclusions

- Our findings suggest that when treating patients with sepsis, LRTI, or both, PCT values do not appear to correlate with clinicians' antibiotic prescribing behavior indicating minimal practical utility in real-world clinical practice.

- It is prudent that providers regard the whole patient presentation rather than a single laboratory value when deciding therapy. PCT can perhaps be useful in certain clinical scenarios as one component of an aggregate of clinical factors and tests.

- More robust data and clearer guidelines are likely prerequisites to the use of PCT as a truly useful instrument.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

References

1. Becker KL, Snider R, Nylen ES. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. *Crit Care Med*. 2008;36(3):941-952. doi:10.1097/CCM.0B013E318165BABB
2. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. *Lancet*. 1993;341(8844):515-518. doi:10.1016/0140-6736(93)90277-n
3. Covington EW, Roberts MZ, Dong J. Procalcitonin Monitoring as a Guide for Antimicrobial Therapy: A Review of Current Literature. *Pharmacotherapy*. 2018;38(5):569-581. doi:10.1002/phar.2112
4. Hamade B, Huang DT. Procalcitonin: Where Are We Now? *Crit Care Clin*. 2020;36(1):23-40. doi:10.1016/j.ccc.2019.08.003
5. Schuetz P, Wirz Y, Sager R, et al. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. *Cochrane Database Syst Rev*. 2017;10(10):CD007498-CD007498. doi:10.1002/14651858.CD007498.pub3
6. 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). doi:10.1186/s13054-018-2125-7
7. Prkno A, Wacker C, Brunkhorst FM, Schlattmann P. Procalcitonin-guided therapy in intensive care unit patients with severe sepsis and septic shock – a systematic review and meta-analysis. *Crit Care*. 2013;17(6):R291. doi:10.1186/cc13157
8. Zhang T, Wang Y, Yang Q, Dong Y. Procalcitonin-guided antibiotic therapy in critically ill adults: a meta-analysis. *BMC Infect Dis*. 2017;17(1). doi:10.1186/s12879-017-2622-3
9. Huang HB, Peng JM, Weng L, Wang CY, Jiang W, Du B. Procalcitonin-guided antibiotic therapy in intensive care unit patients: a systematic review and meta-analysis. *Ann Intensive Care*. 2017;7(1). doi:10.1186/s13613-017-0338-6
10. Schuetz P, Briel M, Christ-Crain M, et al. Procalcitonin to Guide Initiation and Duration of Antibiotic Treatment in Acute Respiratory Infections: An Individual Patient Data Meta-Analysis. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2012;55(5):651-662. doi:10.1093/cid/cis464
11. Discussion and Recommendations for the Application of Procalcitonin to the Evaluation and Management of Suspected Lower Respiratory Tract Infections and Sepsis. *Gaithersburg Md FDA Exec Summ*. Published online 2016.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

References

12. Stolz D, Smyrnios N, Eggimann P, et al. Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study. *Eur Respir J*. 2009;34(6):1364-1375. doi:10.1183/09031936.00053209
13. Bloos F, Trips E, Nierhaus A, et al. Effect of Sodium Selenite Administration and Procalcitonin-Guided Therapy on Mortality in Patients With Severe Sepsis or Septic Shock: A Randomized Clinical Trial. *JAMA Intern Med*. 2016;176(9):1266-1276. doi:10.1001/jamainternmed.2016.2514
14. de Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. *Lancet Infect Dis*. 2016;16(7):819-827. doi:10.1016/S1473-3099(16)00053-0
15. Daubin C, Valette X, Thiollière F, et al. Procalcitonin algorithm to guide initial antibiotic therapy in acute exacerbations of COPD admitted to the ICU: a randomized multicenter study. *Intensive Care Med*. 2018;44(4):428-437. doi:10.1007/s00134-018-5141-9
16. Huang DT, Yealy DM, Filbin MR, et al. Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection. *N Engl J Med*. 2018;379(3):236-249. doi:10.1056/NEJMoa1802670
17. Hey J, Thompson-Leduc P, Kirson NY, et al. Procalcitonin guidance in patients with lower respiratory tract infections: a systematic review and meta-analysis. *Clin Chem Lab Med CCLM*. 2018;56(8):1200-1209. doi:10.1515/cclm-2018-0126
18. "American Society for Clinical Pathology." Choosing Wisely – Promoting conversations between providers and patients, September 25, 2018.
19. Christ-Crain M, Jaccard-Stolz D, Bingisser R, et al. Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial. *Lancet Lond Engl*. 2004;363(9409):600-607. doi:10.1016/S0140-6736(04)15591-8
20. Christ-Crain M, Stolz D, Bingisser R, et al. Procalcitonin Guidance of Antibiotic Therapy in Community-acquired Pneumonia. *Am J Respir Crit Care Med*. 2006;174(1):84-93. doi:10.1164/rccm.200512-1922OC

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

References

21. Corti C, Fally M, Fabricius-Bjerre A, et al. Point-of-care procalcitonin test to reduce antibiotic exposure in patients hospitalized with acute exacerbation of COPD. *Int J Chron Obstruct Pulmon Dis*. 2016;11:1381-1389. doi:10.2147/COPD.S104051
22. Long W, Deng X, Zhang Y, Lu G, Xie J, Tang J. Procalcitonin guidance for reduction of antibiotic use in low-risk outpatients with community-acquired pneumonia. *Respirol Carlton Vic*. 2011;16(5):819-824. doi:10.1111/j.1440-1843.2011.01978.x
23. Schuetz P, Christ-Crain M, Thomann R, et al. Effect of Procalcitonin-Based Guidelines vs Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections: The ProHOSP Randomized Controlled Trial. *JAMA*. 2009;302(10):1059-1066. doi:10.1001/jama.2009.1297
24. Branche AR, Walsh EE, Vargas R, et al. Serum Procalcitonin Measurement and Viral Testing to Guide Antibiotic Use for Respiratory Infections in Hospitalized Adults: A Randomized Controlled Trial. *J Infect Dis*. 2015;212(11):1692-1700. doi:10.1093/infdis/jiv252
25. Briel M, Schuetz P, Mueller B, et al. Procalcitonin-guided antibiotic use vs a standard approach for acute respiratory tract infections in primary care. *Arch Intern Med*. 2008;168(18):2000-2007; discussion 2007-2008. doi:10.1001/archinte.168.18.2000
26. Burkhardt O, Ewig S, Haagen U, et al. Procalcitonin guidance and reduction of antibiotic use in acute respiratory tract infection. *Eur Respir J*. 2010;36(3):601-607. doi:10.1183/09031936.00163309
27. Kristoffersen KB, Søgaard OS, Wejse C, et al. Antibiotic treatment interruption of suspected lower respiratory tract infections based on a single procalcitonin measurement at hospital admission--a randomized trial. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis*. 2009;15(5):481-487. doi:10.1111/j.1469-0691.2009.02709.x
28. Kyriazopoulou E, Liaskou-Antoniou L, Adamis G, et al. Procalcitonin to Reduce Long-Term Infection-associated Adverse Events in Sepsis. A Randomized Trial. *Am J Respir Crit Care Med*. 2021;203(2):202-210. doi:10.1164/rccm.202004-1201OC
29. Covington EW, Eure S, Carroll D, Freeman C. Impact of Procalcitonin Monitoring on Duration of Antibiotics in Patients With Sepsis and/or Pneumonia in a Community Hospital Setting. *J Pharm Technol JPT Off Publ Assoc Pharm Tech*. 2018;34(3):109-116. doi:10.1177/8755122518756333
30. Agarwal R, Schwartz DN. Procalcitonin to guide duration of antimicrobial therapy in intensive care units: a systematic review. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2011;53(4):379-387. doi:10.1093/cid/cir408

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

References

31. Wilson KC, Schoenberg NC, Cohn DL, et al. Community-acquired Pneumonia Guideline Recommendations—Impact of a Consensus-based Process versus Systematic Reviews. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2020;73(7):e1467-e1475. doi:10.1093/cid/ciaa1428
32. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med*. 2021;49(11):e1063. doi:10.1097/CCM.0000000000005337
33. Brennan MB, Osterby K, Schulz L, Lepak AJ. Impact of Low Procalcitonin Results on Antibiotic Administration in Hospitalized Patients at a Tertiary Care Center. *Infect Dis Ther*. 2016;5(2):185-191. doi:10.1007/s40121-016-0114-1
34. Hohn A, Balfer N, Heising B, et al. Adherence to a procalcitonin-guided antibiotic treatment protocol in patients with severe sepsis and septic shock. *Ann Intensive Care*. 2018;8:68. doi:10.1186/s13613-018-0415-5
35. Ulrich RJ, McClung D, Wang BR, Winters S, Flanders SA, Rao K. Introduction of Procalcitonin Testing and Antibiotic Utilization for Acute Exacerbations of Chronic Obstructive Pulmonary Disease. *Infect Dis*. 2019;12:1178633719852626. doi:10.1177/1178633719852626
36. Chu DC, Mehta AB, Walkey AJ. Practice Patterns and Outcomes Associated With Procalcitonin Use in Critically Ill Patients With Sepsis. *Clin Infect Dis*. 2017;64(11):1509-1515. doi:10.1093/cid/cix179
37. Schroeder S, Hochreiter M, Koehler T, et al. Procalcitonin (PCT)-guided algorithm reduces length of antibiotic treatment in surgical intensive care patients with severe sepsis: results of a prospective randomized study. *Langenbecks Arch Surg*. 2009;394(2):221-226. doi:10.1007/s00423-008-0432-1
38. Hochreiter M, Köhler T, Schweiger AM, et al. Procalcitonin to guide duration of antibiotic therapy in intensive care patients: a randomized prospective controlled trial. *Crit Care Lond Engl*. 2009;13(3):R83. doi:10.1186/cc7903
39. Jensen JU, Hein L, Lundgren B, et al. Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: a randomized trial. *Crit Care Med*. 2011;39(9):2048-2058. doi:10.1097/CCM.0b013e31821e8791
40. Self WH, Balk RA, Grijalva CG, et al. Procalcitonin as a Marker of Etiology in Adults Hospitalized With Community-Acquired Pneumonia. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2017;65(2):183-190. doi:10.1093/cid/cix317

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.