Opinion Paper

Philipp Schuetz*

How to best use procalcitonin to diagnose infections and manage antibiotic treatment

https://doi.org/10.1515/cclm-2022-1072
Received October 25, 2022; accepted October 26, 2022;
published online November 2, 2022

Abstract

Objectives: Procalcitonin (PCT) is a host-response biomarker that has shown clinical value for assessing the likelihood of bacterial infections and guiding antibiotic treatment. Identifying situations where PCT can improve clinical care is therefore highly important.
Methods: The aim of this narrative review is to discuss strategies for the usage and integration of PCT into clinical routine, based on the most recent clinical evidence.
Results: Although PCT should not be viewed as a traditional diagnostic marker, it can help differentiate bacterial from non-bacterial infections and inflammation states – particularly in respiratory illness. Several trials have found that PCT-guided antibiotic stewardship reduces antibiotic exposure and associated side-effects among patients with respiratory infection and sepsis. Studies have demonstrated that patient-specific decisions regarding antibiotic usage is highly complex. Factors to consider include: the clinical situation (with a focus on the pretest probability for bacterial infection), the acuity and severity of presentation, as well as PCT test results. Low PCT levels help rule out bacterial infection in patients with both low pretest probability for bacterial infection and low-risk general condition. In high-risk individuals and/or high pretest probability for infection, empiric antibiotic treatment is mandatory. Subsequent monitoring of PCT helps track the resolution of infection and guide decisions regarding early termination of antibiotic treatment.
Conclusions: PCT possesses high potential to improve decision-making regarding antibiotic treatment – when combined with careful patient assessment, evidence-based clinical algorithms, and continuous notification and regular feedback from all antibiotic stewardship stakeholders. Medical Journals such as *Clinical Chemistry and Laboratory Medicine* (*CCLM*) have played a critical role in reviewing and dissemination the high-quality evidence about assays for PCT measurement, observational research regarding association with outcomes among different populations, and interventional research proofing its effectiveness for patient care.

Keywords: antibiotic stewardship; bacterial infection; biomarker; procalcitonin; respiratory tract infections; sepsis.

Introduction

Acute respiratory tract illnesses and suspected sepsis often prompt initiation of empiric antibiotic treatment. In many cases, however, a bacterial pathogen cannot be detected, as viruses account for a large proportion of respiratory illnesses [1, 2]. The same is true in patients presenting with systemic inflammatory response syndrome (SIRS) and possible sepsis – where other inflammatory or viral illnesses may be the cause of a significant proportion of cases. Despite technological advances and the wide availability of rapid molecular diagnostics [3], antibiotics are often over-prescribed due to concerns about bacterial coinfections and the risk of withholding therapy. Once started, physicians often prescribe prolonged courses of antibiotics due to lack of proof that the infection has been resolved. Unnecessarily long treatment also often results from the application of antibiotic regimens advocated by standard practice guidelines. Individualizing antibiotic treatment may potentially improve antibiotic stewardship efforts to encourage judicious and correct usage of these agents. This would further mitigate the emergence of multi-drug resistant pathogens – a situation directly linked to antibiotic overuse and one of the most urgent health threats worldwide [4].

Regarding clinical care of patients with acute respiratory illnesses and sepsis, the integration of host response markers which correlate with the likelihood of bacterial infection has strong potential to improve individual antibiotic therapy decision-making [5]. Among such host-

***Corresponding author: Philipp Schuetz**, MD, MPH, Department of Internal Medicine, Kantonsspital Aarau, Aarau, Switzerland; and University of Basel, Basel, Switzerland, Phone: +41 (0) 79 365 10 06, Fax: +41 (0) 62 838 9524, E-mail: Philipp.Schuetz@unibas.ch

response markers, Procalcitonin (PCT) has generated much interest due to its higher specificity towards bacterial infection compared to C-reactive protein (CRP) or white blood cell count (WBC) [6, 7]. PCT also has a superior prognostic [8] and kinetic profile to track infections – making it useful to assess response to treatment [7, 9–12].

The goal of this narrative review is to discuss different studies and clinical trials that have investigated clinical effects of using PCT for the purpose of antibiotic stewardship, and to provide practical advice on how to best integrate PCT into clinical care. Thereby, several milestone studies about PCT that were published in *Clinical Chemistry and Laboratory Medicine (CCLM)* over the last years are particularly highlighted and critically discussed.

Clinical trials investigating PCT-guided antibiotic stewardship

In addition to a large body of observational data [13], several interventional trials have compared PCT protocols with control groups regarding antibiotic use and clinical outcomes [14, 15]. Most trials focused on patients with respiratory infection and/or sepsis. Although the protocols followed slightly different PCT guidelines, there were some similarities: PCT cut-off values in low risk patients were used to identify individuals for whom bacterial infection was unlikely and antibiotic treatment could be stopped, or withheld [16]. If the probability for bacterial infection was high, the protocol focused on PCT kinetics and cessation of antibiotics when PCT levels dropped to normal ranges, or by at least 80–90%. PCT protocols had varying cut-offs for low or higher acuity/severity: for emergency department and medical ward patients, a PCT<0.25 μg/L recommended no use of antibiotics, while in intensive care patients a PCT<0.5 μg/L advocated discontinuation of antibiotics.

There are several meta-analyses which have investigated the effectiveness and safety of utilizing PCT to guide antibiotic treatment. One individual patient data meta-analysis of 26 trials focusing on respiratory infections reported that PCT guidance was associated with a 2.4-day reduction in antibiotic exposure (5.7 vs. 8.1 days). This was due to decreased rates of antibiotic initiation in low-risk patient (i.e., bronchitis or COPD patients) and shorter treatment courses in high risk patients (i.e., pneumonia patients) [7, 15]. Importantly, use of PCT resulted in reductions of antibiotic-related side-effects (16 vs. 22%), and in significantly lowered mortality (286 [9%] deaths in 3,336 procalcitonin-guided patients vs. 336 [10%] in 3,372 controls [p=0.037]). Similar effects were also seen for other respiratory infections and clinical settings.

Another meta-analysis of 11 trials and 4,482 patients investigated the effects of applying PCT in patients with sepsis [14]. Those randomized to the PCT protocol experienced an earlier discontinuation of antibiotics and significant reductions in mean treatment duration from 10.4 to 9.3 days. Here again, mortality in PCT-guided patients was significantly lower compared to the control group (21.1 vs. 23.7%, p=0.03). In a further meta-analysis of individuals with positive blood cultures, PCT reduced both antibiotic exposure (by 2.86 days) and mortality (16.6 vs. 20.0%) [17]. A subgroup analysis demonstrated the strongest effects for pneumonia caused by *Streptococcus pneumoniae* (–4.52 days) and urogenital infections caused by *Escherichia coli* (–4.21 days).

How to implement PCT in clinical practice

Based on these trials, important considerations for PCT use in clinical practice must be made. The interpretation of PCT results varies according to clinical setting, specific patient situation, and type of illness.

In low risk patients in primary care, a marker such as PCT can rule out bacterial disease and reduce antibiotic initiation [18]. Two large primary care PCT trials examined a total of 1,008 patients with lower and upper respiratory tract infections – whereby a low PCT of ≤0.25 μg/L prohibited the use of antibiotics [18, 19]. Antibiotic initiation was reduced from 63% in control group patients to 23% in PCT-guided patients; with a significant reduction in antibiotic exposure from 4.6 to 1.6 days and no difference in clinical outcomes. Currently, the most significant limitation to the use of PCT in primary care is the lack of highly sensitive point-of-care tests. Furthermore, other markers such as CRP – where tests are more widely available and less expensive – have shown benefit in primary care patients despite their lower specificity regarding bacterial infections [20]. As corresponding large scale head-to-head trials are lacking, further study is needed to compare PCT-guided care with other biomarkers such as CRP. Cost-effectiveness and country-specific reimbursement of PCT must also be addressed.

Several trials of mostly respiratory infection patients have investigated PCT in the emergency department

setting. A study of over 500 patients with bronchitis found significant reduction in initiation of antibiotics (26 vs. 66%) when PCT was used as guideline [15]. Similarly for COPD exacerbation, an analysis of more than 1,200 patients found significant reduction in the application of antibiotics with PCT-guided care (43 vs. 72%). PCT may also help emergency department personnel to discriminate between chronic heart failure patients with decompensation vs. respiratory infection [21, 22]. For cases with pneumonia, baseline PCT levels obtained in the emergency department help assess kinetics over time and guide duration of antibiotic therapy.

Several trials on pneumonia patients admitted to medical wards have found that serial PCT measurements and the termination of antibiotics when PCT dropped by ≥80% (or to <0.25 μg/L) resulted in shorter treatment durations, lower risk of adverse drug events, and improved survival rates [23]. One meta-analysis of more than 3,000 pneumonia patients reported reductions in antibiotic treatment from 10.4 day to 7.5 days, and improvements in treatment failure (22 vs. 26%) and mortality (12 vs. 14%) [15]. The positive impact of PCT-guided antibiotic management on mortality may be explained by various factors; including a reduction of direct toxic effects of antibiotics, a lowering of risk for antibiotic related *Clostridium difficile* infections, and changes in diagnostic and therapeutic monitoring and management based on prognostic information. Less trial data is available regarding the use of PCT in surgical patients [24] – where it is important to understand that inflammatory stress-induced increases in PCT concentrations correlate with the extent of surgery [10]. One study indicated that PCT was highest on the second day postop and typically declined thereafter in patients with uncomplicated recoveries. Persistently elevated PCT levels have been conversely associated with the development of postsurgical infection [25, 26]. The acquisition of more data is necessary before PCT is broadly implemented to assist management of postsurgical complications.

The intensive care unit is another important setting where clinical trial data has demonstrated the usefulness of PCT for antibiotic decision-making. Here, PCT-guided care does not focus on the initiation of antibiotics, but rather on determining clinical response to treatment and possible discontinuation of therapy [27]. Several large multicenter trials have found PCT helpful in reducing antibiotic exposure [28, 29]. Most trials stopped antibiotic treatment when PCT decreased by ≥80% from its peak value; or to a level of ≤0.5 μg/L. A recent meta-analysis of PCT-guided antibiotic treatment found reductions in both duration of treatment and mortality [14, 30].

Practical considerations

Decisions regarding antibiotic use in individual patients is complex and should be based on several considerations including: the pretest probability for bacterial infection (based on clinical examination and microbiological findings), the severity of presentation, and PCT test results. Figure 1 provides a practical guide for the rational use of PCT in both high and low risk settings; in conjunction with clinical assessment including interpretation of PCT, and recommendations for antibiotic use as discussed at a consensus conference of international experts [16, 31].

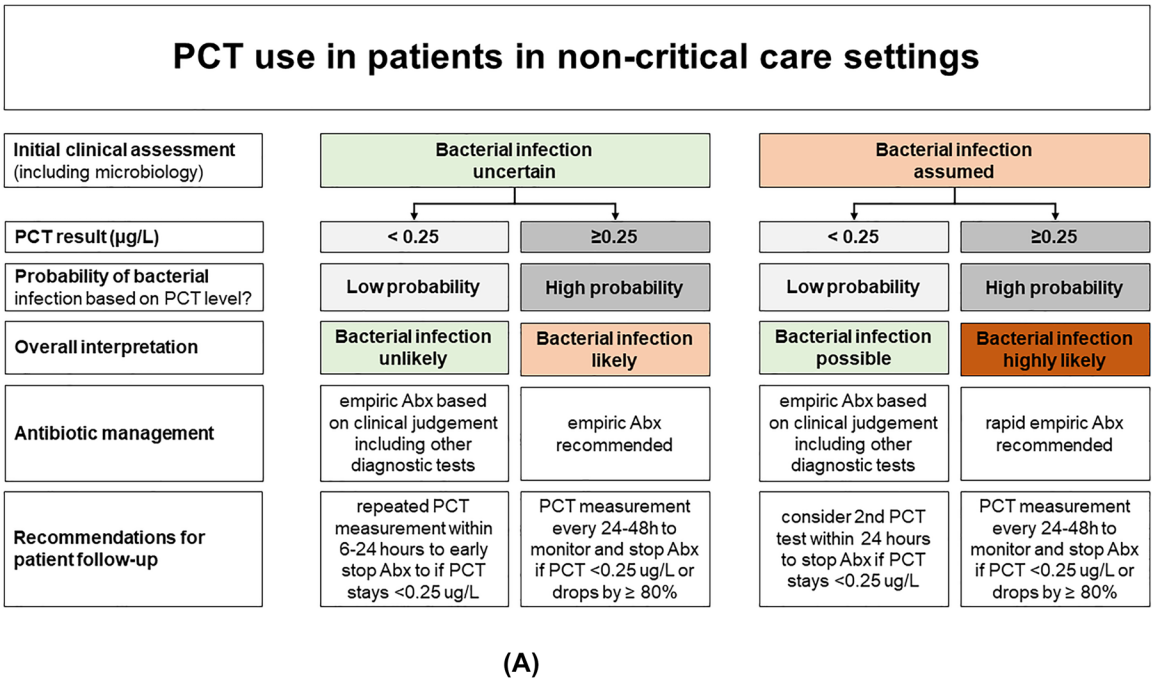
In low-risk situations (e.g., patient in primary care or on the medical ward) and a minimal pretest probability for bacterial infections (e.g., individuals presenting with bronchitis), low PCT levels <0.25 μg/L help rule out bacterial infection and empiric antibiotic therapy should be avoided. PCT should be retested if the patient does not improve clinically. Antibiotics should be considered if PCT increases, or initial clinical assessment indicates high probability of bacterial infection. PCT testing can then be undertaken every 24–48 h, with discontinuation of antibiotics if levels drop to ≤0.25 μg/L or decrease by 80% or more from peak values.

Concerning high-risk patient with sepsis, initial antibiotics should be used irrespective of PCT results – but low PCT values may prompt additional diagnostic measures to rule out other non-bacterial causes of illness. In these situations, monitoring of PCT over time helps track resolution of infection and decision-making regarding early termination of antibiotic treatment.

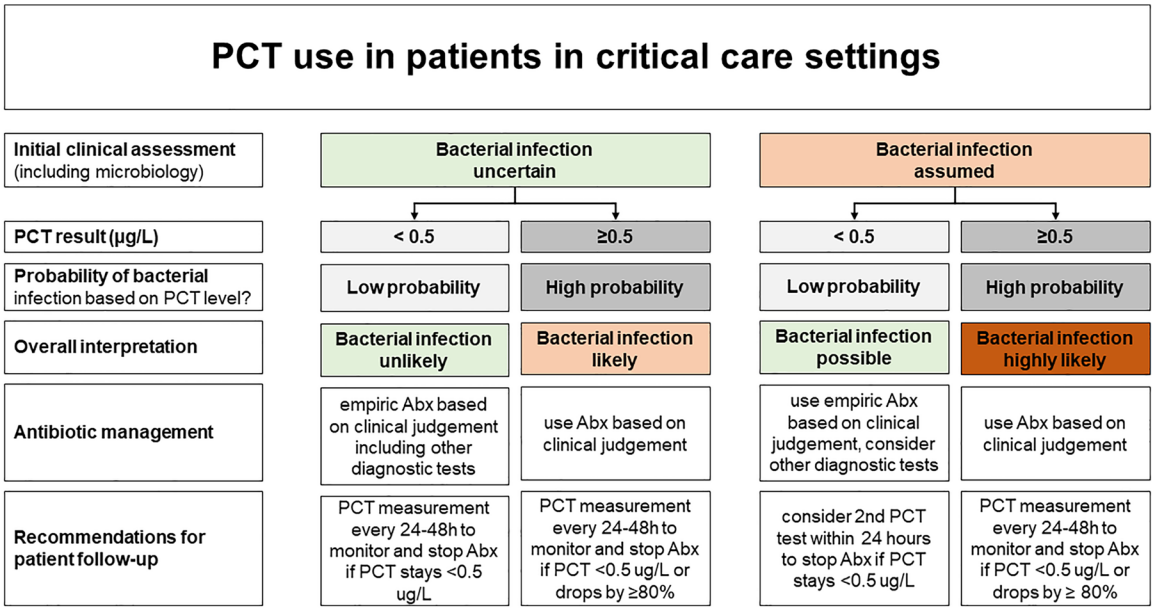
Finally, while most studies are performed in Europe and the US, it is important to adapt existing algorithms for differences in type of infections in regions with tropical diseases [32].

Limitations of procalcitonin

Most PCT studies investigate individuals with respiratory infections or sepsis, and data is limited for immunosuppressed patients [11]. In addition, various non-infectious conditions such as C-cell carcinoma or trauma can cause systemic inflammation and increases in PCT [33]. Also, PCT-guided stewardship should not be applied to patients with chronic infections such as osteomyelitis or endocarditis, as observational studies have not shown positive results and interventional research is lacking [31]. For emerging infections such as COVID-19, the role of PCT as a stewardship tool requires further study [34]. PCT is



(A)



(B)

Figure 1: Clinical algorithm for PCT use in different clinical settings. (A) Suggested PCT protocol in low and moderate severity patients [31]. (B) Suggested PCT protocol in critical care patients [31].

also relatively low in some atypical infections – including mycoplasma [35]. Some clinical conditions such as kidney failure and dialysis may influence PCT kinetics [36], although one large individual patient meta-analysis suggested that use of PCT in patients with impaired kidney function works well and is associated with shorter antibiotic courses and lower mortality rates [37]. Finally, a large number of new PCT immunoassays are currently being developed (including point-of-care tests [38]), which will require careful analysis and clinical evaluation [39–45]. The expansion of PCT assays also necessitates evaluation of result comparability among tests and standardized calibration to support safe usage of PCT in clinical routine [46–48]. Finally, cost-effectiveness

analyses are needed to evaluate how widespread PCT testing would affect health care budgets – in comparison with the resulting benefits for clinical outcomes and antibiotic resistance patterns [49, 50].

Concluding remarks

The medical community is highly interested in reducing unnecessary antibiotic exposure in patients with acute respiratory illness and low risk for bacterial infection, as well as shortening therapy in cases of known bacterial infections. Essentially, the aim is to shift from fixed antibiotic doses to individualized treatment. As a marker of host defense response, PCT has shown promising results for respiratory infections and sepsis. PCT should not be used as a substitute for good clinical practice, but rather be part of the overall assessment of a patient. Decisions pertaining to initiation and cessation of antibiotic treatment remains strongly dependent on evaluating all available clinical and diagnostic parameters, including a thorough assessment of the patient and severity of illness. Furthermore, PCT usage should not delay or impede initiation of empirical treatment in high-risk situations. Host response markers such as PCT, however, remain the best line of defense against diagnostic uncertainty and antibiotic overuse. Further research is needed to explore the optimal application of biomarkers in combination with pathogen-directed tests. Importantly, medical Journals such as *Clinical Chemistry and Laboratory Medicine* (*CCLM*) have played a critical role in reviewing and dissemination the high-quality evidence about assays for PCT measurement, observational research regarding association with outcomes among different populations, and interventional research proofing its effectiveness for patient care.

Research funding: None declared.
Author contributions: Single author contribution.
Competing interests: Dr. Schuetz reports grants from bioMerieux, Thermofisher, and Roche Diagnostics (paid to the Institution).
Informed consent: Not applicable.
Ethical approval: Not applicable.

References

1. Musher DM, Thorner AR. Community-acquired pneumonia. N Engl J Med 2014;371:1619–28.
2. Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, Bramley AM, et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. N Engl J Med 2015;373:415–27.
3. Mitsuma SF, Mansour MK, Dekker JP, Kim J, Rahman MZ, Tweed-Kent A, et al. Promising new assays and technologies for the diagnosis and management of infectious diseases. Clin Infect Dis 2013;56:996–1002.
4. Jee Y, Carlson J, Rafai E, Musonda K, Huong TTG, Daza P, et al. Antimicrobial resistance: a threat to global health. Lancet Infect Dis 2018;18:939–40.
5. Hey J, Thompson-Leduc P, Kirson NY, Zimmer L, Wilkins D, Rice B, et al. Procalcitonin guidance in patients with lower respiratory tract infections: a systematic review and meta-analysis. Clin Chem Lab Med 2018;56:1200–9.
6. Bartoletti M, Antonelli M, Bruno Blasi FA, Casagranda I, Chieregato A, Fumagalli R, et al. Procalcitonin-guided antibiotic therapy: an expert consensus. Clin Chem Lab Med 2018;56: 1223–9.
7. Zhydkov A, Christ-Crain M, Thomann R, Hoess C, Henzen C, Werner Z, et al. Utility of procalcitonin, C-reactive protein and white blood cells alone and in combination for the prediction of clinical outcomes in community-acquired pneumonia. Clin Chem Lab Med 2015;53:559–66.
8. Sager R, Wirz Y, Amin D, Amin A, Hausfater P, Huber A, et al. Are admission procalcitonin levels universal mortality predictors across different medical emergency patient populations? Results from the multi-national, prospective, observational TRIAGE study. Clin Chem Lab Med 2017;55:1873–80.
9. Schuetz P, Birkhahn R, Sherwin R, Jones AE, Singer A, Kline JA, et al. Serial procalcitonin predicts mortality in severe sepsis patients: results from the multicenter procalcitonin MOnitoring SEpsis (MOSES) study. Crit Care Med 2017;45:781–9.
10. Sager R, Kutz A, Mueller B, Schuetz P. Procalcitonin-guided diagnosis and antibiotic stewardship revisited. BMC Med 2017; 15:15.
11. Lippi G, Cervellin G. Procalcitonin for diagnosing and monitoring bacterial infections: for or against? Clin Chem Lab Med 2018;56: 1193–5.
12. Schuetz P, Hausfater P, Amin D, Amin A, Haubitz S, Faessler L, et al. Biomarkers from distinct biological pathways improve early risk stratification in medical emergency patients: the multinational, prospective, observational TRIAGE study. Crit Care 2015;19:377.
13. Schuetz P, Aujesky D, Muller C, Muller B. Biomarker-guided personalised emergency medicine for all – hope for another hype? Swiss Med Wkly 2015;145:w14079.
14. Wirz Y, Meier MA, Bouadma L, Luyt CE, Wolff M, Chastre J, 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;22:191.
15. Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. Lancet Infect Dis 2018;18:95–107.
16. Schuetz P, Bolliger R, Merker M, Christ-Crain M, Stolz D, Tamm M, et al. Procalcitonin-guided antibiotic therapy algorithms for different types of acute respiratory infections based on previous trials. Expert Rev Anti Infect Ther 2018;16:555–64.
17. Meier MA, Branche A, Neeser OL, Wirz Y, Haubitz S, Bouadma L, et al. Procalcitonin-guided antibiotic treatment in patients with positive blood cultures: a patient-level meta-analysis of randomized trials. Clin Infect Dis 2019;69:388–96.

18. Odermatt J, Friedli N, Kutz A, Briel M, Bucher HC, Christ-Crain M, et al. Effects of procalcitonin testing on antibiotic use and clinical outcomes in patients with upper respiratory tract infections. An individual patient data meta-analysis. Clin Chem Lab Med 2017;56:170–7.
19. Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, et al. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Syst Rev 2017;10: CD007498.
20. Do NT, Ta NT, Tran NT, Than HM, Vu BT, Hoang LB, et al. Point-of-care C-reactive protein testing to reduce inappropriate use of antibiotics for non-severe acute respiratory infections in Vietnamese primary health care: a randomised controlled trial. Lancet Global Health 2016;4:e633–41.
21. Schuetz P, Daniels LB, Kulkarni P, Anker SD, Mueller B. Procalcitonin: a new biomarker for the cardiologist. Int J Cardiol 2016;223:390–7.
22. Schuetz P, Kutz A, Grolimund E, Haubitz S, Demann D, Vogeli A, et al. Excluding infection through procalcitonin testing improves outcomes of congestive heart failure patients presenting with acute respiratory symptoms: results from the randomized ProHOSP trial. Int J Cardiol 2014;175:464–72.
23. Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M, Widmer I, 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; 302:1059–66.
24. Aoki Y, Taniai N, Yoshioka M, Kawano Y, Shimizu T, Kanda T, et al. Serum procalcitonin concentration within 2 days postoperatively accurately predicts outcome after liver resection. Clin Chem Lab Med 2018;56:1362–72.
25. Hunziker S, Hugle T, Schuchardt K, Groeschl I, Schuetz P, Mueller B, et al. The value of serum procalcitonin level for differentiation of infectious from noninfectious causes of fever after orthopaedic surgery. J Bone Joint Surg 2010;92:138–48.
26. Bouaicha S, Blatter S, Moor BK, Spanaus K, Dora C, Werner CM. Early serum procalcitonin level after primary total hip replacement. Mediat Inflamm 2013;2013:927636.
27. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 2013;39:165–228.
28. Landman GW, Kleefstra N. Procalcitonin in intensive care units: the PRORATA trial. Lancet 2010;375:1606. author reply-7.
29. de Jong E, van Oers JA, Beishuizen A, Vos P, Vermeijden WJ, Haas LE, 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;16:819–27.
30. Wirz Y, Branche A, Wolff M, Welte T, Nobre V, Reinhart K, et al. Management of respiratory infections with use of procalcitonin: moving toward more personalized antibiotic treatment decisions. ACS Infect Dis 2017;3:875–9.
31. Schuetz P, Beishuizen A, Broyles M, Ferrer R, Gavazzi G, Gluck EH, et al. Procalcitonin (PCT)-guided antibiotic stewardship: an international experts consensus on optimized clinical use. Clin Chem Lab Med 2019;57:1308–18.
32. Lee CC, Kwa ALH, Apisarnthanarak A, Feng JY, Gluck EH, Ito A, et al. Procalcitonin (PCT)-guided antibiotic stewardship in Asia-Pacific countries: adaptation based on an expert consensus meeting. Clin Chem Lab Med 2020;58:1983–91.
33. Kratzsch J, Willenberg A, Frank-Raue K, Kempin U, Rocktaschel J, Raue F. Procalcitonin measured by three different assays is an excellent tumor marker for the follow-up of patients with medullary thyroid carcinoma. Clin Chem Lab Med 2021;59: 1861–8.
34. Dolci A, Robbiano C, Aloisio E, Chibireva M, Serafini L, Falvella FS, et al. Searching for a role of procalcitonin determination in COVID-19: a study on a selected cohort of hospitalized patients. Clin Chem Lab Med 2020;59:433–40.
35. Neeser OL, Vukajlovic T, Felder L, Haubitz S, Hammerer-Lercher A, Ottiger C, et al. A high C-reactive protein/procalcitonin ratio predicts Mycoplasma pneumoniae infection. Clin Chem Lab Med 2019;57:1638–46.
36. Ceccarelli G, Alessandri F, Sargentini V, D'Alessandro MD, Spaziante M, Bachetoni A, et al. Impact of continuous renal replacement therapy (CRRT) and other extracorporeal support techniques on procalcitonin guided antibiotic therapy in critically ill patients with septic shock. Clin Chem Lab Med 2019;57:e86–7.
37. Heilmann E, Gregoriano C, Wirz Y, Luyt CE, Wolff M, Chastre J, et al. Association of kidney function with effectiveness of procalcitonin-guided antibiotic treatment: a patient-level meta-analysis from randomized controlled trials. Clin Chem Lab Med 2020;59:441–53.
38. Kutz A, Hausfater P, Oppert M, Alan M, Grolimund E, Gast C, et al. Comparison between B.R.A.H.M.S PCT direct, a new sensitive point-of-care testing device for rapid quantification of procalcitonin in emergency department patients and established reference methods – a prospective multinational trial. Clin Chem Lab Med 2016;54:577–84.
39. Schuetz P, Bretscher C, Bernasconi L, Mueller B. Overview of procalcitonin assays and procalcitonin-guided protocols for the management of patients with infections and sepsis. Expert Rev Mol Diagn 2017;17:593–601.
40. Lippi G, Salvagno GL, Gelati M, Pucci M, Lo Cascio C, Demonte D, et al. Two-center comparison of 10 fully-automated commercial procalcitonin (PCT) immunoassays. Clin Chem Lab Med 2019;58: 77–84.
41. Dupuy AM, Ruffel L, Bargnoux AS, Badiou S, Cristol JP. Analytical evaluation of the performances of a new procalcitonin immunoassay. Clin Chem Lab Med 2022;60:77–80.
42. Choi H, Tashpulatova Z, Moon SY, Choi J, Kim JY, Lee SM. Evaluation of the Beckman Coulter access procalcitonin assay: analytical and clinical performance. Clin Chem Lab Med 2022;60:e50–3.
43. Jensch A, Mahla E, Toller W, Herrmann M, Mangge H. Procalcitonin measurement by Diazyme immunturbidimetric and Elecsys BRAHMS PCT assay on a Roche COBAS modular analyzer. Clin Chem Lab Med 2021;59:e362–e6.
44. Yuan S, Zheng N, Zheng W, Jiang Q, Qiao B, Jing H, et al. Analytical evaluation of Reebio procalcitonin latex-enhanced immunoturbidimetric assay on the HITACHI Labospect 008AS. Clin Chem Lab Med 2020;59:e23–6.
45. Schuetz P, Christ-Crain M, Huber AR, Muller B. Long-term stability of procalcitonin in frozen samples and comparison of Kryptor and VIDAS automated immunoassays. Clin Biochem 2010;43:341–4.
46. Huynh HH, Boeuf A, Pfannkuche J, Schuetz P, Thelen M, Nordin G, et al. Harmonization status of procalcitonin measurements: what

do comparison studies and EQA schemes tell us? Clin Chem Lab Med 2021;59:1610–22.
47. Eidizadeh A, Asif AR, von Ahsen N, Binder L, Schnelle M. Differences in procalcitonin measurements between three BRAHMS-partnered immunoassays (Liaison, Elecsys and Architect). Clin Chem Lab Med 2019;57:e207–10.
48. Chambliss AB, Hayden J, Colby JM. Evaluation of procalcitonin immunoassay concordance near clinical decision points. Clin Chem Lab Med 2019;57:1414–21.
49. Stojanovic I, Schneider JE, Wei L, Hong Z, Keane C, Schuetz P. Economic evaluation of procalcitonin-guided antibiotic therapy in acute respiratory infections: a Chinese hospital system perspective. Clin Chem Lab Med 2017;55: 561–70.
50. Schuetz P, Balk R, Briel M, Kutz A, Christ-Crain M, Stolz D, et al. Economic evaluation of procalcitonin-guided antibiotic therapy in acute respiratory infections: a US health system perspective. Clin Chem Lab Med 2015;53:583–92.