

# Procalcitonin in clinical practice: from diagnosis of sepsis to antibiotic therapy

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## ABSTRACT

A diagnostic algorithm that allows for the rapid identification of sepsis and possibly guides the appropriate antimicrobial therapy application is the cornerstone to obtaining effective treatment and better results. The use of emerging surrogate markers could significantly improve clinical practice, but the validity and clinical utility have been proved only for very few of them, and their availability in clinical routine is limited. For this purpose, numerous scientific evidence has indicated procalcitonin as a marker linked to sepsis and its evolution. This review aims to retrace the main evidence relating to the use of procalcitonin in sepsis. We analyzed the primary studies in the literature and the existing meta-analysis evaluating the behavior of procalcitonin as a marker of bacterial sepsis, its prognostic power, and its ability to influence antibiotic therapy. Recent evidence has suggested that procalcitonin could be an efficient marker for diagnosing sepsis and its therapeutic management in many types of patients. The choice of the appropriate timing to initiate and suspend antibiotic therapy, with obvious clinical advantages, the favorable effects could also include reducing health costs, both avoiding the administration of inappropriate antibiotic therapies, and reducing the duration of hospitalization. Moreover, limited studies reported high procalcitonin levels in coronavirus disease 2019 patients with a worse prognosis. Despite the considerable evidence in favor of the potential of procalcitonin as an index for managing septic patients, there are conflicting data that deserve specific and detailed studies.

## Introduction

Serious bacterial infections and their sequels are still a major problem, burdened by a high mortality rate in hospitals; for this reason,<sup>1,2</sup> a diagnostic algorithm that allows for the rapid identification of sepsis, and possibly guides the appropriate application of antimicrobial therapy, is the cornerstone to obtaining effective treatment and better results.

Critical elements for a rapid diagnosis of sepsis are the clinical pattern, imaging results, and biohumoral markers of systemic inflammatory response. The ideal standard for the definition would be the definite isolation of causative microorganisms through positive cultures and/or molecular identification. Unfortunately, the delay in microbiology response and the false-negative rate results make it challenging.<sup>3</sup>

The use of emerging surrogate markers could significantly improve clinical practice, but the validity and clinical utility have been proved only for very few of them, and their availability in clinical routine is limited.<sup>4</sup>

Reliable bio-marker desirable features should be the diagnostic accuracy, management simplicity, prognostic power, and the ability to predict and monitor clinical response to a therapeutic intervention,<sup>5</sup> and affordable costs.

In septic conditions, a complex host immune response, activated by pathogen-related antigens, enhances the production and the release of several inflammatory mediators into the bloodstream, including cytokines and vasoactive molecules, receptor bio-markers, and coagulative factors. Precursors and mature products of these mediators could be useful surrogate markers to improve the diagnosis and assess disease gravity.

Different researchers based on considerable evidence have proposed that procalcitonin possesses adequate potency in predicting bacterial etiology of the infectious process. Procalcitonin is a precursor of calci-

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tonin, whose production increases during infection due to the overexpression of the *CALC 1* gene. The main pathway of procalcitonin secretion<sup>6</sup> is represented by the neuroendocrine cells of the intestine and lung tissue within 4 hours, and its concentration can increase nearly 1000-fold after a severe bacterial infection; based on similar evidence, it was suggested that there might be a link between blood levels of procalcitonin (PCT) and the severity of the infection. PCT has a good kinetic profile compared to C-reactive protein (CRP); its rise is more rapid, and a reduced renal function does not significantly modify blood concentrations. Such behavior would make procalcitonin an ideal marker, both diagnostic and for therapeutic and prognostic management.

### Aim

The aim of this review is to retrace the main evidence relating to the use of procalcitonin in sepsis.

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### Methods of research

We analyzed the main studies in the literature and the existing meta-analysis evaluating the role of procalcitonin in diagnosing bacterial sepsis, its prognostic power in the course of sepsis, and in its ability to influence antibiotic therapy.

The discussion was conducted according to essential points such as the role of PCT as a diagnostic marker of sepsis, prognostic index, and guiding tool of clinical-therapeutic management; furthermore for each point the studies in favor and against were evaluated.

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### Procalcitonin for diagnosis of bacterial sepsis

The link between procalcitonin and its metabolites with bacterial infections was initially observed in a study carried out in 1993; the authors observed an increase in procalcitonin levels during sepsis. Furthermore, these early observations had suggested a possible role as a direct marker of patient prognosis, significantly increasing in more severe infections.<sup>6-8</sup>

Subsequent studies had enjoyed greater accuracy with which serum PCT concentrations were detected in future years, providing even more accurate analyses.

The debate on the diagnostic role of PCT was thus enriched, particularly with the publication of the first prospective studies.

Several studies provided results in favor of procalcitonin utility.<sup>10-29</sup>

In particular, among them, Wanner *et al.*<sup>11</sup> measured the PCT concentrations at the time of admission, demonstrating that these were higher in case of diagnosis of sepsis or severe multiorgan dysfunction syndrome related to influenza.

However, there are also other prospective studies<sup>30-36</sup>

that have shown contrary results to the previous ones, with negative results regarding the role of PCT as a diagnostic marker.

In recent years, various authors compared PCT with other well-established indicators of inflammation and infection, such as CRP<sup>37</sup> and high-sensitivity CRP,<sup>38</sup> pre-sepsin,<sup>37</sup> neutrophil CD64,<sup>39</sup> lactate levels,<sup>40</sup> white blood cells and neutrophil count,<sup>41,42</sup> interleukin (IL)-6<sup>43</sup>.

Meisner *et al.*<sup>43</sup> investigated the relationship between PCT and inflammatory markers, such as CRP, in 40 subjects with systemic inflammation complicated with multiple organ failure over 15 days. Investigators reported that PCT levels of non-surviving patients significantly increased after the fourth day, whereas CRP was not different between surviving and non-surviving subjects; these findings supported that measurement of PCT concentrations during multiple organ dysfunction syndrome could describe the illness course better than CRP.

Further evidence was provided in a prospective cohort study conducted by Muller,<sup>44</sup> on 101 critically ill medical patients. The research aimed to compare the diagnostic power of PCT to other markers of inflammation, such as CRP, IL-6, and lactate levels, in the case of sepsis.

Serum procalcitonin levels proved to be the most efficient marker for identifying patients suffering from sepsis, compared to other variables. Moreover, a cut-off equal to 1 ng/mL showed the best power (sensitivity 89% and specificity 94%) for diagnosis. In addition to selecting septic patients over other critically ill patients, the elevated serum PCT concentrations were predictive of poor prognosis.

Similar data were provided by Ibrahim *et al.*<sup>45</sup> The group of researchers conducted a prospective cohort study on critically ill patients (73) admitted to a medical-surgical intensive care unit to identify the pattern of blood parameters that faithfully identified sepsis. Standard blood parameters (blood cell count and CRP) did not have the same diagnostic capability as PCT.

Furthermore, confirming data from other studies, the PCT cut-off >1 ng/mL had the greatest diagnostic and prognostic accuracy (75% diagnostic accuracy, 72% specificity, and 76% sensitivity).

When procalcitonin was tested in specific clinical settings, such as populations of community-acquired pneumonia, to evaluate both the potential benefits of diagnostic speed and accuracy and optimize clinical management in lower respiratory tract infections, the authors have obtained conflicting results.<sup>46-48</sup>

A relevant proposal has been provided by Muller *et al.*, suggesting a different behavior of serum procalcitonin levels between bacterial rather than viral pneumonia.

Analyzing a population of patients with a suspected clinical pattern for lower respiratory tract infection, the authors reported that procalcitonin had shown diagnostic

superiority over other markers in recognizing bacterial pneumonia. In detail, PCT showed greater diagnostic accuracy [area under the curve (AUC), 0.88 (0.84-0.93)], compared to high sensitivity CRP [AUC, 0.76 (0.69-0.83);  $P < 0.001$ ] and total white blood cell count [AUC, 0.69 (0.62-0.77);  $P < 0.001$ ].

Additionally, higher PCT levels were reported for bacteremia, even compared to high sensitivity CRP blood levels, white blood cell counts, and body temperature. In confirmation of the previous data, which wanted PCT as a prognostic marker, Muller *et al.* showed that PCT identified patients suffering from pneumonia with the worst course.<sup>49</sup>

Further insights into the diagnostic accuracy of PCT and its ability to identify patients with high mortality were provided by The Diagnostic and Prognostic Utility of Procalcitonin in Patients Presenting to the Emergency Department with Dyspnea (DPUP) study.<sup>50</sup>

The investigated population is made up of symptomatic patients for dyspnea who went to the emergency room. Of the total of 453, 30 patients presented a clinical pattern compatible with isolated pneumonia (6.6%), while for another 30 (6.6%), dyspnea resulted from a clinical pattern compatible with exacerbation of heart failure secondary to pneumonia. In both groups, pneumonia was associated with elevated PCT levels, compared to the other causes of dyspnea; PCT also provided a good diagnostic capability of pneumonia compared to dyspnea from other causes.

Similarly, other studies showed that the value of 0.10 ng/mL was recognized as the optimal cut-off (sensitivity 80% and specificity 77%, respectively) for the diagnosis of pneumonia. Interesting data concern the increase in the diagnostic power of PCT when associated with other markers. Furthermore, PCT is shown to be able to implement the differential diagnosis of dyspnea, discriminating between cardiac and infectious causes.

A study of similar design is the BACH study, conducted by Maisel *et al.*<sup>51</sup> It is a prospective, international study conducted on a population of 1641 subjects enrolled in the emergency room for the onset of dyspnea.

PCT has proved to be a powerful aid in the differential diagnosis of dyspnea, considering its high ability to identify pneumonia. Furthermore, an antibiotic therapy algorithm guided by PCT, could prove to be an adequate choice precisely in cases of diagnostic uncertainty to optimize its use. In particular, if patients showed high PCT ( $>0.21$  ng/mL) or low PCT levels ( $<0.05$  ng/mL), the prognosis was worse or better, if not treated with antibiotics ( $P=0.046$ ), or treated ( $P=0.049$ ), respectively. Accordingly, other studies showed an improvement in the accuracy of diagnosis and severity assessment of community acquired pneumonia for the approaches using PCT.<sup>46,52,53</sup>

Moreover, in the context of the diagnosis of pneumonia, contrary to the studies presented so far, Le Ben

*et al.* have shown evidence that PCT is not an adequate marker. In detail, the study in question is part of a sub-analysis related to a prospective multicenter study that evaluates the role of thoracic CT in the diagnosis of pneumonia in a population of 200 patients.<sup>52</sup>

Another clinical context in which PCT has been extensively evaluated is the one concerning abdominal infections, particularly the surgical patient. Elevated PCT levels have been found in subjects with abdominal infections, in both medical and surgical patients. In particular, its high predictive value for sepsis arising after abdominal surgery procedures was identified.<sup>54</sup>

Data conflict in cardiac surgery. In detail, in a study conducted on a population of 400 surgical patients, elevated PCT levels were strongly suggestive of post-cardiac surgical infection.<sup>26</sup> Also, in a population of cardiac surgery patients, elevated PCT values were more predictive of a septic shock than CRP.<sup>25</sup> On the other hand, the results of Dorge *et al.* were negative, which did not show a statistically significant relationship between PCT and sepsis.<sup>32</sup>

Sepsis of renal origin has also been the subject of investigation. In an analysis conducted on 49 patients with pyelonephritis complicating renal lithiasis, the predictive strength of PCT was confirmed statistically significant even after multivariate analysis. The analysis included different variables, such as blood cell count, renal function index, inflammatory markers, assessed as a marker of sepsis; at receiver operating characteristic (ROC) analysis, PCT showed the highest accuracy (AUC: 0.929 vs 0.822) and the cut-off value of 0.52 ng/mL, presented the best diagnostic power.<sup>55</sup>

The authors of the PBC-PCI study published relevant data. In particular, researchers conducted a retrospective analysis of data concerning 422 subjects enrolled in the emergency room for the suspicion of infection. The diagnostic accuracy of PCT in predicting blood culture positivation was statistically significant. The cut-off value of 0.5 ng/mL was associated with a positivation rate of the cultures of 34.0%.<sup>56</sup>

In the context of medical patients with multiple comorbidities, for which a systemic fungal superinfection may be hypothesized, the data of a retrospective case-control study (64 cases vs 128 controls) stand out, in which the authors demonstrated a negative predictive value of PCT  $>2.5$  ng/mL for identification of *Candida* species from blood cultures [AUC of 0.76 (0.68-0.84) 95% confidence interval (CI)].<sup>57</sup>

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### Meta-analyses on the diagnostic role of procalcitonin

Since 2006, meta-analyses evaluated both the diagnostic role of serum concentrations of PCT and the use of PCT-based algorithms in optimizing therapies in septic patients, providing conflicting results.<sup>58-67</sup> The

main meta-analyses that provided results in favor of the usefulness of PCT as a diagnostic marker are discussed in more detail below.<sup>58-66</sup>

First, the meta-analysis by Uzzan *et al.*<sup>58</sup> was conducted on a large population, for a total of 1826 patients from intensive care or predominantly surgical settings, suffering from sepsis of different severity. The control group consisted of 1545 patients with inflammatory response syndrome. The published data, although it must be taken into account that medical and immunosuppressed patients were excluded from the analysis, are statistically in favor of PCT as a marker of all the various clinical degrees of sepsis, even more so than CRP.

In the analysis conducted, a broad correction lacks multiple confounding factors; in particular, no sub-analysis takes into account the patient's clinical context and site of infection.

Studies investigating the use of PCT-based strategies<sup>61-64</sup> reported positive results.

In another relevant meta-analysis conducted by Wacker *et al.*<sup>65</sup> on a population of 3244 patients derived from 30 different clinical studies, authors suggested that PCT may have adequate diagnostic power for sepsis, particularly in critically ill patients. However, a correct clinical contextualization for an adequate interpretation of data is fundamental. This limitation was due essentially to the heterogeneity of the studies analyzed.

In a recent meta-analysis,<sup>66</sup> the role of CRP and PCT was compared in the optimization of differential fever diagnostics by analyzing data from 17 different studies. High values of both markers were found in patients with infection probably of bacterial origin, compared to the group with a fever of unknown origin; however, the sensitivity of PCT was greater than that of CRP, showing itself to be a more reliable marker, as can be easily seen from the ROC curves, for PCT [0.82 (95% CI, 0.78-0.86)] and CRP, respectively [0.78 (95% CI, 0.70-0.78)].

The extensive meta-analysis by Schuetz *et al.*<sup>67</sup> was conducted on a total population of 6708 derived from 26 different multicenter international studies to evaluate PCT levels for multiple endpoints concerning the presence of acute airways infection.

The utility of PCT has been tested not only in relation to its diagnostic capacity; in particular, it was investigated whether PCT levels could optimize therapeutic choices, guide patient management in the event of therapeutic failure, and, furthermore, identify patients at greater risk for poor prognosis.

In fact, the group of patients in which the diagnostic and therapeutic management was conducted based on PCT levels showed a better prognosis than the control group, whose path was conducted according to standard protocol. The use of PCT as an index to es-

tablish the duration of antimicrobial therapy also made it possible to optimize the duration [5.7 vs 8.1 days (95% CI -2.71 to -2.15),  $P < 0.0001$ ] and thus reduce the iatrogenic adverse effects [16% vs 22%, adjusted odds ratio (OR) 0.68 (95% CI 0.57 to 0.82),  $P < 0.0001$ ], compared to the control group.

However, although the evidence listed so far is substantially in favor of the role of PCT in the management of the infectious patient, data published by Tang *et al.*<sup>59</sup> are in contrast.

The data published by this group of researchers provided results of non-superiority of PCT compared to a standard marker panel, showing both low sensitivity and low diagnostic power. In particular, the analysis was conducted on a large population derived from 18 different studies, having however excluded from analyses all the cases concerning abdominal sepsis, pancreatitis, meningitis or septic shock; low values of sensitivity and specificity, equal to 71% (95% CI 67-76), and an area under the curve of 0.78 (95% CI 0.73-0.83) were reported.

Only Jones *et al.* reported inconclusive results.<sup>60</sup>

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### Prognostic role of procalcitonin in sepsis

The potential of PCT as a prognostic marker, *i.e.*, capable of identifying patients at risk of an inauspicious course of infectious disease or with a clinical pattern of relevant severity since presentation to the emergency department triage, has been widely debated.

In particular, since the nineties, various investigations have been carried out in this regard, which have provided conflicting results.

Most of the prospective studies,<sup>9,10,11-17,18-29,44,68-80</sup> showed a statistically significant correlation between serum procalcitonin concentrations and disease severity or outcome.

Prospective data on 246 patients with post-surgical abdominal infection confirmed a relationship between elevated PCT levels and mortality, with a statistically significant difference for PCT levels in patients not surviving compared to those with a better prognosis ( $P < 0.01$ ).<sup>70</sup>

In the TRIAGE study,<sup>71</sup> a recent observational, prospective, cohort, multicenter study, a PCT-based approach identified patients with worse prognosis (AUC 0.75), rapid clinical deterioration requiring admission to intensive care (AUC 0.62) or critical presentation since admission to the emergency room (AUC 0.58). These results were unaffected by other clinical variables, including age and different comorbidities.

When assessed during severe sepsis or septic shock, the kinetics of PCT assays in the first 72 hours after admission was considered a useful prognostic marker, rather than isolated measurements at patient

entry;<sup>72</sup> in particular, the percentage change in PCT between hospitalization and 72 hours and between 24 hours after admission and the following 72 hours, was an adequate mortality index at 30 days.<sup>72</sup> Confirming these data, Becker *et al.*<sup>73</sup> also reported that serial measurements of PCT and PCT kinetics were more useful in determining disease severity and prognosis<sup>73</sup> than absolute isolated samples; furthermore, the role of borderline or early-collected PCT values was downsized.

A PCT-based algorithm proposed in a work by De Jong *et al.*<sup>74</sup> provided new evidence of the utility of PCT regarding mortality in comparison with standard care. In more detail, the authors conducted a prospective intervention trial on 1575 critically ill patients admitted to the Intensive Care Unit (ICU); published results provided consistent evidence that clinical management monitoring PCT values in progress were associated with greater diagnostic accuracy and optimization in terms of therapeutic efficacy and safety. In particular, this approach allowed the early reduction of antibiotic therapy in 71% of patients [5 days (3-9) *versus* 7 days (4-11)], with the consequent reduction of adverse effects; moreover, the therapy was aimed at suspected cases, to increase its effectiveness with a consequent reduction in mortality at 28 days and 1 year.

By contrast, other prospective studies by Sudhir *et al.*,<sup>35</sup> Whang *et al.*,<sup>81</sup> Selberg *et al.*,<sup>68</sup> Castelli *et al.*,<sup>69</sup> and Dahaba *et al.*<sup>82</sup> found low or no correlation between serum concentrations of PCT and prognosis in sepsis.

### Meta-analysis and prognostic role of procalcitonin

In recent years, several studies<sup>75-89</sup> have investigated whether PCT levels were associated with different mortality endpoints in the septic patient. The several data available have highlighted that high PCT concentrations are associated with a worse prognosis, with a relative risk ranging from 1.38 to 24.62.

In particular, it was found that PCT changes over time are statistically significant in terms of mortality.<sup>90</sup>

Based on these data, PCT clearance was investigated in nine different studies,<sup>91-98</sup> for a total population of 868 patients. Subjects who had reduced PCT clearance at subsequent controls had a high risk of poor prognosis, as evidenced by the aggregate relative risk (RR) for mortality 3.05 (95% CI, 2.35-3.95). These studies are burdened by numerous limitations that do not fully clarify the potential of PCT as a prognostic marker. First, the accuracy of PCT could not be adequately estimated to predict death in emergency room patients; furthermore, the inability to perform subgroup analyses, in particular based on different admission categories or different infection sites, did not allow to de-

cline the potential of PCT in these different areas; as the last element, a cut-off value was not provided.

Similar data were obtained from a recent meta-analysis conducted on a large population of 3994 patients from 23 studies, in which both high PCT concentrations [2.60 (95% CI, 30)], and a reduced PCT clearance [RR was 3.05 (95% CI, 2.35-3.95)] are adequate markers of all-cause mortality in ongoing sepsis.<sup>99</sup>

### Procalcitonin and antibiotic therapy

The appropriate use of antibiotics is fundamental for ensuring the efficiency of treatment,<sup>100</sup> avoiding the development of drug resistance,<sup>101</sup> and improving patient safety.<sup>102</sup> Several pieces of evidence suggested the role of procalcitonin in targeting the correct use of antimicrobials in clinical therapy,<sup>103</sup> in comparison with other biomarkers.<sup>104</sup>

The role of serum PCT concentrations in monitoring for complications of sepsis has been evaluated in several prospective trials in the last 20 years.

In particular, the studies that have proposed to evaluate the relationship between PCT and management of antibiotic therapy have questioned whether this marker was able to indicate both when to start antibiotic therapy, its suspension and, therefore, its optimal duration.

In a study conducted on 165 patients hospitalized in a medical setting for community-acquired infections, a cut-off of 0.4 ng/mL showed the best negative predictive value (98.8%) compared to standard inflammatory markers.<sup>105-108</sup>

In a very select group of patients, such as those suffering from chronic obstructive pulmonary disease exacerbation, a decision algorithm based on PCT, aimed at identifying exacerbations on an infectious basis, managed to contain antibiotic prescriptions (40% *vs* 72%, respectively;  $P < 0.0001$ ), but without limiting the patient's recovery. Instead, an improvement was observed in terms of adverse effects related to therapy and inappropriate prescriptions, compared to a standard approach.<sup>48</sup>

Accordingly, Schroeder *et al.*<sup>109</sup> reported similar evidence. The authors elaborated a prospective randomized case-control study, conducted on 27 patients admitted to surgical intensive care, in which antibiotic therapy was started after positive culture tests, while PCT levels guided discontinuation of therapy with severe sepsis.<sup>109</sup> As in other studies, the PCT-led approach made it possible to reduce the duration of antibiotic therapy for the benefit of clinical safety and by optimizing the use of drug therapy, without significant differences in mortality.

In addition to the benefits in terms of clinical outcome and mortality, a rationalization of the use of antibiotic therapy has also shown a positive impact on

costs, expressed as a shorter length of hospitalization and less waste of pharmacological resources.<sup>107</sup>

However, caution is a must, considering other data in which an apparently targeted therapy did not improve the mortality rates of the populations examined.<sup>108,109</sup>

To confirm this, a study conducted on 1200 critically ill patients admitted to intensive care for different clinical reasons reported that a reduction in antimicrobial therapy, based on PCT, led to numerous complications, recorded in terms of organ failure, and an increased length of hospitalization and mortality.<sup>110,111</sup>

Other studies have also conservatively confirmed the benefit alone in reducing the duration of antibiotic therapy, and finally decreasing total hospital spending, cutting down unnecessary tests, procedures, and admission length, but without significantly affecting patient survival.<sup>112, 113</sup>

## Procalcitonin and COVID-19

The trend of procalcitonin levels in patients with severe acute respiratory syndrome-related coronavirus 2 infection has been recently investigated. In a retrospective study of 140 patients, divided into mild and severe clinical presentations, the latter had higher procalcitonin levels. However, these results are burdened by the smallness of the sample. The authors proposed as an explanation for this relationship that the most severe clinical presentation is associated with bacterial superinfection.<sup>114</sup> The results of a meta-analysis are in agreement with these data.<sup>115</sup> A ferritin/procalcitonin score was proposed as a diagnostic tool to differentiate COVID-19 from bacterial pneumonia in a case-control study. However, further studies are needed to clarify the real diagnostic scope<sup>116</sup> (Table 1<sup>11,20,23,26,27,32,70,108,117-122</sup>).

**Table 1. Different clinical uses of procalcitonin and related studies.**

Authors	Study population	Setting	Study parameters
Wanner <i>et al.</i> , 2000 <sup>11</sup>	133	Emergency Department and Trauma Intensive Care Unit	PCT was considered an early indicator of septic complication in trauma patients
Reith <i>et al.</i> , 2000 <sup>70</sup>	246	Surgical Intensive Care Unit	PCT as an indicator of complications, such as peritonitis, in septic patients, s/p abdominal surgery
Dorge <i>et al.</i> , 2003 <sup>32</sup>	80	Surgical Intensive Care Unit	PCT was an early predictor of postoperative complications
Benoist <i>et al.</i> , 1998 <sup>20</sup>	21	Surgical Intensive Care Unit	PCT identified sepsis in trauma patients
Rothenburger <i>et al.</i> , 1999 <sup>23</sup>	59	Surgical Intensive Care Unit	PCT indicated sepsis in postoperative cardiac patients
Baykut <i>et al.</i> , 2000 <sup>26</sup>	400	Surgical Intensive Care Unit	PCT was a predictor of sepsis in postoperative cardiac patients
Boeken <i>et al.</i> , 2000 <sup>27</sup>	74	Surgical Intensive Care Unit	PCT predicted sepsis in postoperative cardiac patients
Meisner <i>et al.</i> , 2002 <sup>117</sup>	208	Surgical Intensive Care Unit	PCT as an indicator of sepsis in postoperative cardiac patients
Hensler <i>et al.</i> , 2003 <sup>118</sup>	138	Trauma Intensive Care Unit and Surgical Intensive Care Unit	PCT as an early indicator of sepsis in major trauma patients
Mokart <i>et al.</i> , 2005 <sup>119</sup>	50	Surgical Intensive Care Unit	PCT was considered an indicator of postoperative infectious complication
Reith <i>et al.</i> , 1998 <sup>120</sup>	70	Surgical Intensive Care Unit	PCT as an early indicator of postoperative infectious complication
Castelli <i>et al.</i> , 2006 <sup>121</sup>	255	Medical and Surgical Intensive Care Unit	PCT was used in monitoring for sepsis in ICU patients
Lavrentieva <i>et al.</i> , 2007 <sup>108</sup>	43	Burn Intensive Care Unit	PCT as an early predictor of septic complication in burnpatients
Novotny <i>et al.</i> , 2009 <sup>122</sup>	104	Surgical Intensive Care Unit	PCT as an indicator for determining if repeat laparotomy is needed inpatients with prior laparotomy for infective source

PCT, procalcitonin; ICU, Intensive Care Unit.

## Conclusions

Recent evidence has suggested the role of procalcitonin in the rapid detection of septic conditions and in the management of antimicrobial therapy in different clinical settings. Significantly, the favorable effects of such approach led to an improvement in clinical outcomes; moreover, a reduction of health costs was obtained avoiding the administration of inappropriate antibiotic therapies and reducing the duration of hospitalization. However, there are conflicting data, which deserve further study and analysis.

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