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Corresponding author:

Victor Incze

vicincze@yahoo.com

Author Affiliation:"Iuliu Hatieganu" University of
Medicine and Pharmacy.

Popa, SL; Incze, V; Ismaiel, A; Surdea-Blaga, T; Grad, S; Turtoi, DC; Amarie, DS; David, L; Brata, VD; Leucuta, DC; Abdelghafar, A; Gherman, CD; Zahan, MR; Dumitrascu, DI.

ADMINISTRATIVE INFORMATION**Support** - This research received no external funding.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202620023**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 February 2026 and was last updated on 5 February 2026.**INTRODUCTION**

Review question / Objective Its objectives are to categorize the major clinical contexts in which procalcitonin rises in the absence of infection, to elucidate the underlying biological mechanisms contributing to these elevations, and to delineate the diagnostic scenarios in which procalcitonin may be misleading if interpreted without adequate clinical nuance.

Condition being studied Procalcitonin has become firmly established as a biomarker of substantial clinical importance in the assessment of systemic inflammatory responses, particularly in the differentiation of bacterial infections from inflammation of non-infectious origin.

METHODS

Participant or population Human participants across all age groups who have been evaluated for

non-infectious conditions associated with procalcitonin elevation.

Intervention N/A.

Comparator N/A.

Study designs to be included Eligible study designs included observational studies (prospective or retrospective cohort studies and case-control studies), clinical trials, and case series with ≥ 5 patients.

Eligibility criteria Studies were eligible if they met all of the following criteria: (i) conducted in human participants; (ii) published in English; (iii) reported quantitative PCT measurements (e.g., absolute values, ranges, or summary statistics); and (iv) investigated non-infectious contexts in which PCT may be elevated, including (but not limited to) trauma, surgery, shock, pancreatitis, burns, malignancy, and autoimmune/inflammatory

diseases. Eligible study designs included observational studies (prospective or retrospective cohort studies and case-control studies), clinical trials, and case series with ≥ 5 patients.

Studies were excluded if they: (i) focused exclusively on infectious etiologies of PCT elevation; (ii) were conducted in animals or in vitro without direct clinical correlation in humans; (iii) were reviews, editorials, letters, or conference abstracts without original patient-level data; or (iv) did not provide sufficient information to interpret PCT results (e.g., absence of measurement details and/or sampling time points).

Information sources A comprehensive literature search was performed in the following electronic databases: PubMed/MEDLINE, Embase, Web of Science, and Scopus.

Main outcome(s) For each included study, the following information was collected: (i) publication details (first author, year, country); (ii) study design and setting; (iii) sample size; (iv) participant characteristics (age, sex, clinical condition); (v) details of PCT assessment (assay or analytical method when reported, sampling time points relative to the clinical event, and reported PCT values/summary statistics); (vi) the non-infectious etiology associated with elevated PCT; (vii) mechanistic explanations proposed by the study authors; and (viii) clinical outcomes when available (e.g., severity measures, complications, mortality, length of stay).

Quality assessment / Risk of bias analysis

Methodological quality (risk of bias) was assessed at the study level using design-appropriate tools. The Newcastle-Ottawa Scale (NOS) was applied to cohort and case-control studies, and the Joanna Briggs Institute (JBI) critical appraisal checklist was applied to case series.

Strategy of data synthesis Findings were organized into clinically meaningful categories (trauma, surgery, shock, pancreatitis, burns, malignancy, autoimmune/inflammatory diseases). Where reported, PCT values were summarized descriptively (e.g., ranges, medians, means) and interpreted in relation to timing and clinical context. Proposed mechanistic pathways underlying non-infectious PCT elevation were extracted and synthesized across studies.

Subgroup analysis A quantitative meta-analysis was not undertaken due to heterogeneity and inconsistent reporting of effect measures. Findings were organized into clinically meaningful categories (trauma, surgery, shock, pancreatitis,

burns, malignancy, autoimmune/inflammatory diseases).

Sensitivity analysis A quantitative meta-analysis was not undertaken due to heterogeneity and inconsistent reporting of effect measures.

Country(ies) involved Romania.

Keywords procalcitonin; non-infectious inflammation; systemic inflammatory response; trauma; surgery; shock; acute pancreatitis; malignancy; renal failure; transplantation.

Contributions of each author

Author 1 - Stefan Lucian Popa.

Author 2 - Victor Incze.

Author 3 - Abrulrahman Ismaiel.

Author 4 - Teodora Surdea-Blaga.

Author 5 - Simona Grad.

Author 6 - Daria Claudia Turtoi.

Author 7 - Darius-Stefan Amarie.

Author 8 - Liliana David.

Author 9 - Vlad Dumitru Brata.

Author 10 - Daniel Corneliu Leucuta.

Author 11 - Ahmed Abdelghafar.

Author 12 - Claudia Diana Gherman.

Author 13 - Mihai Razvan Zahan.

Author 14 - Dinu Luliu Dumitrascu.