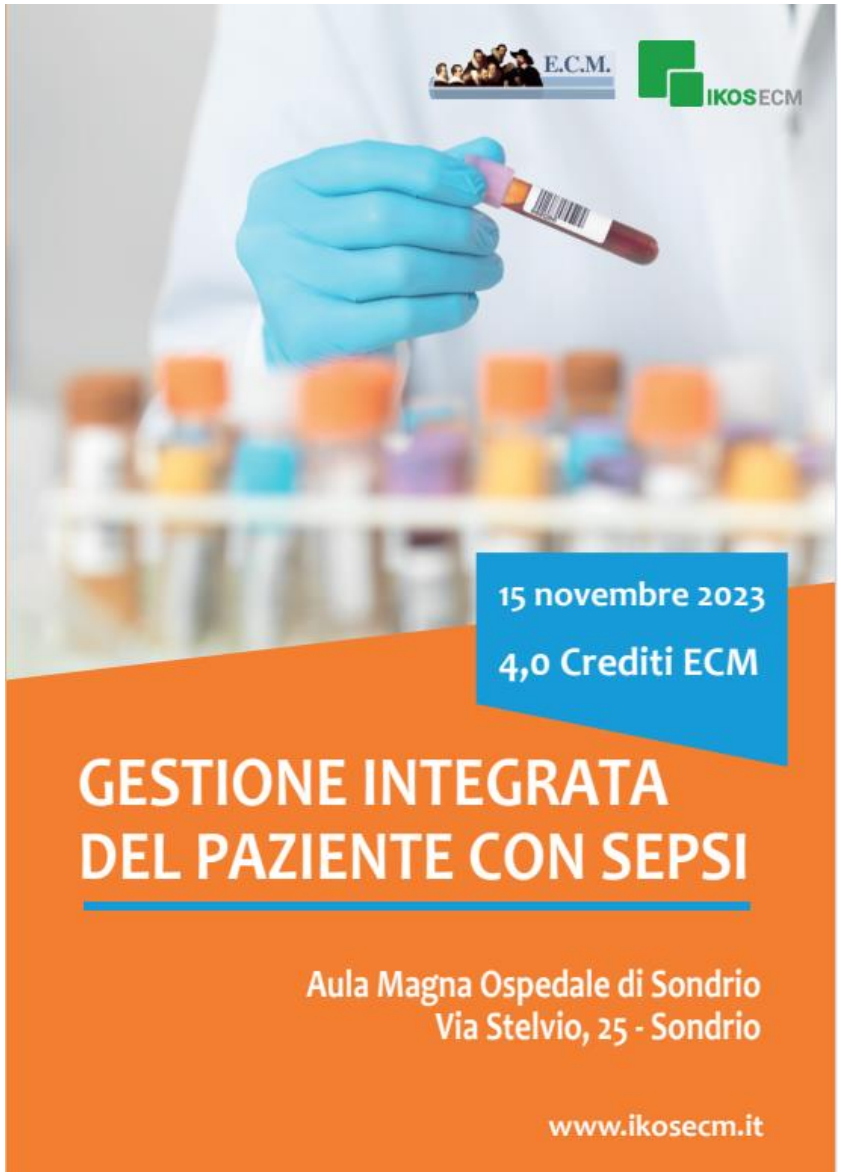
Fondazione IRCCS Policlinico San Matteo

Sistema Socio Sanitario

Regione Lombardia

# Biomarkers in "Acute Care Surgery and Trauma" (ACS&T)



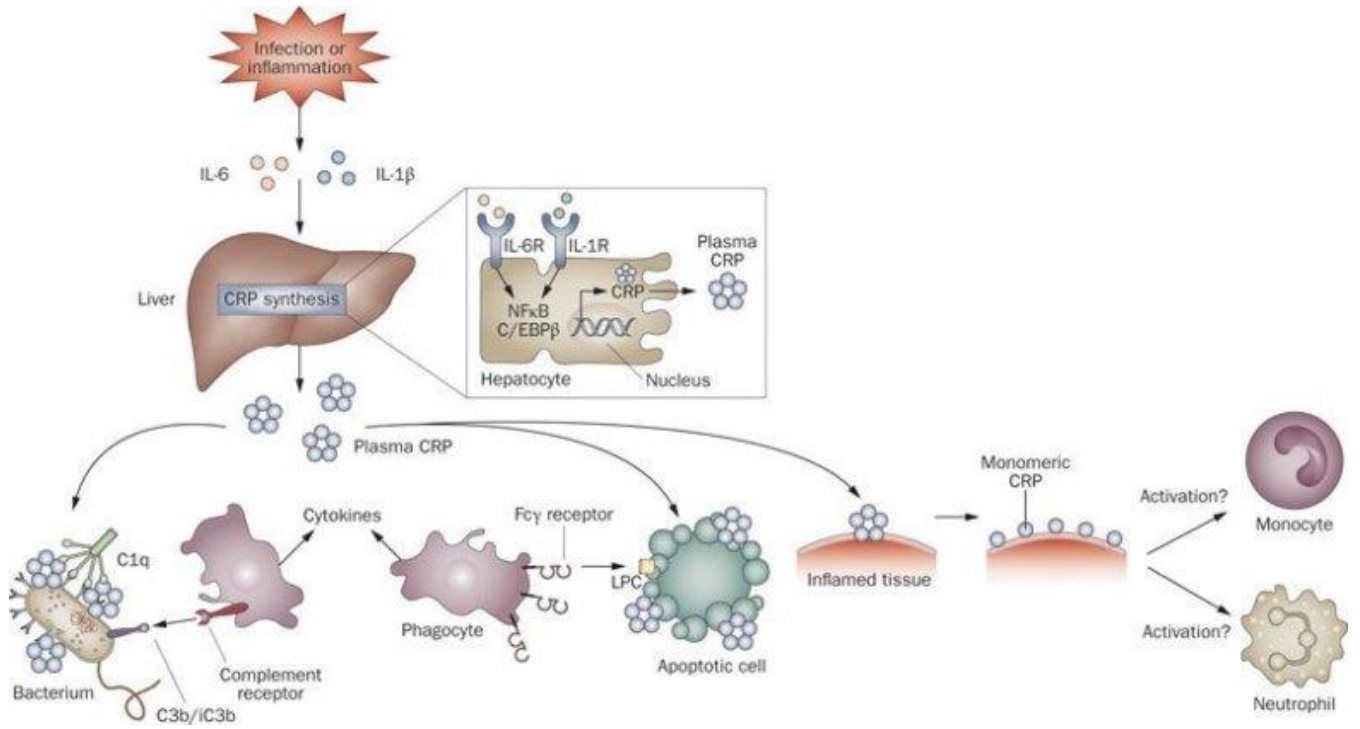

UNIVERSITÀ DI PAVIA


## Prof. Luca Ansaloni

Head, General Surgery I,
IRCCS San Matteo Hospital Foundation,
University of Pavia,
Italy

# Background: CRP and PTC

- ✓ among several markers of inflammation and sepsis, procalcitonin (PCT) and C-reactive protein (CRP) markers are being studied to investigate their accuracy for diagnosis of bacterial infections
- ✓ CRP is synthesized by liver, mainly in response to IL-6, which is produced not only during infection but also in many types of inflammation and binds to polysaccharides in pathogens, activating the classical complement pathway. CRP is an acute-phase reactant, and CRP level measurements are frequently used to aid in the diagnosis of bacterial infections.

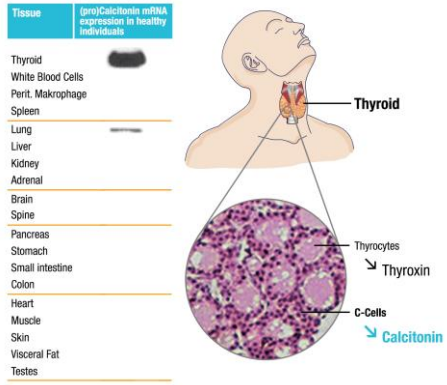


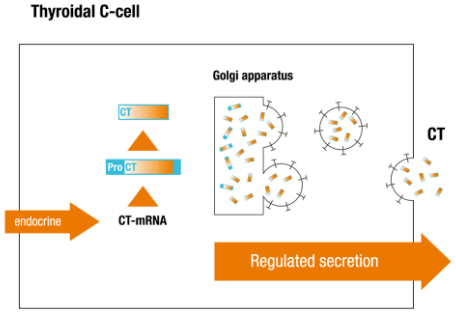


Whicher J, et al. Procalcitonin as an acute phase marker. Ann Clin Biochem 2001; 38:483–93.
Nijsten MW, et al. Procalcitonin behaves as a fast responding acute phase protein in vivo and in vitro. Crit Care Med 2000; 28:458–61.
Oberhoffer M, et al. Procalcitonin expression in human peripheral blood mononuclear cells and its modulation by lipopolysaccharides and sepsis-related cytokines in vitro. J Lab Clin Med 1999 ; 134:49–55.
Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation 2003; 107:363–9

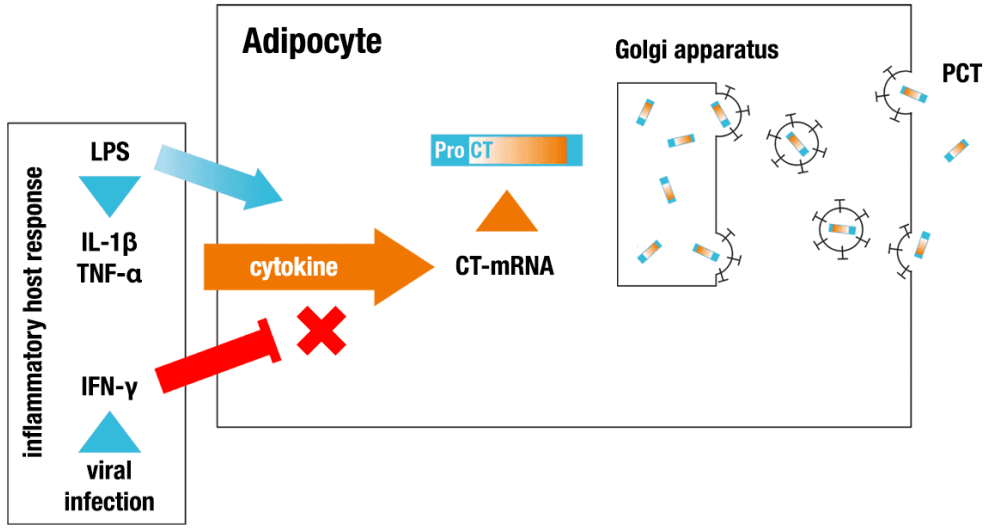
# Background: CRP and PTC

- ✓ PCT is calcitonin prehormone, which is normally secreted by thyroid C cells in response to hypercalcemia; under these normal conditions, negligible serum PCT concentrations are detected. The mechanism proposed for PCT production after inflammation and its role are still not completely known. It is believed that PCT is produced by liver and peripheral blood mononuclear cells, modulated by lipopolysaccharides and sepsis-related cytokines.
- ✓ reported diagnostic accuracy of PCT and CRP for the diagnosis of bacterial infections has varied across studies.









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Oberhoffer M, et al. Procalcitonin expression in human peripheral blood mononuclear cells and its modulation by lipopolysaccharides and sepsis-related cytokines in vitro. J Lab Clin Med 1999 ; 134:49–55.
Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation 2003; 107:363–9

# Background: CRP and PTC

**diagnostic accuracy of PCT is higher than that of CRP among pts hospitalized for suspected bacterial infections**

REVIEW ARTICLE

Clinical Infectious Diseases 2004; 39:206–17

## Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis

Liliana Simon,[1] France Gauvin, [2] Devendra K. Amre,[2] Patrick Saint-Louis,[3] and Jacques Lacroix[2]

[1]Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut; and Departments of [2]Pediatrics and [3]Clinical Biochemistry, University of Montreal, Quebec

**A meta-analysis was performed to evaluate the accuracy of determination of procalcitonin (PCT) and C-reactive protein (CRP) levels for the diagnosis of bacterial infection. The analysis included published studies that evaluated these markers for the diagnosis of bacterial infections in hospitalized patients. PCT level was more sensitive (88% [95% confidence interval {CI}, 80%–93%] vs. 75% [95% CI, 62%–84%]) and more specific (81% [95% CI, 67%–90%] vs. 67% [95% CI, 56%–77%]) than CRP level for differentiating bacterial from noninfective causes of inflammation. The Q value for PCT markers was higher (0.82 vs. 0.73). The sensitivity for differentiating bacterial from viral infections was also higher for PCT markers (92% [95% CI, 86%–95%] vs. 86% [95% CI, 65%–95%]); the specificities were comparable (73% [95% CI, 42%–91%] vs. 70% [95% CI, 19%–96%]). The Q value was higher for PCT markers (0.89 vs. 0.83). PCT markers also had a higher positive likelihood ratio and lower negative likelihood ratio than did CRP markers in both groups. On the basis of this analysis, the diagnostic accuracy of PCT markers was higher than that of CRP markers among patients hospitalized for suspected bacterial infections.**

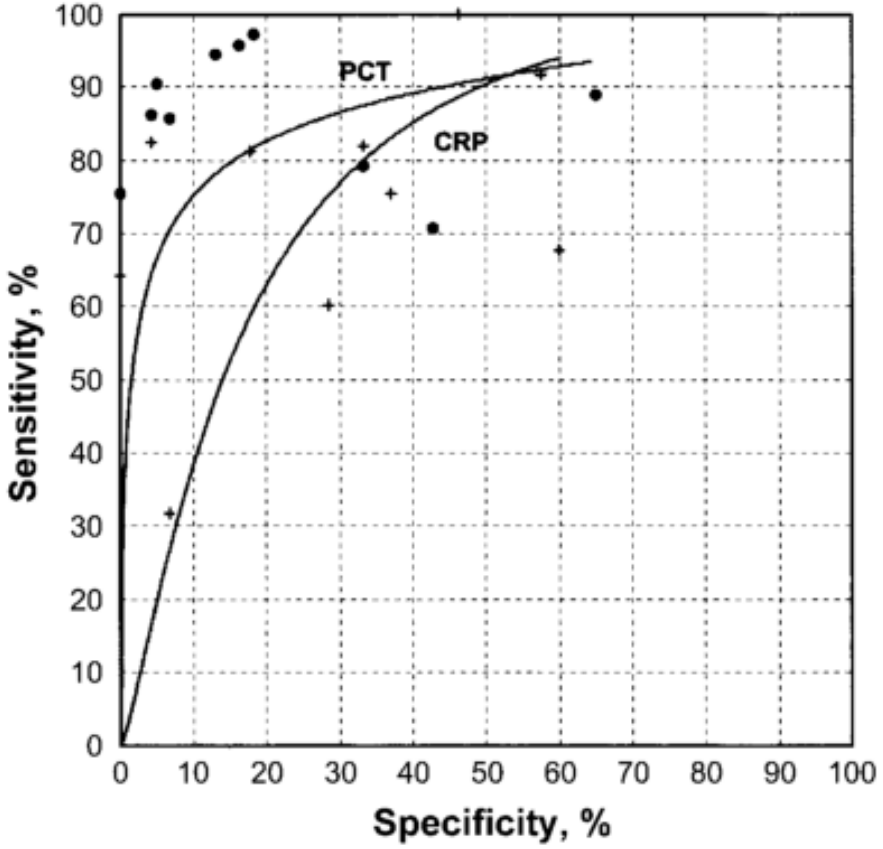



**Figure 1.** Summary receiver operating characteristic (SROC) curves comparing serum procalcitonin (PCT; ●) and C-reactive protein (CRP; +) markers for detection of bacterial infections versus noninfective causes of inflammation. Each point contributing to the SROC curve represents 1 study.

# Background: CRP and PTC

*J Antimicrob Chemother* 2011; **66** Suppl 2: ii33–ii40
doi:10.1093/jac/dkq523

Journal of Antimicrobial Chemotherapy

## Diagnostic and prognostic biomarkers of sepsis in critical care

**Savitri Kibe [1], Kate Adams [1] and Gavin Barlow [1,2]***

[1]*Department of Infection & Tropical Medicine, Castle Hill Hospital, Hull and East Yorkshire Hospitals NHS Trust, Cottingham, East Yorkshire, UK;* [2]*Hull York Medical School, Hull, UK*

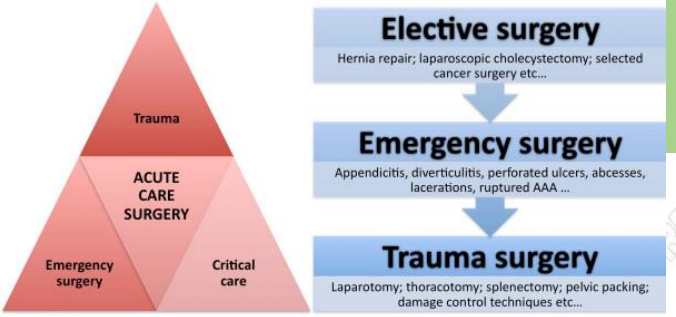
*Corresponding author. Tel: +44-1482-875875 ext. 2267; Fax: +44-1482-622492; E-mail: gavin.barlow@hey.nhs.uk

Sepsis is a leading cause of mortality in critically ill patients. Delay in diagnosis and initiation of antibiotics have been shown to increase mortality in this cohort. However, differentiating sepsis from non-infectious triggers of the systemic inflammatory response syndrome (SIRS) is difficult, especially in critically ill patients who may have SIRS for other reasons. It is this conundrum that predominantly drives broad-spectrum antimicrobial use and the associated evolution of antibiotic resistance in critical care environments. It is perhaps unsurprising, therefore, that the search for a highly accurate biomarker of sepsis has become one of the holy grails of medicine. Procalcitonin (PCT) has emerged as the most studied and promising sepsis biomarker. For diagnostic and prognostic purposes in critical care, PCT is an advance on C-reactive protein and other traditional markers of sepsis, but is not accurate enough for clinicians to dispense with clinical judgement. There is stronger evidence, however, that measurement of PCT has a role in reducing the antibiotic exposure of critical care patients. For units intending to incorporate PCT assays into routine clinical practice, the cost-effectiveness of this is likely to depend on the pre-implementation length of an average antibiotic course and the subsequent impact of implementation on emerging antibiotic resistance. In most of the trials to date, the average baseline duration of the antibiotic course was longer than is currently standard practice in many UK critical care units. Many other biomarkers are currently being investigated. To be highly useful in clinical practice, it may be necessary to combine these with other novel biomarkers and/or traditional markers of sepsis.

**Keywords:** procalcitonin, intensive care, antibiotic stewardship

- In the diagnosis and prognosis of sepsis in critically ill pts, PCT is an improvement on CRP and other traditional markers, but, based on current evidence, it lacks the necessary accuracy to be used without clinical judgement, which should retain a pivotal role in clinical decision-making.
- This is particularly important in pts who present early in the course of illness or have focal rather than systemic infection and in surgical pts in whom various cut-off points have been identified for different diagnoses.
- PCT may be better employed to rule out rather than rule in systemic sepsis in the critical care environment, particularly if repeated measures are used.
- There is stronger evidence for its use as a tool to reduce antibiotic course length and it is perhaps in this role that it will prove most useful. However, the cost-effectiveness of PCT as an antibiotic stewardship tool is likely to depend on baseline antibiotic course length and its, as yet unknown, impact on antibiotic resistance. Critical care units intending to use PCT should consider these issues pre-implementation.

# What about ACS&T: INTRAABDOMINAL SEPSIS TREATMENT




**Elective surgery**
Hernia repair; laparoscopic cholecystectomy; selected cancer surgery etc...

**Emergency surgery**
Appendicitis, diverticulitis, perforated ulcers, abcesses, lacerations, ruptured AAA ...

**Trauma surgery**
Laparotomy; thoracotomy; splenectomy; pelvic packing; damage control techniques etc...



## The "TEMPLE"
## The sacred rules of sepsis tx

**early & appropriate**

CRP dosing can guide the clinician in the diagnosis of intra-abdominal infections.

1

# Acute appendicitis +/-
# Acute diverticulitis +/-

Sartelli et al. World Journal of Emergency Surgery (2020) 15:32
https://doi.org/10.1186/s13017-020-00313-4

World Journal of Emergency Surgery

REVIEW Open Access

## 2020 update of the WSES guidelines for the management of acute colonic diverticulitis in the emergency setting

Massimo Sartelli[1*], Dieter G. Weber[2], Yoram Kluger[3], Luca Ansaloni[4], Federico Coccolini[5], Fikri Abu-Zidan[6], Goran Augustin[7], Offir Ben-Ishay[3], Walter L. Biffl[8], Konstantinos Bouliaris[9], Rodolfo Catena[10], Marco Ceresoli[11,12], Osvaldo Chiara[13], Massimo Chiarugi[5], Raul Coimbra[14], Francesco Cortese[15], Yunfeng Cui[16], Dimitris Damaskos[17], Gian Luigi de' Angelis[18], Samir Delibegovic[19], Zaza Demetrashvili[20], Belinda De Simone[21], Francesco Di Marzo[22], Salomone Di Saverio[23], Therese M. Duane[24], Mario Paulo Faro[25], Gustavo P. Fraga[26], George Gkiokas[27], Carlos Augusto Gomes[28], Timothy C. Hardcastle[29], Andreas Hecker[30], Aleksandar Karamarkovic[31], Jeffry Kashuk[32], Vladimir Khokha[33], Andrew W. Kirkpatrick[34], Kenneth Y. Y. Kok[35], Kenji Inaba[36], Arda Isik[37], Francesco M. Labricciosa[38], Rifat Latifi[39], Ari Leppäniemi[40], Andrey Litvin[41], John E. Mazuski[42], Ronald V. Maier[43], Sanjay Marwah[44], Michael McFarlane[45], Ernest E. Moore[46], Frederick A. Moore[47], Ionut Negoi[48], Leonardo Pagani[49], Kemal Rasa[50], Ines Rubio-Perez[51], Boris Sakakushev[52], Norio Sato[53], Gabriele Sganga[54], Walter Siquini[1], Antonio Tarasconi[10], Matti Tolonen[40], Jan Ulrych[55], Sannop K. Zachariah[56] and Fausto Catena[10]

Di Saverio et al. World Journal of Emergency Surgery (2020) 15:27
https://doi.org/10.1186/s13017-020-00306-3

World Journal of Emergency Surgery

REVIEW Open Access

## Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines

Salomone Di Saverio[1,2*], Mauro Podda[3], Belinda De Simone[4], Marco Ceresoli[5], Goran Augustin[6], Alice Gori[7], Marja Boermeester[8], Massimo Sartelli[9], Federico Coccolini[10], Antonio Tarasconi[4], Nicola de' Angelis[11], Dieter G. Weber[12], Matti Tolonen[13], Arianna Birindelli[14], Walter Biffl[15], Ernest E. Moore[16], Michael Kelly[17], Kjetil Soreide[18], Jeffry Kashuk[19], Richard Ten Broek[20], Carlos Augusto Gomes[21], Michael Sugrue[22], Richard Justin Davies[1], Dimitrios Damaskos[23], Ari Leppäniemi[13], Andrew Kirkpatrick[24], Andrew B. Peitzman[25], Gustavo P. Fraga[26], Ronald V. Maier[27], Raul Coimbra[28], Massimo Chiarugi[10], Gabriele Sganga[29], Adolfo Pisanu[3], Gian Luigi de' Angelis[30], Edward Tan[20], Harry Van Goor[20], Francesco Pata[31], Isidoro Di Carlo[32], Osvaldo Chiara[33], Andrey Litvin[34], Fabio C. Campanile[35], Boris Sakakushev[36], Gia Tomadze[37], Zaza Demetrashvili[37], Rifat Latifi[38], Fakri Abu-Zidan[39], Oreste Romeo[40], Helmut Segovia-Lohse[41], Gianluca Baiocchi[42], David Costa[43], Sandro Rizoli[44], Zsolt J. Balogh[45], Cino Bendinelli[45], Thomas Scalea[46], Rao Ivatury[47], George Velmahos[48], Roland Andersson[49], Yoram Kluger[50], Luca Ansaloni[51] and Fausto Catena[4]

Sartelli et al. World Journal of Emergency Surgery (2017) 12:29
DOI 10.1186/s13017-017-0141-6

World Journal of Emergency Surgery

REVIEW Open Access

## The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections

Massimo Sartelli[1*], Alain Chichom-Mefire[2], Francesco M. Labricciosa[3], Timothy Hardcastle[4], Fikri M. Abu-Zidan[5], Abdulrashid K. Adesunkanmi[6], Luca Ansaloni[7], Miklosh Bala[8], Zsolt J. Balogh[9], Marcelo A. Beltrán[10], Offir Ben-Ishay[11], Walter L. Biffl[12], Arianna Birindelli[13], Miguel A. Cainzos[14], Gianbattista Catalini[1], Marco Ceresoli[7], Asri Che Jusoh[15], Osvaldo Chiara[16], Federico Coccolini[7], Raul Coimbra[17], Francesco Cortese[18], Zaza Demetrashvili[19], Salomone Di Saverio[13], Jose J. Diaz[20], Valery N. Egiev[21], Paula Ferrada[22], Gustavo P. Fraga[23], Wagih M. Ghnnam[24], Jae Gil Lee[25], Carlos A. Gomes[26], Andreas Hecker[27], Torsten Herzog[28], Jae Il Kim[29], Kenji Inaba[30], Arda Isik[31], Aleksandar Karamarkovic[32], Jeffry Kashuk[33], Vladimir Khokha[34], Andrew W. Kirkpatrick[35], Yoram Kluger[36], Kaoru Koike[37], Victor Y. Kong[38], Ari Leppaniemi[39], Gustavo M. Machain[40], Ronald V. Maier[41], Sanjay Marwah[42], Michael E. McFarlane[43], Giulia Montori[7], Ernest E. Moore[44], Ionut Negoi[45], Iyiade Olaoye[46], Abdelkarim H. Omari[47], Carlos A. Ordonez[48], Bruno M. Pereira[23], Gerson A. Pereira Júnior[49], Guntars Pupelis[50], Tarcisio Reis[51], Boris Sakakushev[52], Norio Sato[53], Helmut A. Segovia Lohse[40], Vishal G. Shelat[54], Kjetil Søreide[55,56], Waldemar Uhl[28], Jan Ulrych[56], Harry Van Goor[57], George C. Velmahos[58], Kuo-Ching Yuan[59], Imtiaz Wani[60], Dieter G. Weber[61], Sanoop K. Zachariah[62] and Fausto Catena[63]

**Abstract**

Intra-abdominal infections (IAIs) are common surgical emergencies and have been reported as major contributors to non-trauma deaths in the emergency departments worldwide.
The cornerstones of effective treatment of IAIs are early recognition, adequate source control, and appropriate antimicrobial therapy. Prompt resuscitation of patients with ongoing sepsis is of utmost important.
In hospitals worldwide, non-acceptance of, or lack of access to, accessible evidence-based practices and guidelines result in overall poorer outcome of patients suffering IAIs.
The aim of this paper is to promote global standards of care in IAIs and update the 2013 WSES guidelines for management of intra-abdominal infections.

**Keywords:** Intra-abdominal infections, Sepsis, Peritonitis, Antibiotics

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Full list of author information is available at the end of the article

CRP dosing can guide the clinician in the diagnosis of intra-abdominal infections.

## Acute appendicitis

## Complicated

Int. J. Med. Sci. 2012, 9 909

IVYSPRING INTERNATIONAL PUBLISHER

International Journal of Medical Sciences

2012; 9(10):909-915. doi: 10.7150/ijms.4733

Research Paper

### The Diagnostic Value of D-dimer, Procalcitonin and CRP in Acute Appendicitis

Bulent Kaya[1], Baris Sana[2], Cengiz Eris[3], Koray Karabulut[4], Orhan Bat[5], Riza Kutanis[6]

### Role of Alvarado score and biological indicators of C-reactive protein, procalicitonin and neopterin in diagnosis of acute appendicitis

Fatih Dal, M.D.,[1] Yusuf Çiçek, M.D.,[2] Salih Pekmezci, M.D.,[2] Bekir Kocazeybek, M.D.,[3] Hrisi Bahar Tokman, M.D.,[3] Dildar Konukoğlu, M.D.,[4] Osman Şimşek, M.D.,[2] Zeynep Taner, M.D.,[3] Serhat Sirekbasan, M.D.,[3] Server Sezgin Uludağ, M.D.[2]

Ulus Travma Acil Cerrahi Derg, May 2019, Vol. 25, No. 3

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

2019

### The value of ischemia-modified albumin and oxidative stress markers in the diagnosis of acute appendicitis in adults

Hakan Hakkoymaz, MD[a,*], Selçuk Nazik, MD[b], Muhammed Seyithanoğlu, MD[c], Özlem Güler, MD[a], Ahmet Rıza Şahin, MD[b], Emrah Cengiz, MD[d], Fatih Mehmet Yazar, MD[e]

PCT dosing can guide the clinician in the diagnosis of intra-abdominal infections.

Complicated+++

European Journal of Trauma and Emergency Surgery
https://doi.org/10.1007/s00068-019-01116-2

ORIGINAL ARTICLE

## Procalcitonin as an excellent differential marker between uncomplicated and complicated acute appendicitis in adult patients

Yanxiu Li[1,2] · Zhongwen Zhang[3] · Iokfai Cheang[1] · Xinli Li[1]

Received: 10 January 2019 / Accepted: 26 March 2019


**Abstract**

**Purpose** The aim of this study was to assay the variation of procalcitonin (PCT) in adult patients with uncomplicated and complicated acute appendicitis.

**Methods** In total, 336 patients who underwent appendectomy from January 2016 to December 2017 were enrolled. Levels of inflammatory markers, the highest body temperature within the first 24 h of admission ($BT^m$) and the duration of operation were recorded. All appendectomy specimens were sent for histopathological examination. According to the histopathological results, 336 patients who underwent appendectomy were divided into uncomplicated acute appendicitis (UAA) group (246 cases) and complicated acute appendicitis (CAA) group (90 cases) for further analysis. The relationships of procalcitonin (PCT) and related indicators with UAA and CAA were evaluated by receiver operating characteristic (ROC) and binary logistic regression analysis.

**Results** Age, the levels of PCT, and CRP were significantly higher in CAA group ($P < 0.05$). Spearman correlation analysis showed that PCT was positively correlated with age ($r = 0.452$, $P < 0.01$) and CRP ($r = 0.715$, $P < 0.01$). The area under the curve (AUC) of PCT, CRP and age were 0.987, 0.902, and 0.748, respectively. ROC analysis showed when PCT > 0.42 ng/ml, it maximized the sensitivity and specificity. Logistic regression analysis indicated that PCT remained an independent risk factor for diagnosing CAA after adjusting with age and CRP ($P < 0.05$).

**Conclusions** Serum PCT levels increased significantly in patients with CAA. PCT could provide convenient evaluation method for the optimal treatment of acute appendicitis.

**Keywords** Procalcitonin (PCT) · Complicated acute appendicitis (CAA) · Treatment · Appendectomy · ROC curve

CIRUGIA Y CIRUJANOS

ORIGINAL ARTICLE

## Predictive biomarkers for complicated acute appendicitis: A prospective Ecuadorian study

*Biomarcadores predictores de apendicitis aguda complicada: estudio prospectivo en Ecuador*

*Juan Orellana-Henriquez[1], Ivan Robalino-Rodriguez[2], Hugo Sanchez-Alban[2], John Franco-Orellana[3], Roberto Oleas[4], Jorge Baquerizo-Burgos[4], Mario Patiño-Aquin[3], Carlos Torres-Herrera[5], and Miguel Puga-Tejada[4]**

[1]Faculty of Medical Sciences "Enrique Ortega Moreira", Universidad de Especialidades Espíritu Santo (UEES), Samborondón; [2]Faculty of Medical Sciences, Universidad Católica de Santiago de Guayaquil (UCSG), Guayaquil; [3]Teaching Department, Hospital Teodoro Maldonado Carbo (HTMC), Guayaquil, Ecuador; [4]Clinical Research, Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador; [5]Faculty of Social Sciences, Universidad de Palermo (UP), Buenos Aires, Argentina*

**Abstract**

**Aim:** *The aim of the study was to determine the usefulness of known biomarkers as pre-operative predictors of complicated acute appendicitis (CAA) and perforated appendicitis (PA).* **Materials and methods:** *This was an observational, analytic, cross-sectional, and prospective study at Hospital Teodoro Maldonado Carbo (August 2016-December 2017). Evaluated biomarkers: white blood cells count, neutrophil percentage (N%), neutrophil-to-lymphocyte ratio, glucose, total bilirubin, C-reactive protein, and procalcitonin (PCT). The statistical analysis was performed by means of the area under the receiver operating characteristics (AUROC) curve estimation. Biomarkers' cutoff point was identified using Youden's index. Sensitivity, specificity, positive, and negative predictive value (NPV) (positive predictive value [PPV] and NPV) were estimated.* **Results:** *One hundred and twenty-eight cases were included (median age 30 years, 44% female), 70 cases (54%) corresponded to CAA (PA 38/70). N% and PCT obtained an AUROC of 78% and 80% for CAA (PA 76% and 81%), respectively. A N% > 78.1% predicted CAA with a sensitivity, specificity, PPV, and NPV of 82%, 62%, 72%, and 72% (> 74.9%, PA: 94%, 53%, 46%, and 96%), respectively. PCT > 0.14 ng/dL predicted CAA with sensitivity, specificity, PPV, and NPV of 69%, 79%, 80%, and 68% (PA: 84%, 69%, 53%, and 91%).* **Conclusion:** *The N% and PCT represent useful pre-operative biomarkers for discarding PA when an acute appendicitis is suspected.*

Acute appendicitis

PCT dosing can guide the clinician in the diagnosis of intra-abdominal infections.

Acute appendicitis in children

Diagnosis+
Complicated+++

Cui et al. Italian Journal of Pediatrics (2019) 45:78
https://doi.org/10.1186/s13052-019-0673-3

Italian Journal of Pediatrics

REVIEW Open Access

## Diagnostic accuracy of procalcitonin for overall and complicated acute appendicitis in children: a meta-analysis

Wei Cui[1,2], Haipeng Liu[1,2*], Hong Ni[1,2], Xianhui Qin[3] and Liran Zhu[1,2]

**Abstract**

**Background:** Diagnostic value of procalcitonin (PCT) for acute appendicitis (AA) has been evaluated in adult patients, but the application in children remains controversial. The aim of this study was to evaluate the diagnostic value of PCT for overall and complicated AA in children.

**Methods:** The PubMed, EMBASE, Web of Science, Cochrane Database of Systematic Reviews, Chinese National Knowledge Infrastructure, and Wanfang were searched along with reference lists of relevant articles up to January 2018 without language restrictions. Original articles that reported the performance of PCT in the diagnosis of pediatric AA and associated complications were selected. To assess the diagnostic value of PCT, sensitivity, specificity, diagnostic odds ratios (DORs), summary receiver operating characteristic (ROC) curves, area under the curve (AUC), and 95% confidence intervals (95% CIs) were estimated.

**Results:** Seven qualifying studies (504 confirmed AA and 368 controls) from 6 countries for overall AA and 4 studies (187 complicated AA and 185 uncomplicated AA) for complicated AA from 3 countries were identified. The pooled sensitivity and specificity of PCT for the diagnosis of pediatric AA were 0.62 (95% CI: 0.57–0.66) and 0.86 (95% CI: 0.82–0.89), respectively. The DOR was 21.4 (95% CI: 3.64–126.1) and the AUC was 0.955. PCT was more accurate in diagnosing complicated appendicitis, with a pooled sensitivity of 0.89 (95% CI: 0.84–0.93), specificity of 0.90 (95% CI: 0.86–0.94), and DOR of 76.73 (95% CI: 21.6–272.9).

**Conclusion:** This meta-analysis showed that PCT may have potential value in diagnosing pediatric AA. Moreover, PCT had greater diagnostic value in identifying pediatric complicated appendicitis.

**Keywords:** Acute appendicitis, Diagnosis, Meta-analysis, Pediatric, Procalcitonin

PTC dosing can guide the clinician in the diagnosis of cholecystitis severity

2

Acute cholecystitis severity +++

ORIGINAL PAPERS

**Can inflammatory biomarkers help in the diagnosis and prognosis of gangrenous acute cholecystitis? A prospective study**

Jose Ángel Díez Ares[1], Rosario Martínez García[1], Nuria Estellés Vidagany[1], Nuria Peris Tomás[1], Manuel Planells Roig[1], Marta Valenzuela Gras[1] and Tomás Ripollés González[2]

*Departments of [1]Surgery and [2]Radiology. Hospital Doctor Peset. Valencia, Spain*

**Received:** 26/05/2020 · **Accepted:** 27/05/2020

**Correspondence:** Jose Ángel Díez Ares. Department of Surgery. Hospital Doctor Peset. Av. Gaspar Aguilar, 90. 46017 Valencia, Spain. **e-mail:** jdiezares@gmail.com

Eurasian J Med 2016; 48: 162-6 — The Eurasian Journal of Medicine — Original Article

**Role of Procalcitonin in Evaluation of the Severity of Acute Cholecystitis**

*Akut Kolesistitin Şiddetini Belirlemede Prokalsitoninin Yeri*

Yucel Yuzbasioglu[1], Hikmet Duymaz[2], Ceren Sen Tanrikulu[3], Huseyin Cahit Halhalli[4], Mirac Ozturk Koc[5], Meral Tandoğan[6], Figen Coskun[7]

Hindawi
Emergency Medicine International
Volume 2020, Article ID 8329310, 6 pages
https://doi.org/10.1155/2020/8329310

*Research Article*

**Plasma Procalcitonin Is Useful for Predicting the Severity of Acute Cholecystitis**

**Saben Sakalar,[1] Engin Ozakın,[1] Arif Alper Cevik,[2] Nurdan Acar,[1] Serkan Dogan,[1] Filiz Baloglu Kaya,[1] and Taylan Kara[1]**

## PTC dosing can guide the clinician in the diagnosis of cholecystitis severity

Acute cholecystitis severity: difficult laparoscopic cholecystectomy and major complications

www.nature.com/scientificreports

SCIENTIFIC REPORTS
nature research

OPEN

### Role of procalcitonin as a predictor in difficult laparoscopic cholecystectomy for acute cholecystitis case: A retrospective study based on the TG18 criteria

Tianchong Wu[1], Minjun Luo[2], Yuehua Guo[1], Jiangang Bi[1], Yusheng Guo[1] & Shiyun Bao[1]

Received: 1 November 2018
Accepted: 17 July 2019
Published online: 29 July 2019

Difficult laparoscopic cholecystectomy (DLC) is difficult to precisely predict before operation. This observational cohort study aimed to evaluate the predictive value of procalcitonin (PCT) for DLC in patients with acute cholecystitis (AC). A total of 115 patients were included in the study from January 2017 to April 2018. Multiple logistic regression and receiver-operating characteristic (ROC) were performed to evaluate the predictive value of PCT levels in DLC. Patients with DLC had significantly higher Tokyo Guidelines 2018 (TG18) grade ($P = 0.002$) and levels of C-reactive protein (CRP) ($P = 0.007$) and PCT ($P < 0.001$). The cut-off value of PCT for predicting DLC was 1.50 ng/ml. The sensitivity and specificity were 91.3% (95% CI 78.3–97.1) and 76.8% (95% CI 64.8–85.8), respectively. The area under ROC curve was 92.7% (95% CI 88.2–97.3, $P < 0.001$). Our results suggested that PCT was a good predictor for DLC in the AC patients, but further research is necessary. Monitoring of PCT trends in AC patients may be useful for preoperative risk assessment.

Langenbeck's Archives of Surgery
https://doi.org/10.1007/s00423-021-02252-3

ORIGINAL ARTICLE

### Role of serum procalcitonin in predicting the surgical outcomes of acute calculous cholecystitis

Pietro Fransvea[1] · Marcello Covino[2,3] · Fausto Rosa[3,4] · Caterina Puccioni[1] · Giuseppe Quero[4] · Valerio Cozza[1] · Antonio La Greca[1,3] · Francesco Franceschi[2,3] · Sergio Alfieri[3,4] · Gabriele Sganga[1,3]

Received: 12 April 2021 / Accepted: 16 June 2021


**Abstract**

**Background** Acute calculous cholecystitis (AC) is a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation. In the preoperative planning, the severity of AC should be considered as well as time of onset of symptoms and patient comorbidities. The aim of the present study was to investigate the role of an early PCT assessment in the emergency department in predicting the outcomes of laparoscopic surgery for AC.

**Study design** Retrospective, mono-centric study conducted in a teaching urban hospital. We evaluated all patients admitted to our ED from January 1st, 2015, to December 31st, 2019, underwent laparoscopic cholecystectomy for AC having a preoperative PCT determination in ED.

**Results** A total of 2285 patients in our ED were admitted for AC. Among them 822 patients were treated surgically, 174 had a PCT determination in ED. Median age was 63 [50–74]. Overall, 33 patients (19.0%) had major complications (MC): 32 needed an open surgery conversion, and 3 among them deceased. Multivariate analysis demonstrated that PCT, WBC, BUN, and CCI were significantly associated to MC in our cohort. When we calculated the area under the ROC curve with regard to MC, a procalcitonin value > 0.09 at admission had sensitivity = 84.8% [68.1–94.9] and specificity = 51.8% [43.2–60.3] for the occurrence of MC.

**Conclusion** Our results, suggest that a PCT > 0.09 ng/mL at ED admission, could be associated to a poor surgical outcome in patients treated by laparoscopic surgery for AC.

# PTC in cholecystitis: diagnosis of severity

WSES 2022 CONGRESS
ABSTRACT SUBMISSION TEMPLATE

## SPRIMACC-P(lus): role of Procalcitonin (PCT) as a prognostic factor in Acute Calculus Cholecistitis (ACC)

*Frassini S.[1,2], Fugazzola P.[2], Stabile A.[1,2], Granieri S.[4], Tomasoni M.[2], Calabretto F.[1,2], Cobianchi L.[1,2,3], Ansaloni L.[1,2,3]*

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SPRIMACC-P(lus) - CholepossumPro: PTC integrated in a score to predict mortality after LPC in pts with ACC (high risk patients to avoid LPC?)

- **Purpose/Introduction:**
  Acute Calculus Cholecystitis (ACC) is one of the most common biliary emergencies, and the clinicians need prompt tools to stratify and properly identify effective management and therapy for high-risk patients. Tokyo guidelines 2018 (TG18) recommended the use of severity grading of ACC for predicting prognosis for these patients. SPRIMACC study – a prospective multicenter observational study by WSES – was conducted to validate a prediction model for post-operative morbidity and mortality after cholecystectomy for ACC. Present study, derived from data from SPRIMACC, aims at evaluating predictive role of procalcitonin (PCT) for peri-/post-operative morbidity.

- **Methodology**:
  Patients included in the SPRIMACC study were evaluated from September 2021 to September 2022 in a retrospective observational study. ROC Curve analysis and multivariate model analysis were performed to identify the role of PCT and other flogistic parameters as predictive factors.

- **Results**:
  124 centres from all over the world participated in the clinical trial and 759 patients have been enrolled; a 30-days follow-up time was reached in 727 patients. PCT value was reported for 376 of them. PCT role as a predictive factor in mortality at 30-days was evidenced by an Area Under the Curve (AUC) of 0.915. The AUC of TG18 ACC grade was 0.660. 30-days major complications, in-hospital major complications and overall mortality were the other outcomes evaluated. A multivariate model was conducted for the other flogistic parameters. Multivariate analysis including PCT value and TG18 ACC severity grade, showed that only PCT was a significant risk factor for 30-days mortality.

- **Conclusion/s:**
  The application of procalcitonin as predictive factor for mortality post-cholecystectomy complications seems to be confirmed by data from our study and it is a reliable tool to identify high risk patients. Results from multivariate analysis suggest that PCT is more reliable than ACC grade to predict mortality. Additional studies are necessary to identify a complete pattern of flogistic parameters and to definitively stratify acute calculus cholecystitis patients.

** tables, figures and/or images are acceptable*
***Do not include references,*

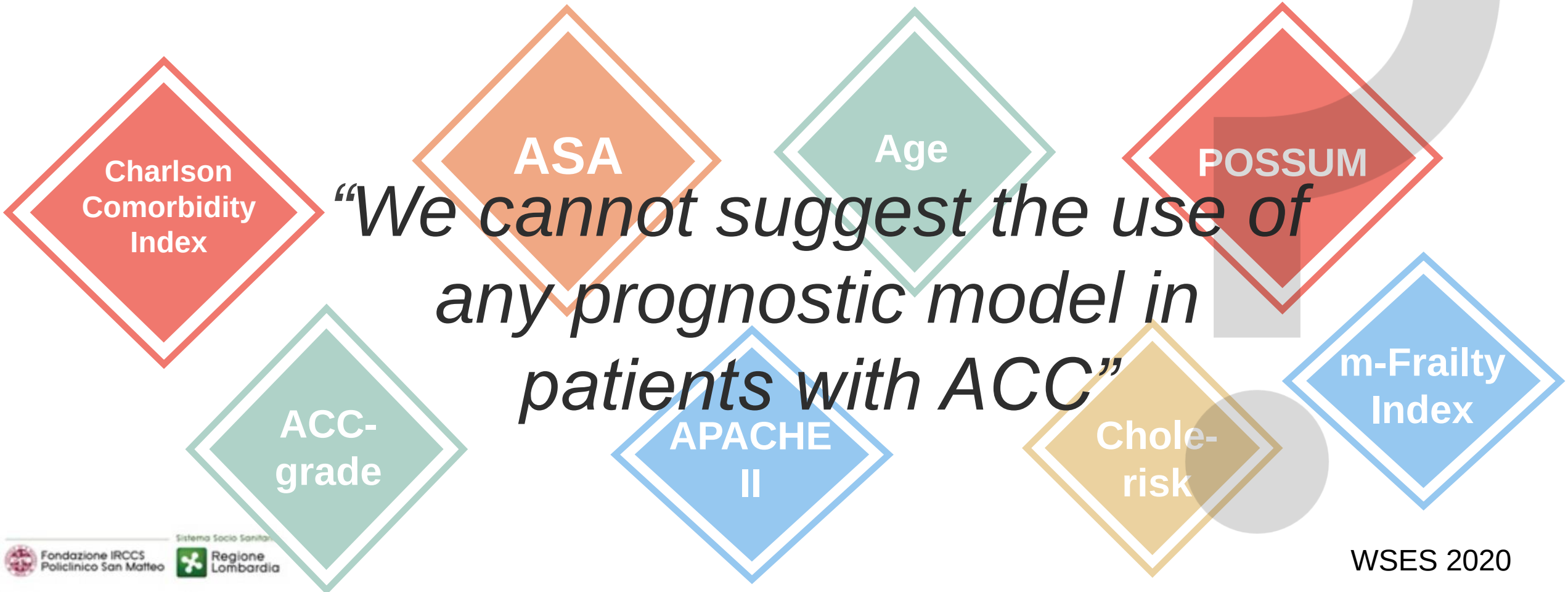
# CHOLE-POSSUM PRO


## Protocol for a prospective multicenter observational study

**Paola Fugazzola & Luca Ansaloni**
**Fondazione IRCCS Policlinico San Matteo, Pavia**

Sistema Socio Sanitario
Fondazione IRCCS Policlinico San Matteo
Regione Lombardia

# How can we select high-risk patients?




*"We cannot suggest the use of any prognostic model in patients with ACC"*

# S.P.Ri.M.A.C.C.

Fondazione IRCCS
Policlinico San Matteo

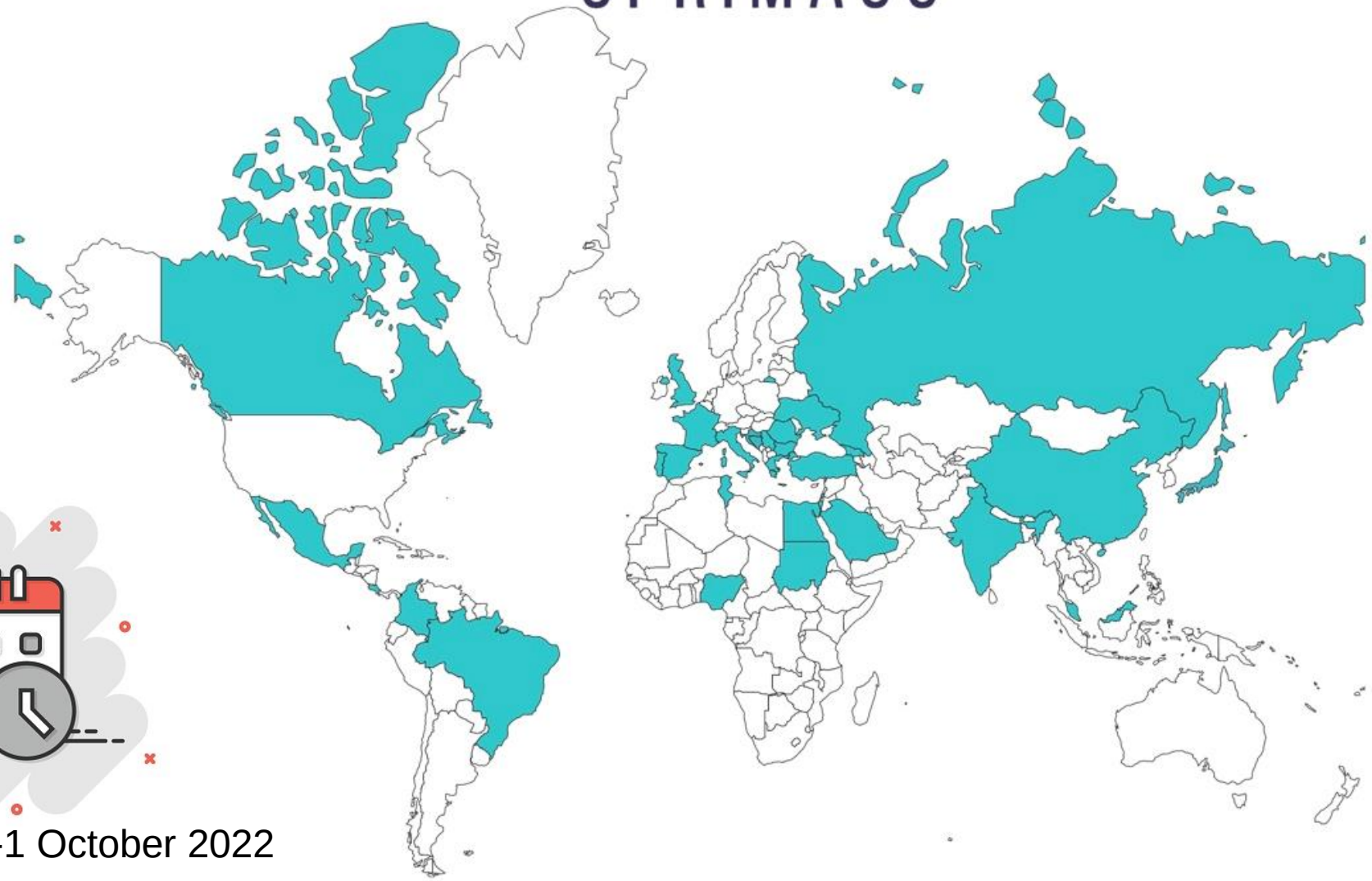
WSES

**Validation and comparison of Scores for Prediction of RIsk for post-operative major Morbidity after cholecystectomy in Acute Calculous Cholecystitis**

SPRIMACC is a prospective multicenter observational study on patients with ACC candidate to EC. The rationale of the study is to validate and compare existing risk prediction models for complicated port-operative course in this population. The calculated sample size is 663 patients.


m-Frailty Index
Risk Factors of Postoperative Complications in Laparoscopic Cholecystectomy for Acute Cholecystitis
Manabu Sato, MD, PhD, Koujin Endo, MD, PhD, Akihiko Harada, MD, PhD, and Masahiro Shijo, MD
POSSUM
Frailty Predicts Morbidity and Mortality After Laparoscopic Cholecystectomy for Acute Cholecystitis: An ACS-NSQIP Cohort Analysis
Check for updates
Alexander M. Fagenson[1] · Benjamin D. Powers[2] · Konstantinos A. Zorbas[3] · Sunil Karhadkar[1] · Andreas Karachristos[4] · Antonio Di Carlo[1] · Kwan N. Lau[1]
Chole-risk
Risk-adjusted treatment selection and outcome of patients with acute cholecystitis
J. I. González-Muñoz[1] · G. Franch-Arcas[1] · M. Angoso-Clavijo[1] · M. Sánchez-Hernández[2] · A. García-Plaza[1] · M. Caraballo-Angeli[1] · L. Muñoz-Bellvís[1]
ASA
Surgery for acute cholecystitis in severely comorbid patients: a population-based study on acute cholecystitis
Erik Osterman[1,4,5*], Louise Helenius[1], Christina Larsson[1], Sofia Jakobsson[3], Tamali Majumder[3], Anders Blomberg[1], Jennie Wickenberg[1] and Fredrik Linder[2,3]
ACC-grade
Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos)
Masamichi Yokoe · Jiro Hata · Tadahiro Takada · Steven M. Strasberg · Horacio J. Asbun · Go Wakabayashi · Kazuto Kozaka · Itaru Endo · Daniel J. Deziel · Fumihiko Miura · Kohji Okamoto · Tsann-Long Hwang · Wayn Shih-Wei Huang · Chen-Guo Ker · Miin-Fu Chen · Ho-Seong Han · Yoo-Seok Yoon · In-Seok Choi · Dong-Sup Yoon · Yoshinori Noguchi · Satoru Shikata · Tomohiko Ukai · Ryota Higuchi · Toshifumi Gabata · Yasuhisa Mori · Yukio Iwashita · Taizo Hibi · Palepu Jagannath · Eduard Jonas · Kui-Hin Liau · Christos Dervenis · Dirk J. Gouma · Daniel Cherqui · Giulio Belli · O. James Garden · Mariano Eduardo Giménez · Eduardo de Santibañes · Kenji Suzuki · Akiko Umezawa · Avinash Nivritti Supe · Henry A. Pitt · Harjit Singh · Angus C. W Chan · Wan Yee Lau · Anthony Yuen Bun Teoh · Goro Honda · Atsushi Sugioka · Koji Asai · Harumi Gomi · Takao Itoi · Seiki Kiriyama · Masahiro Yoshida · Toshihiko Mayumi · Naoki Matsumura · Hiromi Tokumura · Seigo Kitano · Koichi Hirata · Kazuo Inui · Yoshinobu Sumiyama · Masakazu Yamamoto
The quality of cholecystectomy in Denmark: outcome and risk factors for 20,307 patients from the national database
Kirstine Moll Harboe · Linda Bardram
Charlson Comorbidity Index
Optimal treatment strategy for acute cholecystitis based on predictive factors: Japan-Taiwan multicenter cohort study
Itaru Endo, Tadahiro Takada, Tsann-Long Hwang, Kohei Akazawa, Rintaro Mori, Fumihiko Miura, Masamichi Yokoe, Takao Itoi, Harumi Gomi, Miin-Fu Chen, Yi-Yin Jan, Chen-Guo Ker, Hsiu-Po Wang, Seiki Kiriyama, Keita Wada, Hiroki Yamaue, Masaru Miyazaki, Masakazu Yamamoto
APACHE II
Gallbladder perforation: morbidity, mortality and preoperative risk prediction
F. Ausania · S. Guzman Suarez · H. Alvarez Garcia · P. Senra del Rio · E. Casal Nuñez

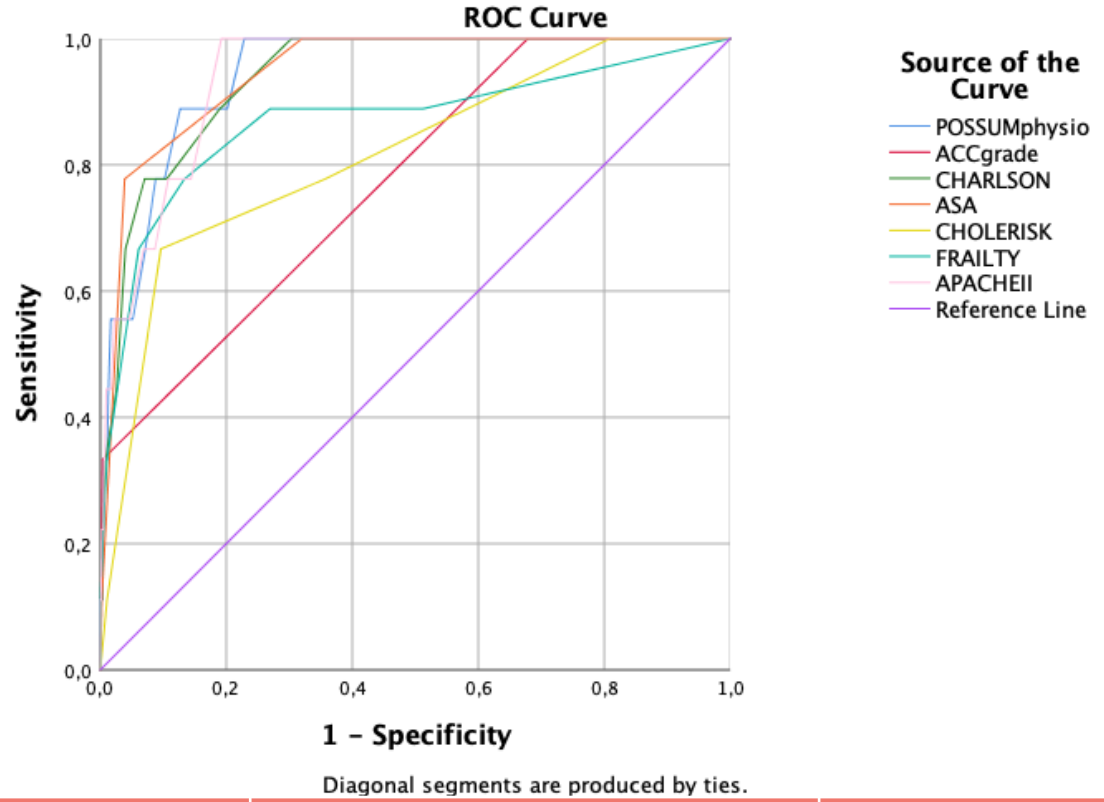
# SPRIMACC



1 September 2021-1 October 2022

## 19 Countries 77 Centers 1253 Patients

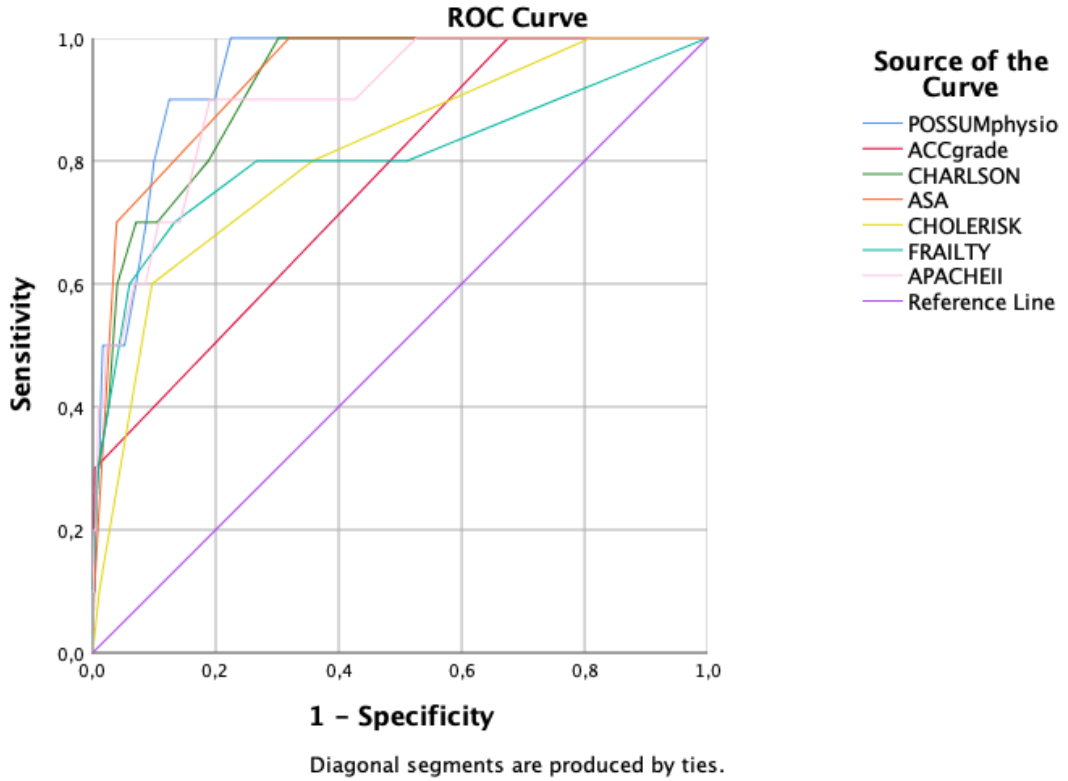
# INHOSPITAL MORTALITY




Diagonal segments are produced by ties.

| TEST | AUC | P |
|---|---|---|
| ASA | 0,946 | <0,001 |
| POSSUM PHYSIO | 0,944 | <0,001 |
| APACHE II | 0,942 | 0,023 |
| CHARLSON C.I. | 0,940 | 0,027 |
| M-FRAILTY | 0,870 | <0,001 |
| CHOLE-RISK | 0,815 | 0,001 |
| ACC GRADE (TG) | 0,772 | 0,005 |

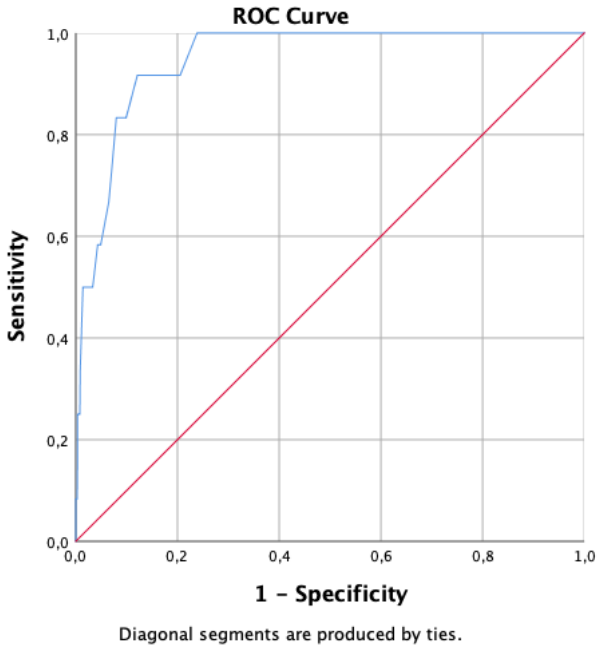
# 30DAYS MORTALITY




Diagonal segments are produced by ties.

| TEST | AUC | P |
|---|---|---|
| POSSUM PHYSIO | 0,941 | <0,001 |
| ASA | 0,934 | <0,001 |
| CHARLSON C.I. | 0,922 | <0,001 |
| APACHE II | 0,900 | <0,001 |
| CHOLE-RISK | 0,811 | 0,001 |
| M-FRAILTY | 0,808 | 0,001 |
| ACC GRADE (TG) | 0,762 | 0,004 |

## INHOSPITAL MORTALITY (AUC = 0,944)

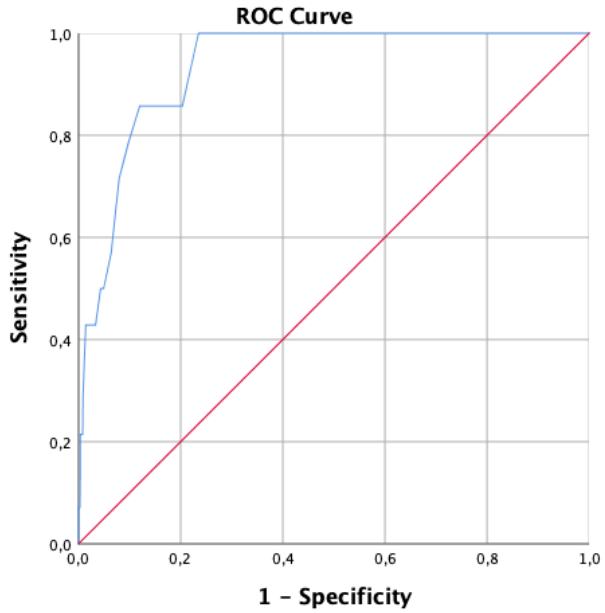



# BEST CUT-OFF FOR CHOLECYSTECTOMY FOR ACC FOR ALL OUTCOMES:

# 25

# (<25 vs ≥25)

## 30 DAYS MORTALITY (AUC= 0,941)




POSSUM PHYSIO

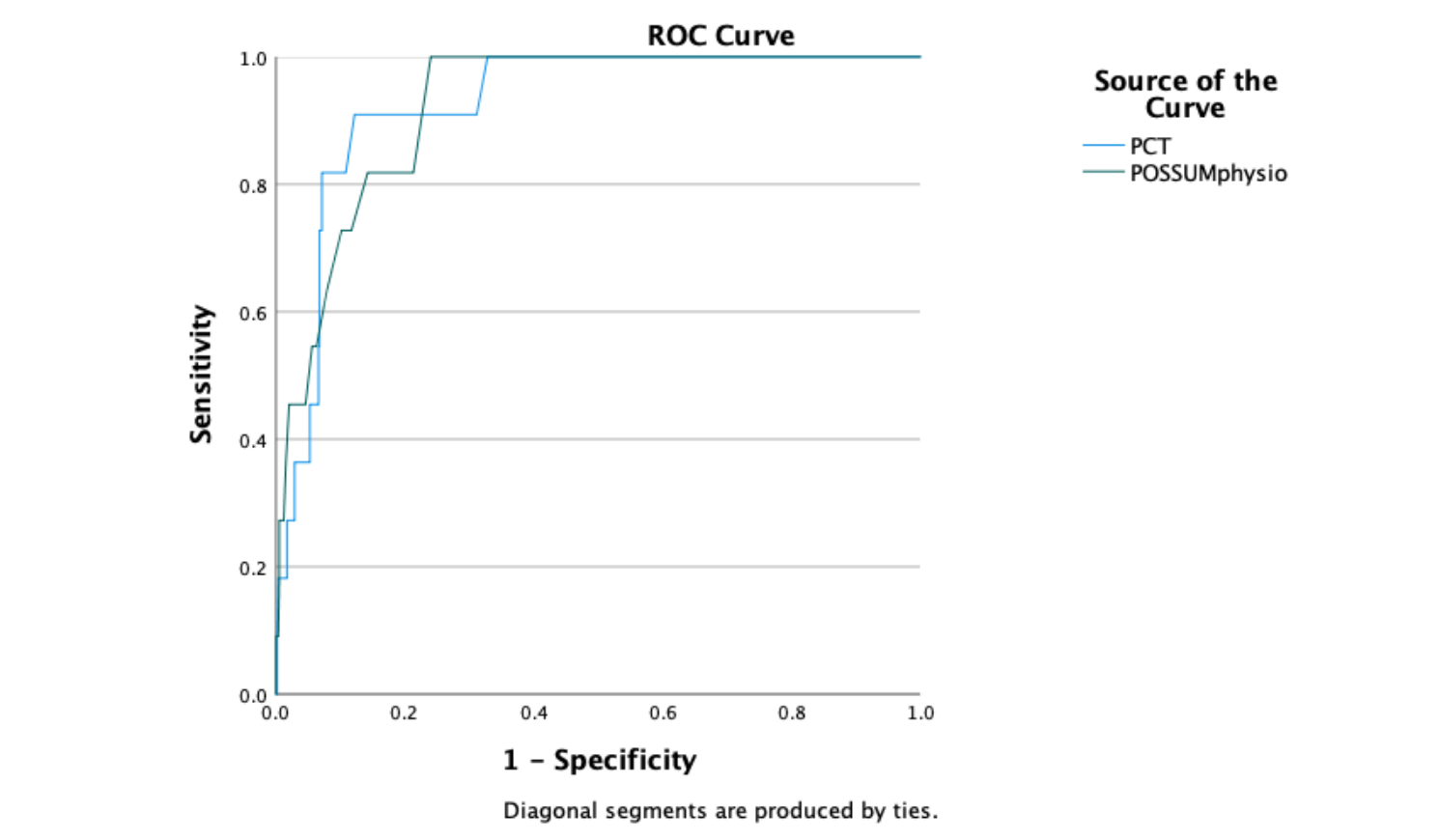
Fondazione IRCCS Policlinico San Matteo
Sistema Socio Sanitario
Regione Lombardia

# POST-HOC ANALYSIS: PCT

612 pts

AUC FOR 30-DAYS MORTALITY: 0.926 (95% CI 0.874-0.978)

BEST CUT-OFF: 4 ng/mL

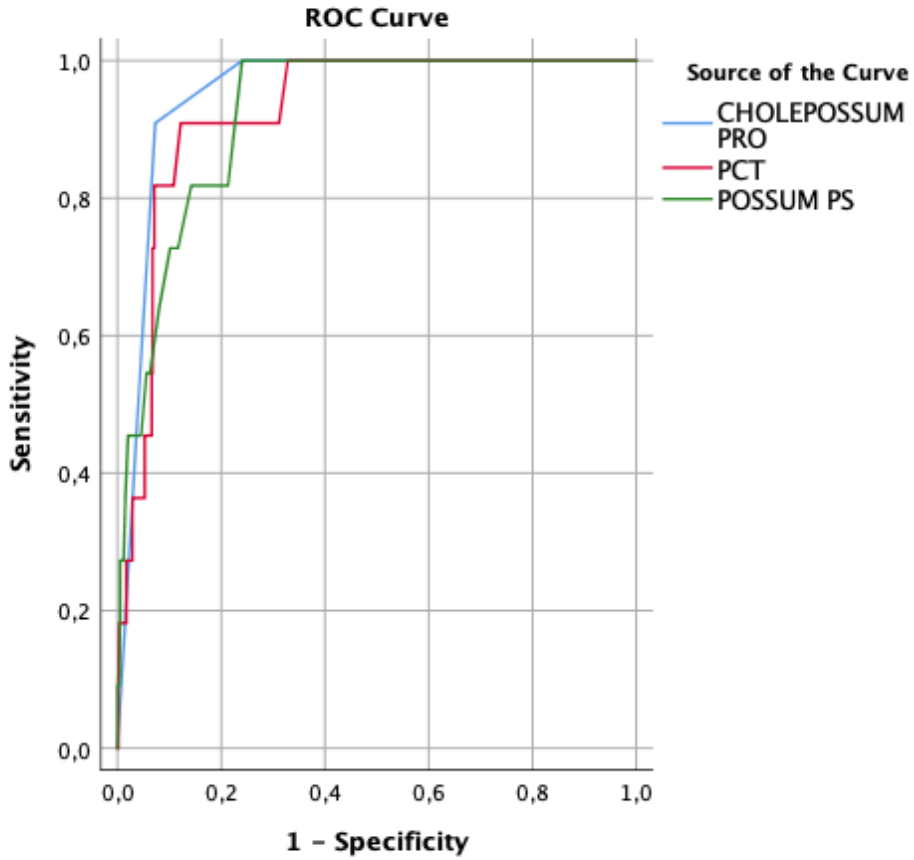


# POST-HOC ANALYSIS: PCT

MULTIVARIATE REGRESSION MODEL

| Variable | Score |
|---|---|
| a) POSSUM-PS ≥ 25 | 2 |
| b) PCT ≥ 4ng/mL | 1 |
| a + b = CHOLE-POSSUM PRO | |

# CHOLE-POSSUM PRO




| Area Under the ROC Curve | | | | | |
|---|---|---|---|---|---|
| | | | | Asymptotic 95% Confidence Interval | |
| Test Result Variable(s) | Area | Std. Error[a] | Asymptotic Sig.[b] | Lower Bound | Upper Bound |
| CHOLEPOSSUM PRO | ,953 | ,014 | ,000 | ,924 | ,981 |
| POSSUM PS | ,924 | ,026 | ,000 | ,874 | ,974 |
| PCT | ,926 | ,027 | ,000 | ,874 | ,978 |

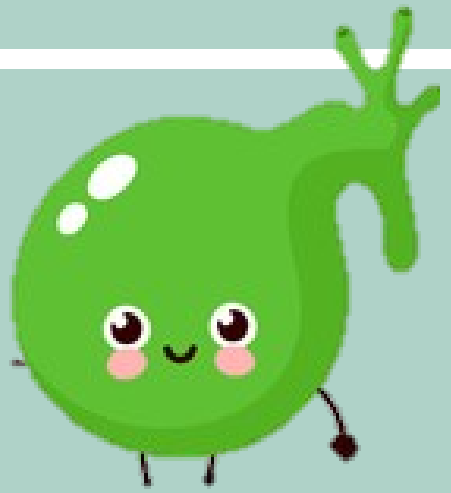
CUT-OFF 2 → sens 100%, spec 76%
CUT-OFF 3 → spec 93%, sens 91%

# CHOLE-POSSUM PRO

Fondazione IRCCS
Policlinico San Matteo

WSES

**CHOLE-POSSUM PRO validation for prediction of mortality after cholecystectomy for acute calculous cholecystitis: protocol for a prospective multicenter observational study**



# Objective

## Objective

- The primary objective of the study is to prospectively validate the CHOLE-POSSUM PRO score for **30-day mortality** after EC in patients with ACC.
- The secondary endpoint is to validate the CHOLE-POSSUM PRO score for **30-days major complications** (Clavien-Dindo >=3).
- The tertiary endpoint is to evaluate the correlation of PCT and CHOLE-POSSUM PRO with **intraoperative complications, duration of surgery, conversion rate, length of stay (LOS), 30-day readmission.**

## Primary end-point measure

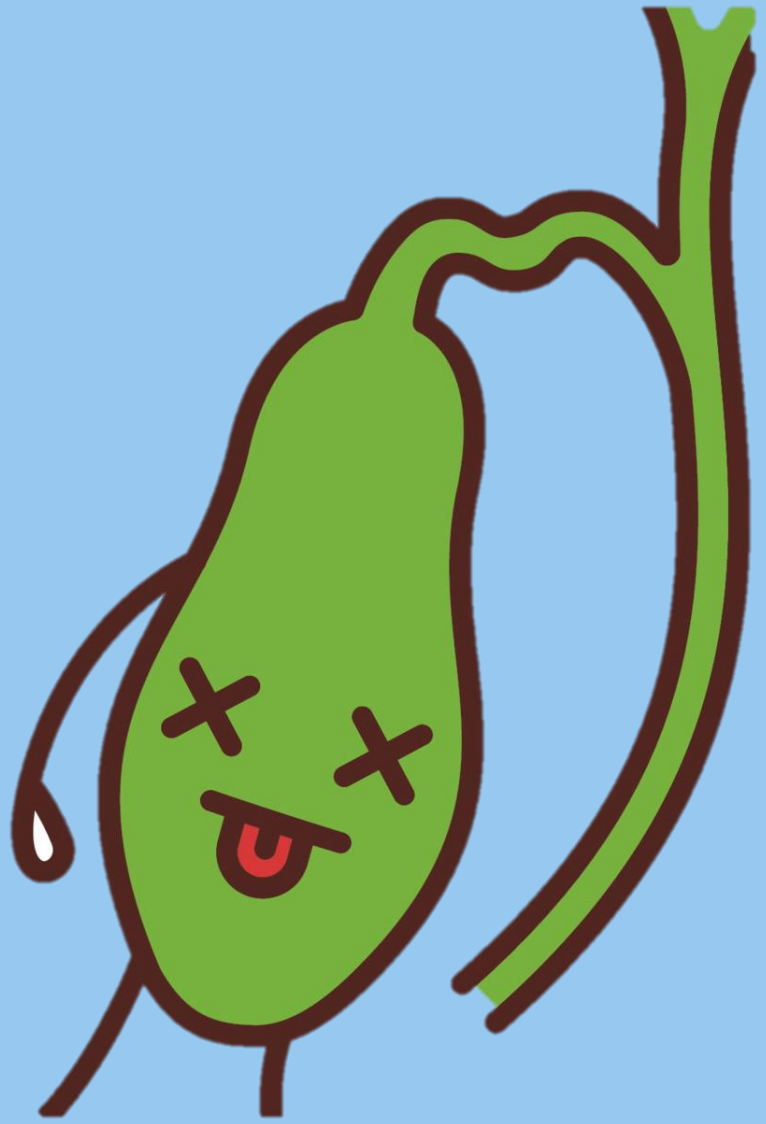
The primary endpoint is the AUC-ROC for 30-days mortality computed in the validating cohort.

The secondary end points is the AUC-ROC for 30-days major complications (Clavien-Dindo □3) rate computed in the validating cohort..

The tertiary endpoints are intraoperative complication rate, conversion rate, duration of surgery (minutes), LOS (days), 30-days readmission rate.

SAMPLE SIZE: 2000-2500 pts

# Inclusion criteria



**01** **Have a diagnosis of Acute Calculous Cholecystitis**

As defined by Tokyo Guidelines 2018 criteria

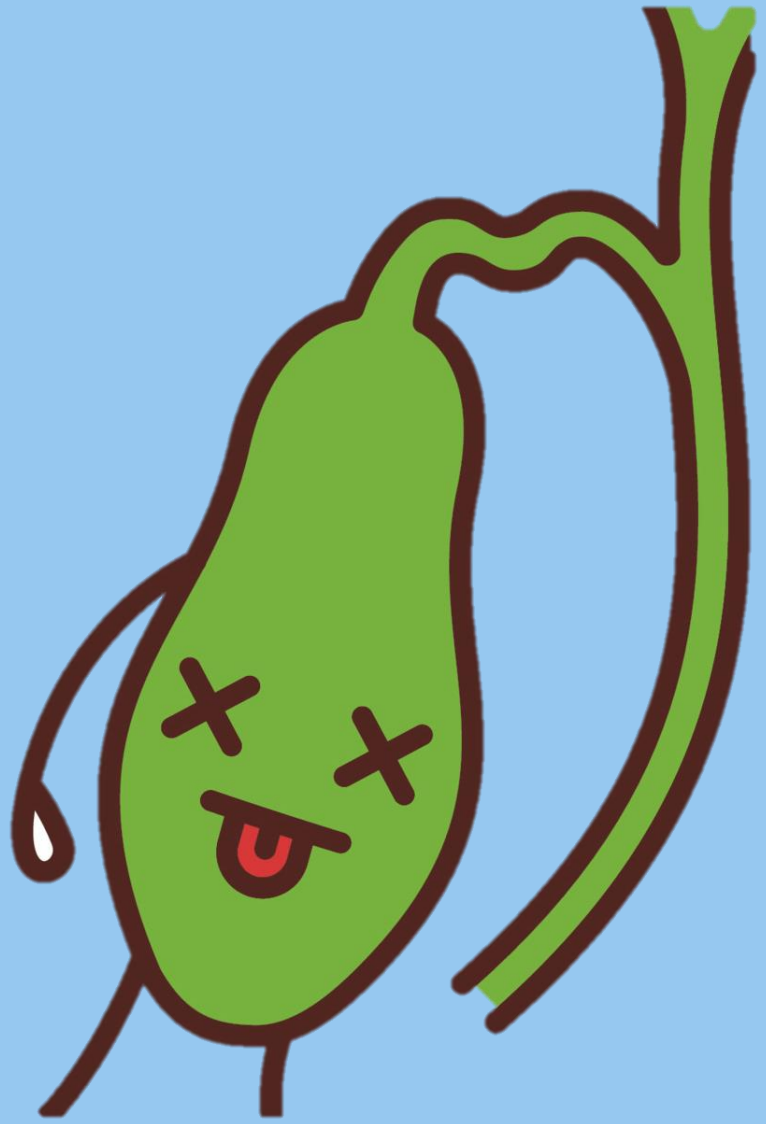
**02** **Be candidate to Early Cholecystectomy during the index admission**

**03** **Be ≥ 18 years old**

**04** **Be stratified for the risk of CBDS**

according to the Israeli Score (30), and, in case of confirmation of CBDS receive pre-operative ERCP.

# Exclusion criteria



**01** **Pregnancy or lactation**

**02** **Acute cholecystitis not related to a gallstone etiology**

**03** **Onset of symptoms >10 days before cholecystectomy**

Patients with ACC associated with common bile duct stones who underwent pre-operative ERCP could be included if they receive EC within 10 days from onset of symptoms.

**04** **Concomitant cholangitis or pancreatitis**

**05** **Intraoperative treatment of common bile duct stones**


CHOLE-POSSUM PRO
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3

PTC dosing can guide the clinician in the diagnosis of complicated diverticulitis (and guiding antibiotic treatment)

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Original article | Published 23 November 2017 | doi:10.4414/smw.2017.14555

Cite this as: Swiss Med Wkly. 2017;147:w14555

Is there a role for procalcitonin in differentiating uncomplicated and complicated diverticulitis in order to reduce antibiotic therapy? A prospective diagnostic cohort study

Jeger Victor[ab], Pop Roxana[a], Forudastan Farschad[d], Barras Jean Pierre[d], Zuber Markus[c], Piso Rein Jan[a]

Acute diverticulitis

Procalcitonin was able to differentiate with a high sensitivity and specificity between complicated and uncomplicated cases of diverticulitis when combined with abdominal CT scans. As most clinicians still treat uncomplicated diverticulitis with antibiotics, procalcitonin could be an interesting parameter for guiding therapy and decreasing antibiotic usage.

4

# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

SURGICAL INFECTIONS
Volume XX, Number X, 2015

DOI: 10.1089/sur.2015.130

## Duration of Antimicrobial Therapy in Treating Complicated Intra-Abdominal Infections: A Comprehensive Review

Massimo Sartelli,[1] Fausto Catena,[2] Luca Ansaloni,[3] Federico Coccolini,[3] Salomone Di Saverio,[4] and Ewen A. Griffiths[5]

**Abstract**

***Background:*** Surgeons managing intra-abdominal infections should always respect the basic principles of antibiotic treatment. An adequate duration of antimicrobial therapy is important to optimize empiric therapy and minimize selective pressures favoring antimicrobial resistance.
***Methods:*** The optimal duration of antibiotic therapy for intra-abdominal infections (IAIs) has been debated in the last years. A literature research, based on PubMed database and limited to English language publications, was performed without restriction of time or type of manuscript.
***Results:*** In stable patients a short course of antimicrobial therapy (3–5 d) after adequate source control, depending on fever and leukocytosis, may be a reasonable option. In critically ill patients with severe sepsis and septic shock, an individualized approach is always mandatory and patient's inflammatory response should be monitored regularly. Procalcitonin may be helpful for guiding antibiotic treatment in critically ill surgical patients and in predicting treatment response.
***Conclusions:*** General surgeons managing intra-abdominal infections should always respect the basic principles of antibiotic treatment. Duration of antimicrobial treatment is an important variable to evaluate in treating complicated intra-abdominal infections.

4

# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

should be considered. Patients who have signs of sepsis beyond 5 to 7 days of treatment warrant aggressive diagnostic investigation to determine if an ongoing uncontrolled source of infection or antimicrobial treatment failure is present. In the management of critically ill patients with sepsis and septic shock clinical signs and symptoms as well as inflammatory response markers such as procalcitonin, although debatable, may assist in guiding antibiotic treatment [293].

Sartelli et al. World Journal of Emergency Surgery (2016) 11:33
DOI 10.1186/s13017-016-0089-y

World Journal of Emergency Surgery

REVIEW Open Access

## Antimicrobials: a global alliance for optimizing their rational use in intra-abdominal infections (AGORA)

Massimo Sartelli[1*], Dieter G. Weber[2], Etienne Ruppé[3], Matteo Bassetti[4], Brian J. Wright[5], Luca Ansaloni[6], Fausto Catena[7], Federico Coccolini[8], Fikri M. Abu-Zidan[9], Raul Coimbra[10], Ernest E. Moore[11], Frederick A. Moore[12], Ronald V. Maier[13], Jan J. De Waele[14], Andrew W. Kirkpatrick[15], Ewen A. Griffiths[16], Christian Eckmann[17], Adrian J. Brink[18], John E. Mazuski[19], Addison K. May[20], Rob G. Sawyer[21], Dominik Mertz[22], Philippe Montravers[23], Anand Kumar[24], Jason A. Roberts[25], Jean-Louis Vincent[26], Richard R. Watkins[27], Warren Lowman[28], Brad Spellberg[29], Iain J. Abbott[30], Abdulrashid Kayode Adesunkanmi[31], Sara Al-Dahir[32], Majdi N. Al-Hasan[33], Ferdinando Agresta[34], Asma A. Althani[35], Shamshul Ansari[36], Rashid Ansumana[37], Goran Augustin[38], Miklosh Bala[39], Zsolt J. Balogh[40], Oussama Baraket[41], Aneel Bhangu[42], Marcelo A. Beltrán[43], Michael Bernhard[44], Walter L. Biffl[45], Marja A. Boermeester[46], Stephen M. Brecher[47], Jill R. Cherry-Bukowiec[48], Otmar R. Buyne[49], Miguel A. Cainzos[50], Kelly A. Cairns[51], Adrian Camacho-Ortiz[52], Sujith J. Chandy[53], Asri Che Jusoh[54], Alain Chichom-Mefire[55], Caroline Colijn[56], Francesco Corcione[57], Yunfeng Cui[58], Daniel Curdo[59], Samir Delibegovic[60], Zaza Demetrashvili[61], Belinda De Simone[62], Sameer Dhingra[63], José J. Diaz[64], Isidoro Di Carlo[65], Angel Dillip[66], Salomone Di Saverio[67], Michael P. Doyle[68], Gereltuya Dorj[69], Agron Dogjani[70], Hervé Dupont[71], Soumitra R. Eachempati[72], Mushira Abdulaziz Enani[73], Valery N. Egiev[74], Mutasim M. Elmangory[75], Paula Ferrada[76], Joseph R. Fitchett[77], Gustavo P. Fraga[78], Nathalie Guessennd[79], Helen Giamarellou[80], Wagih Ghnnam[81], George Gkiokas[82], Staphanie R. Goldberg[76], Carlos Augusto Gomes[83], Harumi Gomi[84], Manuel Guzmán-Blanco[85], Mainul Haque[86], Sonja Hansen[87], Andreas Hecker[88], Wolfgang R. Heizmann[89], Torsten Herzog[90], Adrien Montcho Hodonou[91], Suk-Kyung Hong[92], Reinhold Kafka-Ritsch[93], Lewis J. Kaplan[94], Garima Kapoor[95], Aleksandar Karamarkovic[96], Martin G. Kees[97], Jakub Kenig[98], Ronald Kiguba[99], Peter K. Kim[100], Yoram Kluger[101], Vladimir Khokha[102], Kaoru Koike[103], Kenneth Y. Y. Kok[104], Victory Kong[105], Matthew C. Knox[106], Kenji Inaba[107], Arda Isik[108], Katia Iskandar[109], Rao R. Ivatury[76], Maurizio Labbate[110], Francesco M. Labricciosa[111], Pierre-François Laterre[112], Rifat Latifi[113], Jae Gil Lee[114], Young Ran Lee[115], Marc Leone[116], Ari Leppaniemi[117], Yousheng Li[118], Stephen Y. Liang[119], Tonny Loho[120], Marc Maegele[121], Sydney Malama[122], Hany E. Marei[35], Ignacio Martin-Loeches[123], Sanjay Marwah[124], Amos Massele[125], Michael McFarlane[126], Renato Bessa Melo[127], Ionut Negoi[128], David P. Nicolau[129], Carl Erik Nord[130], Richard Ofori-Asenso[131], AbdelKarim H. Omari[132], Carlos A. Ordonez[133], Mouaqit Ouadi[134], Gerson Alves Pereira Júnior[135], Diego Piazza[136], Guntars Pupelis[137], Timothy Miles Rawson[138], Miran Rems[139], Sandro Rizoli[140], Claudio Rocha[141], Boris Sakakhushev[142], Miguel Sanchez-Garcia[143], Norio Sato[103], Helmut A. Segovia Lohse[144], Gabriele Sganga[145], Boonying Siribumrungwong[146], Vishal G. Shelat[147], Kjetil Soreide[148], Rodolfo Soto[149], Peep Talving[150], Jonathan V. Tilsed[151], Jean-Francois Timsit[152], Gabriel Trueba[153], Ngo Tat Trung[154], Jan Ulrych[155], Harry van Goor[49], Andras Vereczkei[156], Ravinder S. Vohra[157], Imtiaz Wani[158], Waldemar Uhl[90], Yonghong Xiao[159], Kuo-Ching Yuan[160], Sanoop K. Zachariah[161], Jean-Ralph Zahar[162], Tanya L. Zakrison[163], Antonio Corcione[164], Rita M. Melotti[165], Claudio Viscoli[166] and Perluigi Viale[167]

4

# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

**Principles of Appropriate Antibiotic Therapy in Surgical Procedures**

1. The source of infection should always be identified and controlled as soon as possible.
2. Antibiotic empiric therapy should be initiated after a treatable surgical infection has been recognized, because microbiologic data (culture and susceptibility results) may not be available for up to 48–72 hours to guide targeted therapy.
3. In critically ill patients, empiric broad-spectrum therapy to cover the most likely pathogens should be initiated as soon as possible after a surgical infection has been recognized. Empiric antimicrobial therapy should be narrowed once culture and susceptibility results are available and adequate clinical improvement is noted.
4. Empiric therapy should be chosen on the basis of local epidemiology, individual patient risk factors for MDR bacteria and *Candida* spp., clinical severity, and infection source.
5. Specimens for microbiologic evaluation from the site of infection are always recommended for patients with hospital-acquired or with community-acquired infections at risk for resistant pathogens (e.g., previous antimicrobial therapy, previous infection or colonization with a MDR, XDR, and PDR pathogen) and in critically ill patients. Blood cultures should be performed before the administration of antibiotic agents in critically ill patients.
6. The antibiotic dose should be optimized to ensure that PK-PD targets are achieved. This involves prescribing an adequate dose, according to the most appropriate and right method and schedule to maximize the probability of target attainment.
7. The appropriateness and need for antimicrobial treatment should be re-assessed daily.
8. Once source control is established, short courses of antibiotic therapy are as effective as longer courses regardless of signs of inflammation.
   - Intra-abdominal infection—four days are as effective as eight days in moderately ill patients [14]
   - Blood stream infection—five to seven days are as effective as seven to 21 days for most patients [15]
   - Ventilator associated pneumonia—eight days are as effective as 15 days [16,17].
9. Failure of antibiotic therapy in patients having continued evidence of active infection may require a re-operation for a second source control intervention.
10. Biomarkers such as procalcitonin may be useful to guide duration and cessation of antibiotic therapy in critically ill patients.
11. Clinicians with advanced training and clinical experience in surgical infections should be included in the care of patients with severe infections.
12. The IPC measures combined with ASPs should be implemented in surgical departments. These interventions and programs require regular, systematic monitoring to assess compliance and efficacy.

SURGICAL INFECTIONS
Volume 18, Number 8, 2017

DOI: 10.1089/sur.2017.219

***Global Alliance Position Article***

## A Global Declaration on Appropriate Use of Antimicrobial Agents across the Surgical Pathway

Global Alliance for Infections in Surgery Working Group

**Abstract**

This declaration, signed by an interdisciplinary task force of 234 experts from 83 different countries with different backgrounds, highlights the threat posed by antimicrobial resistance and the need for appropriate use of antibiotic agents and antifungal agents in hospitals worldwide especially focusing on surgical infections. As such, it is our intent to raise awareness among healthcare workers and improve antimicrobial prescribing. To facilitate its dissemination, the declaration was translated in different languages.

10. Biomarkers such as procalcitonin may be useful to guide duration and cessation of antibiotic therapy in critically ill patients.

# 4

## PTC has a role in guiding antibiotic therapy in critically «surgical» patients

Prkno *et al. Critical Care* 2013, **17**:R291
http://ccforum.com/content/17/6/R291

CRITICAL CARE

RESEARCH Open Access

### Procalcitonin-guided therapy in intensive care unit patients with severe sepsis and septic shock – a systematic review and meta-analysis

2013

Anna Prkno[1,2], Christina Wacker[1,2], Frank M Brunkhorst[2,3†] and Peter Schlattmann[1,2*†]

**Table 2 PCT assays and algorithms used for procalcitonin (PCT)-guided treatment in the included studies**

| Study | PCT test | Regimen in the PCT group | Regimen in the control group |
|---|---|---|---|
| **Annane *et al.* 2013 [26]** | Brahms PCT Kryptor | **Medical patients:**<br>PCT <0.25 ng/mL: antibiotics not initiated or stopped<br>PCT ≥0.25 and < 0.5 ng/mL: Antibiotics strongly discouraged<br>PCT ≥0.5 and <5 ng/mL: antibiotics recommended<br>PCT ≥5 ng/mL: antibiotics strongly recommended<br>**Surgical patients:**<br>PCT <4 ng/mL: antibiotics not initiated or stopped<br>PCT ≥4 and <9 ng/mL: antibiotics recommended<br>PCT ≥9 ng/mL: antibiotics strongly recommended | Antibiotic treatment at the discretion of the patient's physician |
| **Bouadma *et al.* 2010 [27]** | Brahms PCT Kryptor | **Guidelines for starting of antibiotics:**<br>PCT <0.25 ng/mL: antibiotics strongly discouraged<br>PCT ≥0.25 and <0.5 ng/mL: antibiotics discouraged<br>PCT ≥0.5 and <1 ng/mL: antibiotics encouraged<br>PCT ≥1 ng/mL: antibiotics strongly encouraged<br>**Guidelines for continuing or stopping of antibiotics:**<br>PCT <0.25 ng/mL: stopping of antibiotics strongly encouraged.<br>Decrease by ≥80% from peak concentration, or concentration ≥0.25 and <0.5 ng/mL: stopping of antibiotics encouraged<br>Decrease by <80% from peak concentration and concentration ≥0.5 ng/mL: continuing of antibiotics encouraged<br>Increase of concentration compared with peak concentration and concentration ≥0.5 ng/mL: changing of antibiotics strongly encouraged | Treatment according to international and local guidelines |
| **Hochreiter *et al.* 2009 [28]** | Brahms PCT LIA | PCT < 1 ng/mL: Antibiotics discontinued.<br>PCT >1 ng/mL and dropped to 25 to 35% of the initial value over 3 days: antibiotics discontinued<br>Additionally the infection had to improve clinically | Antibiotic treatment according to standard regimen over 8 days |
| **Jensen *et al.* 2011 [29]** | Brahms PCT Kryptor | Single baseline measurement of PCT ≥1.00 ng/mL or PCT ≥1.00 ng/mL and not decreased at least 10% from the previous day:<br>1) Increasing the antimicrobial spectrum covered<br>2) intensifying the diagnostic effort to find uncontrolled sources of infection<br>PCT <1.00 ng/mL for at least 3 days: de-escalation possible | Antibiotic treatment according to current guidelines |
| **Nobre *et al.* 2008 [30]** | Brahms PCT Kryptor | Patients with PCT <1 ng/mL re-evaluated at day 3: antibiotics discontinued if PCT <0.1 ng/mL<br>Patients with PCT ≥1 ng/mL re-evaluated at day 5: antibiotics discontinued if PCT dropped >90% from the baseline peak level or if PCT <0.25 ng/mL | Antibiotic treatment based on empirical rules |
| **Schroeder *et al.* 2009 [31]** | Brahms PCT LIA | PCT <1 ng/mL and clinical signs of infection improved: antibiotics discontinued<br>PCT dropped to <35% of the initial concentration within 3 days and clinical signs of infection improved: antibiotics discontinued | Antibiotic treatment according to clinical signs and empiric rules |
| **Svoboda *et al.* 2007 [32]** | Brahms PCT-Q | PCT >2 ng/mL: change of antibiotics and catheters<br>PCT ≤2 ng/mL: ultrasonography and/or computer tomography followed by repeated surgical treatment if localized infection was confirmed | Treatment according to contemporary treatment protocol of the institute |

PCT, procalcitonin.

**Table 1 Characteristics of included studies**

| Study | Annane *et al.* 2013 [26] | Bouadma *et al.* 2010 [27] | Hochreiter *et al.* 2009 [28] | Jensen *et al.* 2011 [29] | Nobre *et al.* 2008 [30] | Schroeder *et al.* 2009 [31] | Svoboda *et al.* 2007 [32] |
|---|---|---|---|---|---|---|---|
| **Design** | RCT | RCT | RCT | RCT | RCT | RCT | RCT |
| **Setting** | Surgical and medical ICU | Surgical and medical ICU | Surgical ICU | Surgical and medical ICU | Surgical and medical ICU | Surgical ICU | Surgical ICU |
| **Condition** | Severe sepsis and septic shock | Septic shock | Severe sepsis | Severe sepsis and septic shock | Severe sepsis and septic shock | Severe sepsis | Severe sepsis |
| **Total number of included patients** | 61 | 267 | 110 | 459 | 79 | 27 | 72 |
| **Number of patients** | | | | | | | |
| PCT group/control group | 31/30 | 138/129 (septic shock)<br>55/53 (positive blood culture) | 57/53 | 247/212 | 39/40 | 14/13 | 38/34 |
| **Hospital mortality** | | | | | | | |
| Relative risk (95% CI) | 0.68 (0.30; 1.55) | NA | 1.00 (0.53; 1.86) | NA | 1.03 (0.46; 2.31) | 0.93 (0.23; 3.81) | NA |
| Events PCT group/events control group | 7/10 | | 15/14 | | 9/9 | 3/3 | |
| **28-day mortality** | | | | | | | |
| Relative risk (95% CI) | NA | 1.15 (0.81; 1.63) | NA | 1.02 (0.80; 1.30) | 1.03 (0.43; 2.46) | NA | 0.69 (0.35; 1.36) |
| Events PCT group/events control group | | 48/39 (septic shock) | | 90/76 | 8/8 | | 10/13 |
| **Duration of antibiotic treatment, days** | | | | | | | |
| PCT group/control group | 5/5 (median) | 9.8/12.8 (mean) (only positive blood culture) | 5.9/7.9 (mean) | NA | 6.0/9.5 (median) | 6.6/8.3 (mean) | NA |
| **Length of ICU stay, days** | | | | | | | |
| PCT group/control group | 22/23 (median) | NA | 15.5/17.7 (mean) | 6.0/5.0 (median) | 4.0/7.0 (median) | 16.4/16.7 (mean) | 16.1/19.4 (mean) |
| **Length of hospital stay, days** | | | | | | | |
| PCT group/control group | 27/33 (median) | NA | NA | 23.0/22.0 (median) | 17.0/23.5 (median) | NA | NA |
| **SOFA score** | | | | | | | |
| PCT group/control group | 9.5/10 (median)<br>8.5 to 11/8 to 11 (IQR) | NA | 6.7/7.0 (mean)<br>3.68/3.62 (SD) | NA | 6.4/6.6 (mean)<br>3.3/3.0 (SD) | 7.3/8.3 (mean)<br>3.5/4.2 (SD) | 7.9/9.3 (mean)<br>2.8/3.3 (SD) |
| **Medical patients, %*** | 97% | 89% | 0% | 59% | NA | 0% | 0% |
| **Subgroup of study** | No | Yes | No | Yes | No | No | No |
| **Duration of study, months** | 36 | 12 | 15 | 29 | 15 | 7 | 29 |
| **Study protocol available** | Yes | Yes | Yes | Yes | Yes | No | No |
| **Country** | France | France | Germany | Denmark | Switzerland | Germany | Czech Republic |

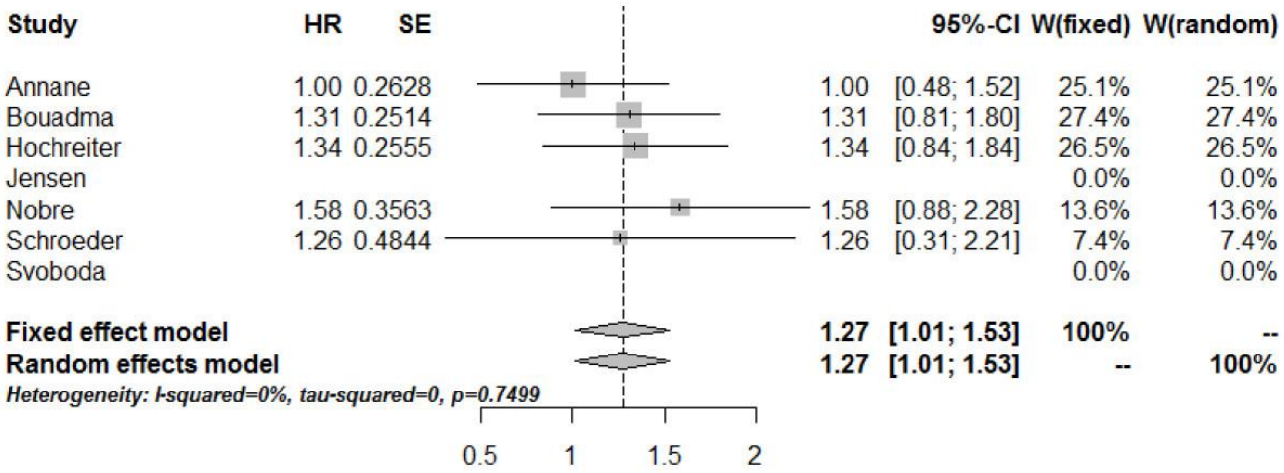
PCT, procalcitonin; RCT, randomized controlled clinical trial; SOFA, sequential organ failure assessment; NA, data were not available; *data were stated in study or calculated from information given in study.

Prkno *et al. Critical Care* 2013, **17**:R291
http://ccforum.com/content/17/6/R291

4

# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

## PCT and duration of antimicrobial therapy



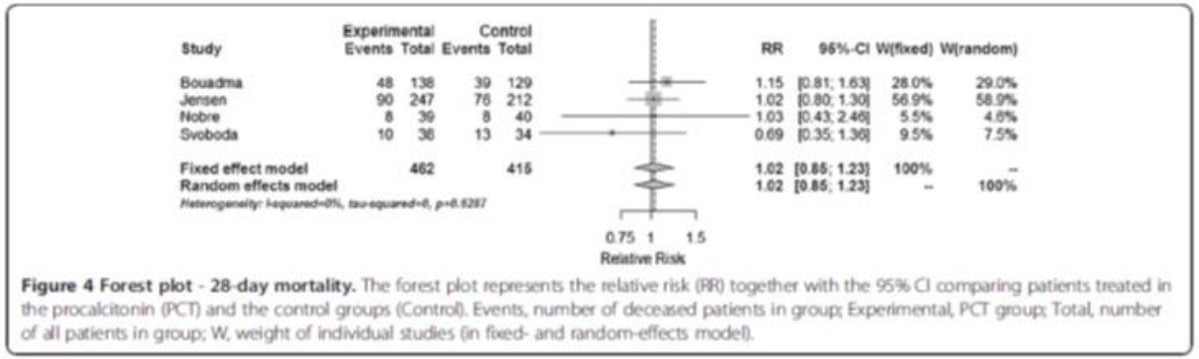




**Figure 4 Forest plot - 28-day mortality.** The forest plot represents the relative risk (RR) together with the 95% CI comparing patients treated in the procalcitonin (PCT) and the control groups (Control). Events, number of deceased patients in group; Experimental, PCT group; Total, number of all patients in group; W, weight of individual studies (in fixed- and random-effects model).

**Conclusion**

An approach along a biomarker-guided treatment algorithm using procalcitonin levels may be helpful to guide antimicrobial treatment in severe sepsis patients, treated in ICUs and reduces the duration of antimicrobial therapy without an obvious increase in mortality. However, more research is urgently needed to investigate the safety and effectiveness in subgroups of surgical and medical severe sepsis patients, treated in ICUs. Most importantly, treatment algorithms differ substantially and have to be clarified in future studies.

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# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

2015

**Table 1** Results of prospective randomized trials

| Country | Author | Ref | Trial name | Year | Number | Population | PCT E | PCT C | Number of fewer days of antibiotic use |
|---|---|---|---|---|---|---|---|---|---|
| Use in respiratory infections | | | | | | | | | |
| Switzerland | Christ-Crain | [20] | None | 2006 | 302 | CAP | 0.57 | 0.44 | Yes, 7 days |
| Switzerland | Briel | [23] | None | 2008 | 458 | resp infect | 0.8 | 0.8 | Yes, 1 day |
| Swiss/USA | Stolz | [25] | None | 2009 | 101 | VAP | 0.6 | 0.7 | Yes, 5 days |
| Switzerland | Schuetz | [26] | ProHosp | 2009 | 1359 | resp infect | 0.24 | 0.24 | Yes, 3 days |
| Use in sepsis | | | | | | | | | |
| Switzerland | Nobre | [21] | None | 2008 | 79 | Sepsis | 8.4 | 5.9 | Yes, 3.5 days |
| Germany | Schroeder | [22] | None | 2008 | 27 | Severe sepsis | 7.0 | 6.0 | Yes, 1.7 days |
| Sepsis in the ICU setting | | | | | | | | | |
| Germany | Hochreiter | [24] | None | 2009 | 110 | SICU | 4.5 | 4.8 | Yes, 2 days |
| France | Bouadma | [27] | PRORATA | 2010 | 621 | ICU | 12.0 | 12.0 | Yes, 3 days |
| Netherlands | De Jong | [28] | SAPS | 2013 | 1816 | ICU | – | – | Results pending |
| Australia | Shehabi | [30] | ProGuard | 2014 | 400 | ICU | 5.7 | 8.8 | No, 2 days not statistically significant |

*Ref* reference number, *n* number of patients enrolled in the study, *CAP* community-acquired pneumonia, *resp infect* respiratory infection, *SICU* surgical intensive care unit, *VAP* ventilator-associated pneumonia, *ICU* intensive care unit, *PCT E* initial procalcitonin level in the experimental group (ng/mL), *PCT C* initial procalcitonin level in the control group (ng/mL)

Carr *Journal of Intensive Care*
DOI 10.1186/s40560-015-0100-9

JOURNAL OF INTENSIVE CARE

REVIEW Open Access

## Procalcitonin-guided antibiotic therapy for septic patients in the surgical intensive care unit

John Alfred Carr

**Abstract**

In critically ill patients, elucidating those patients with the systemic inflammatory response syndrome (SIRS) from an infectious source (sepsis), versus those who have SIRS without infection, can be challenging since the clinical features are the same. Even with strict monitoring and testing, 39–98 % of patients with SIRS will never have bacteriological confirmation of an infection, and 6–17 % of patients with a documented infection will not show signs of SIRS. Due to this overlap, an extensive amount of research has been performed to investigate ways of determining and separating SIRS from infection, compared to SIRS due to trauma, surgical stress, or other non-infectious causes. This review article will discuss the recommended and peer-approved use of procalcitonin in septic patients in the intensive care unit and its use as a guide to antibiotic initiation and termination. The article will focus on the prospective randomized trials (Level 1 evidence) that have been conducted, and lesser levels of evidence will be referenced as needed to substantiate a conclusion. The literature documents multiple benefits of using procalcitonin as a guide to cost savings and appropriate termination of antibiotics by its use as a new objective marker of bacteremia that was previously not available. This article will show that antibiotics should be terminated when the procalcitonin level falls below 0.5 ng/mL.

4

# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

Wirz et al. Critical Care (2018) 22:191
https://doi.org/10.1186/s13054-018-2125-7

2018

Critical Care

REVIEW Open Access

## 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

Yannick Wirz[1†], Marc A. Meier[1†], Lila Bouadma[3], Charles E. Luyt[4], Michel Wolff[3], Jean Chastre[4], Florence Tubach[5], Stefan Schroeder[6], Vandack Nobre[7], Djillali Annane[8], Konrad Reinhart[9], Pierre Damas[10], Maarten Nijsten[11], Arezoo Shajiei[11], Dylan W. deLange[12], Rodrigo O. Deliberato[13], Carolina F. Oliveira[14], Yahya Shehabi[15,16], Jos A. H. van Oers[17], Albertus Beishuizen[18], Armand R. J. Girbes[19], Evelien de Jong[19], Beat Mueller[1,2] and Philipp Schuetz[1,2*]

**Table 1** Characteristics of included trials

| First author (year) | Country | Setting, type of trial | Patients included | Follow-up | Clinical diagnosis | Type of procalcitonin algorithm; procalcitonin cutoffs used (μg/L)[a] | Compliance with the PCT protocol |
|---|---|---|---|---|---|---|---|
| Annane (2013) [7] | France | ICU, multicenter | 62 | Hospital stay | Severe sepsis without overt source of infection and negative blood culture | Initiation and duration; R against AB: < 0.5 (< 0.25); R for AB: > 0.5 (> 5.0) | 63% adherence |
| Bloos (2016) [8] | Germany | ICU, multicenter | 1089 | 3 months | Severe sepsis or septic shock (SIRS and documented infection + criteria for severe sepsis/septic shock) | Discontinuation at days 4, 7, and 10; R against AB: < 1.0 or > 50% drop over previous value | 49.6% adherence |
| Bouadma (2010) [9] | France | ICU, multicenter | 621 | 2 months | Critically ill patients with assumed/proven bacterial infection | Initiation and duration; R against AB: < 0.5 (< 0.25); R for AB: > 0.5 (> 1.0) | 47% adherence |
| De Jong (2016) [10] | The Netherlands | ICU, multicenter | 1546 | 1 year | Critically ill patients with assumed infection | Duration; R against AB: < 0.5 or > 80% drop over peak value | 44% adherence |
| Deliberato (2013) [11] | Brazil | ICU, single center | 81 | ICU discharge or 14 days postrandomization | Sepsis patients with microbiologically confirmed bacterial infection | Duration; R against AB: < 0.5 or > 90% drop over peak value | 47.6% adherence |
| Hochreiter (2009) [14] | Germany | Surgical ICU, single center | 110 | Hospital stay | Sepsis (SIRS and documented infection) | Duration; R against AB: < 1 or > 65% drop over 3 days | not reported |
| Layios (2012) [15] | Belgium | ICU, single center | 379 | 1 month | Critically ill patients with assumed infection | Initiation; R against AB: < 0.5 (< 0.25); R for AB: > 0.5 (> 1.0) | 46.3% adherence |
| Nobre (2008) [17] | Switzerland | ICU, single center | 79 | 1 month | Severe sepsis or septic shock | Duration; R against AB: < 0.5 (< 0.25) or > 80% drop over peak value; R for AB: > 0.5 (> 1.0) | 81% adherence |
| Oliveira (2013) [16] | Brazil | ICU, multicenter | 94 | 28 days or hospital discharge | Severe sepsis or septic shock (SOFA score > 10 and/or bacteremia) | Discontinuation; Initial < 1.0: R against AB: 0.1 at day 4; Initial > 1.0: R against > 90% drop over peak value | 87.8% adherence |
| Schroeder (2009) [13] | Germany | Surgical ICU, single center | 27 | Hospital stay | Severe sepsis following abdominal surgery (SIRS and documented infection + criteria for severe sepsis/septic shock) | Duration; R against AB: < 1 or > 65% drop over 3 days | not reported |
| Shehabi (2014) [1] | Australia | ICU, multicenter | 394 | 3 months | Sepsis (SIRS and documented infection) | Duration; R against AB: < 0.25 (< 0.1) or > 90% drop over peak value | 97% adherence |

*AB* antibiotic, *ICU* intensive care unit, *PCT* procalcitonin, *R* recommendation, *SIRS* systemic inflammation response system, *SOFA* Sequential Organ Failure Assessment
[a] Cutoffs are listed as recommendation (strong recommendation)

4

## PTC has a role in guiding antibiotic therapy in critically «surgical» patients

- PCT-guided antibiotic treatment in ICU pts with infection results in improved survival and shorter antibiotic treatment duration.
- Effects were similar in sepsis pts and among subgroups based on sepsis severity, sepsis treatment modalities, and type of infection.

**Table 2** Baseline characteristics of included patients

| Parameter | Control group ($n = 2230$) | PCT group ($n = 2252$) |
|---|---|---|
| Demographics | | |
| Age (years) | 64.1 ± 15.0 | 63.5 ± 15.2 |
| Male gender | 1281 (57.5%) | 1273 (56.5%) |
| Primary focus of infection | | |
| Respiratory | 1101 (49.4%) | 1102 (48.9%) |
| Urinary | 129 (5.8%) | 118 (5.2%) |
| Abdominal | 417 (18.7%) | 391 (17.4%) |
| Skin/soft tissue | 41 (1.8%) | 32 (1.4%) |
| CNS | 35 (1.6%) | 38 (1.7%) |
| Other/unknown | 440 (19.7%) | 519 (23.0%) |
| Genital/gynecologic | 8 (0.4%) | 3 (0.1%) |
| Catheter-related | 14 (0.6%) | 16 (0.7%) |
| Bloodstream | 36 (1.6%) | 25 (1.1%) |
| Upper respiratory | 9 (0.4%) | 8 (0.4%) |
| Vital signs | | |
| Temperature (°C) | 37.7 ± 1.2 | 37.8 ± 1.1 |
| Sepsis score | | |
| Meeting sepsis 3 definition | 1630 (73.1%) | 1605 (71.3%) |
| SOFA score (points) | 7.4 ± 4.0 | 7.3 ± 4.1 |
| Additional sepsis support | | |
| Vasopressor use | 1593 (76.3%) | 1606 (76.7%) |
| Ventilation support | 1434 (68.1%) | 1478 (69.4%) |
| Renal replacement | 767 (34.4%) | 757 (33.6%) |

Values are presented as mean ± standard deviation or *n* (%) as appropriate
*CNS* central nervous system, *PCT* procalcitonin, *SD* standard deviation, *SOFA* Sequential Organ Failure Assessment

# PTC has a role in guiding antibiotic therapy in critically «surgical» patients

[ Original Research **Critical Care** ]

2019

CHEST

## Procalcitonin-Guided Antibiotic Discontinuation and Mortality in Critically Ill Adults

### A Systematic Review and Meta-analysis

Check for updates

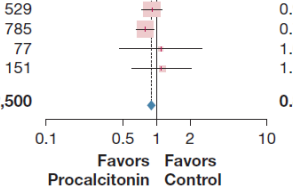
PODCAST

*Dominique J. Pepper, MD; Junfeng Sun, PhD; Chanu Rhee, MD; Judith Welsh, MLS; John H. Powers III, MD; Robert L. Danner, MD; and Sameer S. Kadri, MD*

findings of increased survival and decreased antibiotic utilization associated with PCT-guided antibiotic discontinuation, although with low-certainty evidence and high risk of bias…

| Study | Procalcitonin Events | Procalcitonin Total | Control Events | Control Total | RR | 95%-CI | Weight |
|---|---|---|---|---|---|---|---|
| Nobre | 9 | 39 | 9 | 40 | 1.03 | (0.46-2.31) | 1.7% |
| Hochreiter | 15 | 57 | 14 | 53 | 1.00 | (0.53-1.86) | 2.9% |
| Schroeder | 3 | 14 | 3 | 13 | 0.93 | (0.23-3.81) | 0.6% |
| Stolz | 10 | 51 | 14 | 50 | 0.70 | (0.34-1.43) | 2.2% |
| Bouadma | 65 | 307 | 64 | 314 | 1.04 | (0.76-1.41) | 12.0% |
| Maravic | 3 | 99 | 3 | 100 | 1.01 | (0.21-4.88) | 0.5% |
| Qu | 7 | 35 | 8 | 36 | 0.90 | (0.37-2.22) | 1.4% |
| Annane | 7 | 31 | 10 | 30 | 0.68 | (0.30-1.55) | 1.7% |
| Deliberato | 2 | 42 | 4 | 39 | 0.46 | (0.09-2.39) | 0.4% |
| Liu | 6 | 42 | 5 | 40 | 1.14 | (0.38-3.45) | 0.9% |
| Oliveira | 21 | 49 | 21 | 45 | 0.92 | (0.59-1.44) | 5.6% |
| Shehabi | 30 | 196 | 26 | 198 | 1.17 | (0.72-1.90) | 4.8% |
| Bloos | 140 | 547 | 149 | 529 | 0.91 | (0.75-1.11) | 29.0% |
| deJong | 149 | 761 | 196 | 785 | 0.78 | (0.65-0.95) | 31.9% |
| Xu | 10 | 79 | 9 | 77 | 1.08 | (0.47-2.52) | 1.6% |
| Daubin | 19 | 151 | 17 | 151 | 1.12 | (0.60-2.07) | 3.0% |
| **Random effects model** | | **2,500** | | **2,500** | **0.89** | **(0.83-0.97)** | **100.0%** |

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $P = .97$




2 – *Survival in 16 randomized clinical trials assessing procalcitonin-guided antibiotic discontinuation in critically ill adults. RR = risk ratio.*

5

PTC has a role in guiding antibiotic therapy in pts undergoing surgery for secondary peritonitis

2015

OPEN ACCESS Freely available online

PLOS ONE

## A Procalcitonin-Based Algorithm to Guide Antibiotic Therapy in Secondary Peritonitis following Emergency Surgery: A Prospective Study with Propensity Score Matching Analysis

**Ting-Shuo Huang[1,2], Shie-Shian Huang[3], Yu-Chiau Shyu[4,5], Chun-Hui Lee[2], Shyh-Chuan Jwo[2], Pei-Jer Chen[1], Huang-Yang Chen[2]***

**1** The Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, **2** Division of General Surgery, Department of Surgery, Chang Gung Memorial Hospital, Keelung Branch, Keelung, Taiwan, **3** Division of Infectious Diseases, Department of Medicine, Chang Gung Memorial Hospital, Keelung Branch, Keelung, Taiwan, **4** Institute of Biopharmaceutical Sciences, National Yang-Ming University, Taipei, Taiwan, **5** Department of Education and Research, Taipei City Hospital, Taipei, Taiwan

**Abstract**

***Background:*** Procalcitonin (PCT)-based algorithms have been used to guide antibiotic therapy in several clinical settings. However, evidence supporting PCT-based algorithms for secondary peritonitis after emergency surgery is scanty. In this study, we aimed to investigate whether a PCT-based algorithm could safely reduce antibiotic exposure in this population.

***Methods/Principal Findings:*** From April 2012 to March 2013, patients that had secondary peritonitis diagnosed at the emergency department and underwent emergency surgery were screened for eligibility. PCT levels were obtained pre-operatively, on post-operative days 1, 3, 5, and 7, and on subsequent days if needed. Antibiotics were discontinued if PCT was <1.0 ng/mL or decreased by 80% versus day 1, with resolution of clinical signs. Primary endpoints were time to discontinuation of intravenous antibiotics for the first episode and adverse events. Historical controls were retrieved for propensity score matching. After matching, 30 patients in the PCT group and 60 in the control were included for analysis. The median duration of antibiotic exposure in PCT group was 3.4 days (interquartile range [IQR] 2.2 days), while 6.1 days (IQR 3.2 days) in control ($p < 0.001$). The PCT algorithm significantly improves time to antibiotic discontinuation ($p < 0.001$, log-rank test). The rates of adverse events were comparable between 2 groups. Multivariate-adjusted extended Cox model demonstrated that the PCT-based algorithm was significantly associated with a 87% reduction in hazard of antibiotic exposure within 7 days (hazard ratio [HR] 0.13, 95% CI 0.07–0.21, $p < 0.001$), and a 68% reduction in hazard after 7 days (adjusted HR 0.32, 95% CI 0.11–0.99, $p = 0.047$). Advanced age, coexisting pulmonary diseases, and higher severity of illness were significantly associated with longer durations of antibiotic use.

***Conclusions/Significance:*** The PCT-based algorithm safely reduces antibiotic exposure in this study. Further randomized trials are needed to confirm our findings and incorporate cost-effectiveness analysis.

***Trial Registration:*** Australian New Zealand Clinical Trials Registry ACTRN12612000601831

**Citation:** Huang T-S, Huang S-S, Shyu Y-C, Lee C-H, Jwo S-C, et al. (2014) A Procalcitonin-Based Algorithm to Guide Antibiotic Therapy in Secondary Peritonitis following Emergency Surgery: A Prospective Study with Propensity Score Matching Analysis. PLoS ONE 9(3): e90539. doi:10.1371/journal.pone.0090539

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**Competing Interests:** The authors have declared that no competing interests exist.

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5

# PTC has a role in guiding antibiotic therapy in pts undergoing surgery for secondary peritonitis

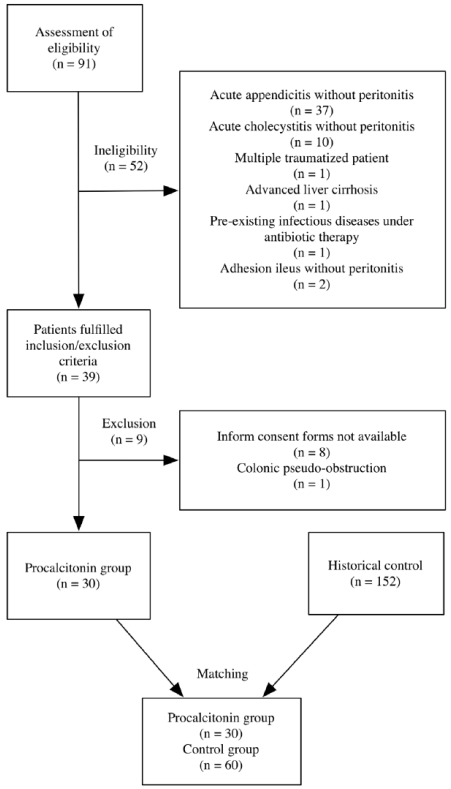


**Figure 1. Flow diagram of the study.**
doi:10.1371/journal.pone.0090539.g001

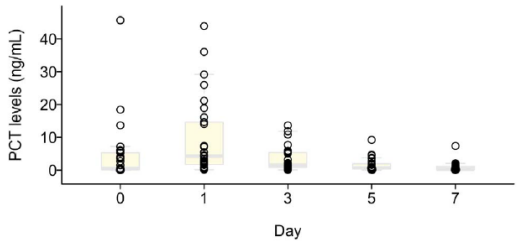


**Figure 2. Box plot of procalcitonin concentrations during pre-operative and post-operative periods.** The majority of day 1 procalcitonin levels declined nearly to physiological levels within 3 to 5

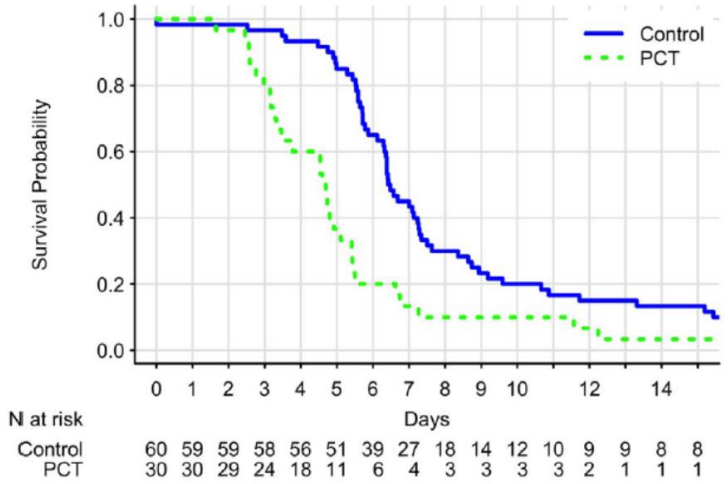


**Figure 3. Kaplan-Meier survival curves.** The results demonstrate that time to antibiotic discontinuation significantly improves in the treatment group ($p < 0.001$, log-rank test). The majority of patients in the control group discontinued antibiotics between postoperative day 4 and day 8. PCT, procalcitonin.
doi:10.1371/journal.pone.0090539.g003

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# PTC has a role in guiding antibiotic therapy in pts undergoing surgery for secondary peritonitis

Journal of Critical Care 30 (2015) 537–542

Contents lists available at ScienceDirect

Journal of Critical Care 2015

journal homepage: www.jccjournal.org

## Procalcitonin-guided therapy may reduce length of antibiotic treatment in intensive care unit patients with secondary peritonitis: A multicenter retrospective study

Emilio Maseda, MD [a,*], Alejandro Suarez-de-la-Rica, MD [a], Víctor Anillo, MD [a], Eduardo Tamayo, MD [b], Carlos A. García-Bernedo, MD [c], Fernando Ramasco, MD [d], Maria-Jose Villagran, MD [a], Genaro Maggi, MD [a], Maria-Jose Gimenez, PhD [e], Lorenzo Aguilar, MD [e], Juan-José Granizo, MD [f], Antonio Buño, MD [g], Fernando Gilsanz, MD [a]

PURPOSE:
Because procalcitonin (PCT) might be surrogate for antimicrobial discontinuation in general intensive care units (ICUs), this study explored its use for secondary peritonitis in 4 surgical ICUs (SICUs).
METHODS:
A retrospective study including all consecutive patients with secondary peritonitis, controlled infection source, requiring surgery, and at least 48-hour SICU admission was performed (June 2012-June 2013). Patients were divided following notations in medical records into PCT-guided (notation of PCT-based antibiotic discontinuation) and non-PCT-guided (no notation) groups.
RESULTS:
A total of 121 patients (52 PCT-guided, 69 non-PCT-guided) were included. No differences in clinical scores, biomarkers, or septic shock (30 [57.7%] PCT-guided vs 40 [58.0%] non-PCT-guided) were found. Length of intra-SICU (median, 5.0 days; both groups) or in-hospital (median, 20.0 vs 17.5 days) stay, and mortality intra-SICU (9.6% vs 13.0%), 28-day (15.4% vs 20.3%), or in-hospital (19.2% vs 29.0%) were not significantly different (PCT-guided vs non-PCT-guided). In septic shock patients, no mortality differences were found (PCT-guided vs non-PCT-guided): 16.7% vs 22.5% (intra-SICU), 26.7% vs 32.5% (28-day), and 33.3% vs 42.5% (in-hospital). Treatment was shorter in the PCT-guided group (5.1 ±2.1 vs 10.2 ± 3.7 days, P < .001), without differences between patients with and without septic shock.
CONCLUSION:
Procalcitonin guidance produced 50% reduction in antibiotic duration (P < .001, log-rank test).

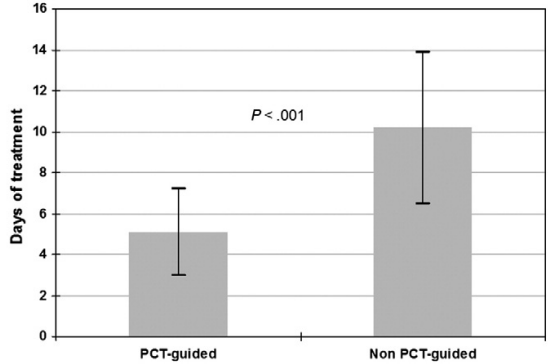


Fig. 3. Length of antimicrobial treatment. Length of antimicrobial treatment in PCT-guided vs non–PCT-guided groups.

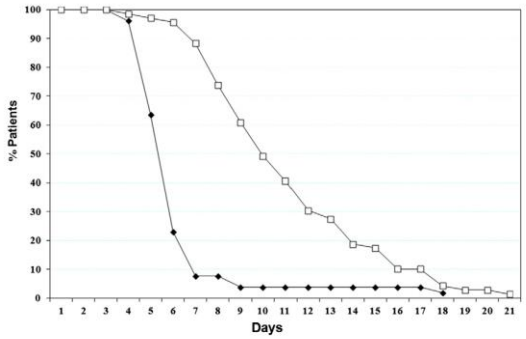


Fig. 2. Patients under antimicrobial treatment over time. Percentage of patients under antimicrobial treatment over time in PCT-guided (solid squares) and non–PCT-guided (open squares) study groups.

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PTC has a role in guiding antibiotic therapy in pts undergoing surgery for secondary peritonitis

Hindawi
Gastroenterology Research and Practice
Volume 2017, Article ID 3457614, 6 pages
https://doi.org/10.1155/2017/3457614

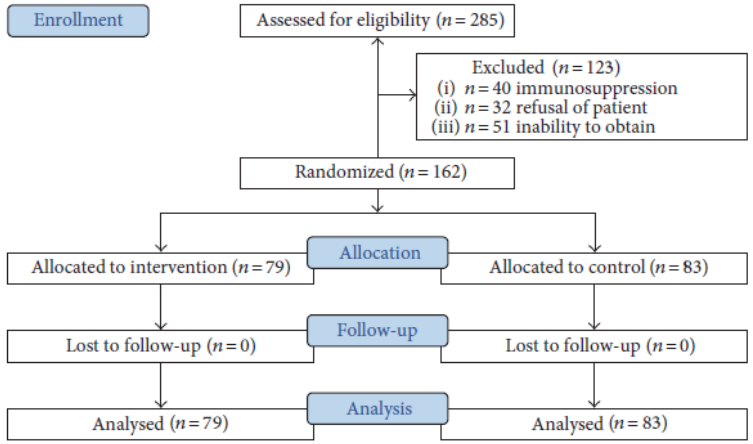
2017

Hindawi

*Clinical Study*

**Procalcitonin-Guided Antibiotics after Surgery for Peritonitis: A Randomized Controlled Study**

**Juliette C. Slieker,[1] Steve Aellen,[2] Philippe Eggimann,[3] Valentine Guarnero,[1] Markus Schäfer,[1] and Nicolas Demartines[1]**




| Indication | Duration | First choice antibiotics |
|---|---|---|
| Perforated appendicitis with peritonitis | 5 days | Amoxicillin/clavulanic acid<br>Allergy: ciprofloxacin + metronidazole |
| Peritonitis due to gastrointestinal perforation | 10 days | Amoxicillin/clavulanic acid. If severe infection: imipenem or piperacillin/tazobactam<br>Allergy: ciprofloxacin + metronidazole |
| Peritonitis due to gastrointestinal perforation, acquired in-hospital | 10 days | Imipenem or piperacillin/tazobactam<br>Allergy: ciprofloxacin + metronidazole |

Table 3: Primary outcome measure: duration of antibiotics (median with interquartile range, days).

| Duration antibiotic treatment | Procalcitonin ($n = 79$) | Control ($n = 83$) | $p$ value |
|---|---|---|---|
| (i) All patients | 8 (5–16) | 10 (6–12) | 0.714 |
| (ii) Subgroup 1: GI perforation | 7 (5–12) | 10 (8.5–12) | 0.065 |
| (iii) Subgroup 2: appendicitis | 8 (5.5–13.5) | 8 (5–11) | 0.573 |
| (iv) Subgroup 3: postoperative | 18.5 (6.75–29.5) | 13 (11–18) | 0.403 |

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# PTC has a role in guiding antibiotic therapy in pts undergoing surgery for secondary peritonitis

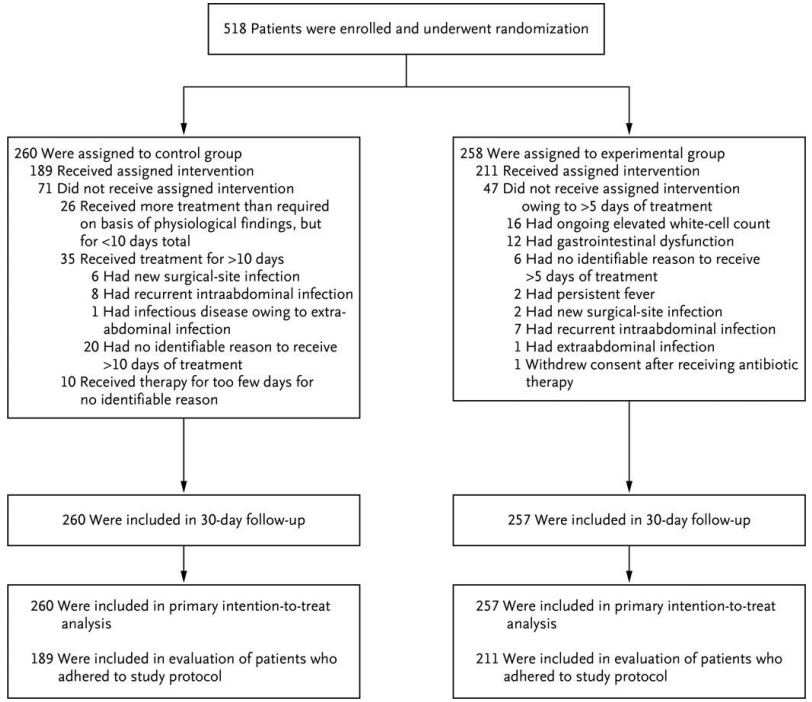
The NEW ENGLAND JOURNAL of MEDICINE

2015

ORIGINAL ARTICLE

## Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection

R.G. Sawyer, J.A. Claridge, A.B. Nathens, O.D. Rotstein, T.M. Duane, H.L. Evans, C.H. Cook, P.J. O'Neill, J.E. Mazuski, R. Askari, M.A. Wilson, L.M. Napolitano, N. Namias, P.R. Miller, E.P. Dellinger, C.M. Watson, R. Coimbra, D.L. Dent, S.F. Lowry,* C.S. Cocanour, M.A. West, K.L. Banton, W.G. Cheadle, P.A. Lipsett, C.A. Guidry, and K. Popovsky




**CONCLUSIONS**

In patients with intraabdominal infections who had undergone an adequate source-control procedure, the outcomes after fixed-duration antibiotic therapy (approximately 4 days) were similar to those after a longer course of antibiotics (approximately 8 days) that extended until after the resolution of physiological abnormalities. (Funded by the National Institutes of Health; STOP-IT ClinicalTrials.gov number, NCT00657566.)

5

PTC has a role in guiding antibiotic therapy in pts undergoing surgery for secondary peritonitis

antibiotics 2023 MDPI

*Review*

# Management of Intra-Abdominal Infections: The Role of Procalcitonin

**Brian W. C. A. Tian [1], Vanni Agnoletti [2], Luca Ansaloni [3], Federico Coccolini [4], Francesca Bravi [5], Massimo Sartelli [6], Carlo Vallicelli [7] and Fausto Catena [8,*]**

[1] Department of General Surgery, Singapore General Hospital, Outram Road, Singapore 169608, Singapore; brianantonytian@gmail.com
[2] Anesthesia and Intensive Care Unit, M. Bufalini Hospital, 47521 Cesena, Italy
[3] Department of Surgery, Pavia University Hospital, 27100 Pavia, Italy
[4] General, Emergency and Trauma Surgery Department, Pisa University Hospital, 56126 Pisa, Italy
[5] Santa Maria Delle Croci Hospital, 48121 Ravenna, Italy
[6] Department of Surgery, Macerata Hospital, Via Santa Lucia 2, 62100 Macerata, Italy
[7] Department of Emergency and Trauma Surgery, M. Bufalini Hospital, 47521 Cesena, Italy
[8] Department of Surgery, "Maurizio Bufalini" Hospital, 47521 Cesena, Italy
* Correspondence: faustocatena@gmail.com

**Abstract:** Patients with intra-abdominal sepsis suffer from significant mortality and morbidity. The main pillars of treatment for intra-abdominal infections are (1) source control and (2) early delivery of antibiotics. Antibiotic therapy should be started as soon as possible. However, the duration of antibiotics remains a matter of debate. Prolonged antibiotic delivery can lead to increased microbial resistance and the development of nosocomial infections. There has been much research on biomarkers and their ability to aid the decision on when to stop antibiotics. Some of these biomarkers include interleukins, C-reactive protein (CRP) and procalcitonin (PCT). PCT's value as a biomarker has been a focus area of research in recent years. Most studies use either a cut-off value of 0.50 ng/mL or an >80% reduction in PCT levels to determine when to stop antibiotics. This paper performs a literature review and provides a synthesized up-to-date global overview on the value of PCT in managing intra-abdominal infections.

**Keywords:** procal; procalcitonin; sepsis; intra-abdominal; infection

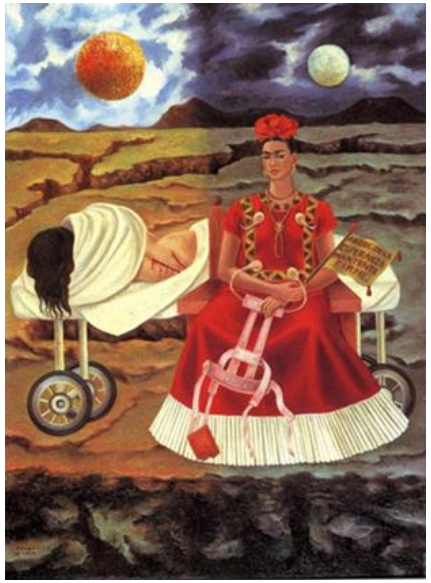
check for updates

**Citation:** Tian, B.W.C.A.; Agnoletti, V.; Ansaloni, L.; Coccolini, F.; Bravi, F.; Sartelli, M.; Vallicelli, C.; Catena, F. Management of Intra-Abdominal Infections: The Role of Procalcitonin. *Antibiotics* **2023**, *12*, 1406. https://doi.org/10.3390/antibiotics12091406

## 1. Introduction

Patients with intra-abdominal sepsis suffer from significant mortality and morbidity.

# 6 PTC has a role in identifying pts at risk of complications after major abdominal surgery



Spoto et al. Medicine (2018) 97:3

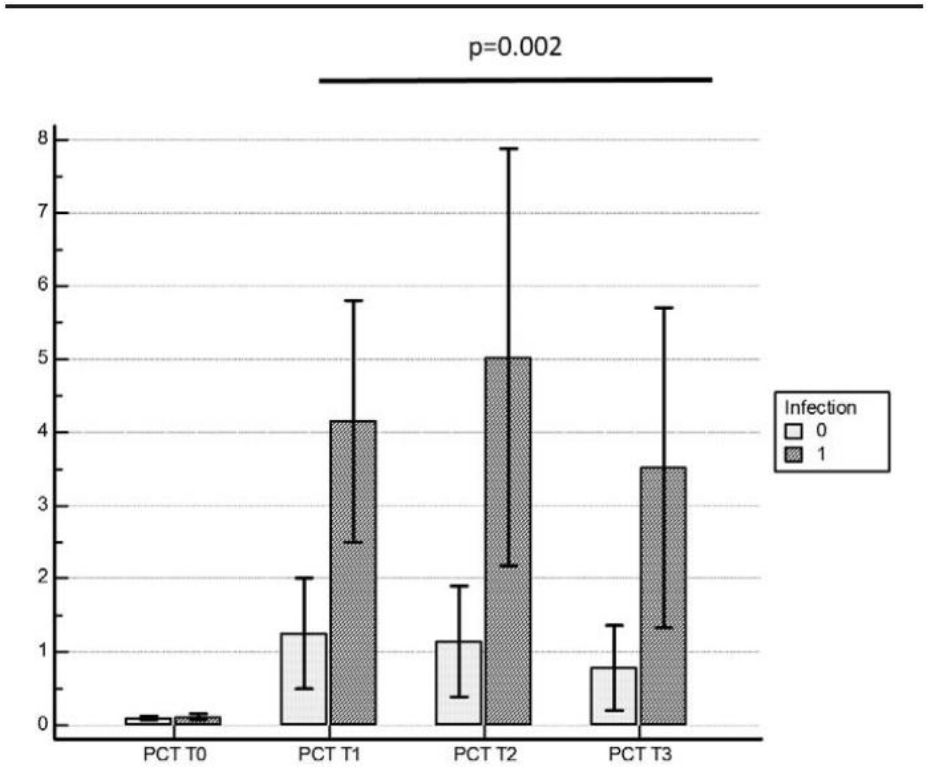



**Figure 4.** ANOVA analysis of variance on PCT measurement at different time points in the 2 groups of patients with and without infection (1,0).

Observational Study 2018 Medicine OPEN

## The role of procalcitonin in the diagnosis of bacterial infection after major abdominal surgery

### Advantage from daily measurement

Silvia Spoto, MD[a], Emanuele Valeriani, MD[b], Damiano Caputo, MD[c], Eleonora Cella, PhD[d,e], Marta Fogolari, MD[e], Elena Pesce, MD[a], Maria Tea Mulè, MD[a], Mariacristina Cartillone, MD[c], Sebastiano Costantino, MD[a], Giordano Dicuonzo, MD[e], Roberto Coppola, MD[c], Massimo Ciccozzi, PhD[e], Silvia Angeletti, MD[e,*]

**Abstract**

Postsurgical infections represent an important cause of morbidity after abdominal surgery. The microbiological diagnosis is not achieved in at least 30% of culture with consequent worsening of patient outcome. In this study, procalcitonin measurement, during the first 3 days after abdominal surgery, has been evaluated for the early diagnosis of postsurgical infection.

Ninety consecutive patients subjected to major abdominal surgery at the University Campus Bio-Medico of Rome, have been included. PCT concentrations were measured by time-resolved amplified cryptate emission (TRACE) assay at admission and at the first, second, and third day after surgery. PCT levels were compared using the Mann–Whitney test and by ANOVA test for variance analysis. Receiver operating characteristic (ROC) analysis was performed to define the diagnostic ability of PCT in case of postsurgical infections.

PCT values resulted significantly different between patients developing or not developing postsurgical infections. PCT >1.0 ng/mL at first or second day after surgery and >0.5 ng/mL at third day resulted diagnostic for infectious complication, whereas a value <0.5 ng/mL at the fifth day after surgery was useful for early and safety discharge of patients.

In conclusion, PCT daily measurement could represent a useful diagnostic tool improving health care in the postsurgical period following major abdominal surgery and should be recommended.

**Abbreviations:** ASA = American Society of Anesthesiologists, AUC = areas under the curves, BMI = body mass index, CONS = *coagulase negative staphylococci*, CRBSI = catheter related bloodstream, CRP = C-reactive protein, MOF = multiple organ failure, PCT = procalcitonin, ROC = receiver operating characteristic, SSIs = surgical site infections, TC = computed tomography, TRACE = time-resolved amplified cryptate emission, WBC = white blood cell.

**Keywords:** early diagnosis, PCT, surgical infections

# 6 PTC has a role in identifying pts at risk of complications after major abdominal surgery

Original paper | General surgery | 2018 | Videosurgery

## Use of inflammatory markers in the early detection of infectious complications after laparoscopic colorectal cancer surgery with the ERAS protocol

Mateusz Wierdak[1,2], Magdalena Pisarska[1,2], Beata Kuśnierz-Cabala[3], Michał Kisielewski[1], Piotr Major[1,2], Jan S. Witowski[1,2], Piotr Ceranowicz[4], Marcin Strzałka[1], Andrzej Budzyński[1,2], Michał Pędziwiatr[1,2]

[1]2nd Department of General Surgery, Jagiellonian University Medical College, Krakow, Poland
[2]Centre for Research, Training and Innovation in Surgery, Krakow, Poland
[3]Department of Diagnostics, Chair of Clinical Biochemistry, Jagiellonian University Medical College, Krakow, Poland
[4]Department of Physiology, Jagiellonian University Medical College, Krakow, Poland

Videosurgery Miniinv 2018; 13 (3): 315–325
DOI: https://doi.org/10.5114/wiitm.2018.75846

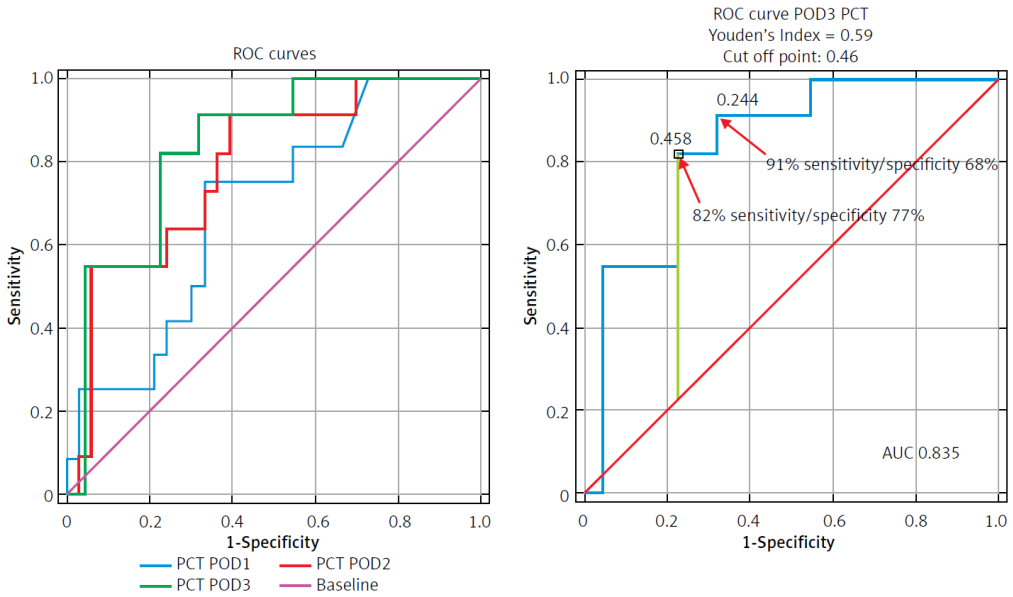



**Figure 7.** ROC curve analysis for PCT on successive PODs. POD3 was observed to achieve the best parameters in AUC evaluation. Established cut-off point is 0.244 ng/l (see text description)

# 6 PTC has a role in identifying pts at risk of complications after major abdominal surgery

DOI:10.22034/APJCP.2017.18.7.1821
Anastomotic Leak

RESEARCH ARTICLE 2017

## Serum Procalcitonin Predicts Anastomotic Leaks in Colorectal Surgery

**Firdaus Hayati[1]*, Zairul Azwan Mohd Azman[2], Dian Nasriana Nasuruddin[3], Luqman Mazlan[2], Andee Dzulkarnaen Zakaria[4], Ismail Sagap[2]**

**Abstract**

**Background:** Anastomotic leaks in colorectal surgery results in a high morbidity and mortality rate. Serum procalcitonin levels is known as a sensitive and specific marker of sepsis and could be use as a marker for early detection of a leak allowing early intervention. It may help a clinician decide to perform a CT scan even earlier especially when the diagnosis of a leak is uncertain. The aim of this study is to determine whether serum procalcitonin is a good predictor of anastomotic leak in colorectal surgery. **Methodology:** Between July 2014 until October 2015, 70 patients undergoing colorectal surgery were prospectively analyzed in a single-center tertiary teaching hospital. Demographic and surgical data were obtained. Serum procalcitonin was taken before surgery and at day 3 (72 hours) postoperatively. During the postoperative period, the patients were observed in the ward for features of anastomotic leak and if present, it was managed accordingly. The primary outcome was to prospectively determine an association between serum procalcitonin levels and an anastomotic leak in patients who underwent colorectal surgery with a primary anastomosis. **Result:** The rate of anastomotic leak was 4.5% (3 patients) with a mortality rate of 4.3% (3 patients). A rise in serum procalcitonin was statistically significant among patients with anastomotic leak. The optimal procalcitonin cut-off level at postoperative day 3 was 5.27 ng/mL, resulting in 100% sensitivity, 85% specificity, 23% positive predictive value and 100% negative predictive value. Nevertheless, none of the variables showed statistical significance with an anastomotic leak. **Conclusion:** Procalcitonin is a reliable biochemical marker to help diagnose anastomotic leak in colorectal surgery. Our study has shown that a level of 5 times beyond normal is statistically significant and a value of more than 5.27 ng/mL is confirmatory of a leak.

**Keywords:** Colon- leak- procalcitonin- rectum- surgery

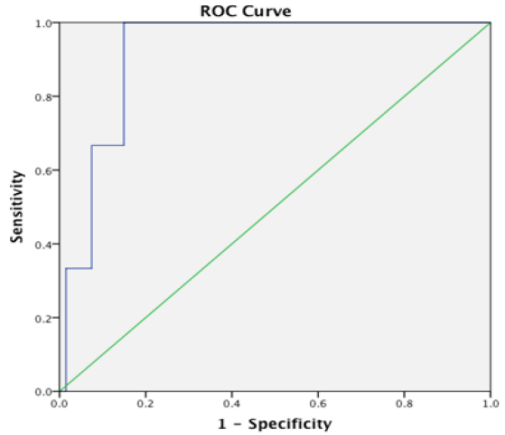



Figure 1. ROC Curve for PCT at Day 3

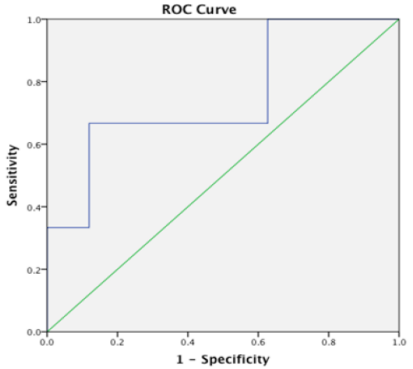



Figure 2. ROC Curve for TWC at Day 3

# PTC has a role in identifying pts at risk of complications after major abdominal surgery

El Zaher *et al.*
*World Journal of Surgical Oncology* (2022) 20:33
https://doi.org/10.1186/s12957-022-02506-4

World Journal of Surgical Oncology

RESEARCH Open Access

## Role of the triad of procalcitonin, C-reactive protein, and white blood cell count in the prediction of anastomotic leak following colorectal resections

Haidi Abd El Zaher[1†], Waleed M. Ghareeb[2,3*†], Ahmed M. Fouad[4], Khaled Madbouly[5*], Hamada Fathy[1], Tomas Vedin[6], Marcus Edelhamre[6], Sameh H. Emile[7*] and Mohammed Faisal[1,8]

2022

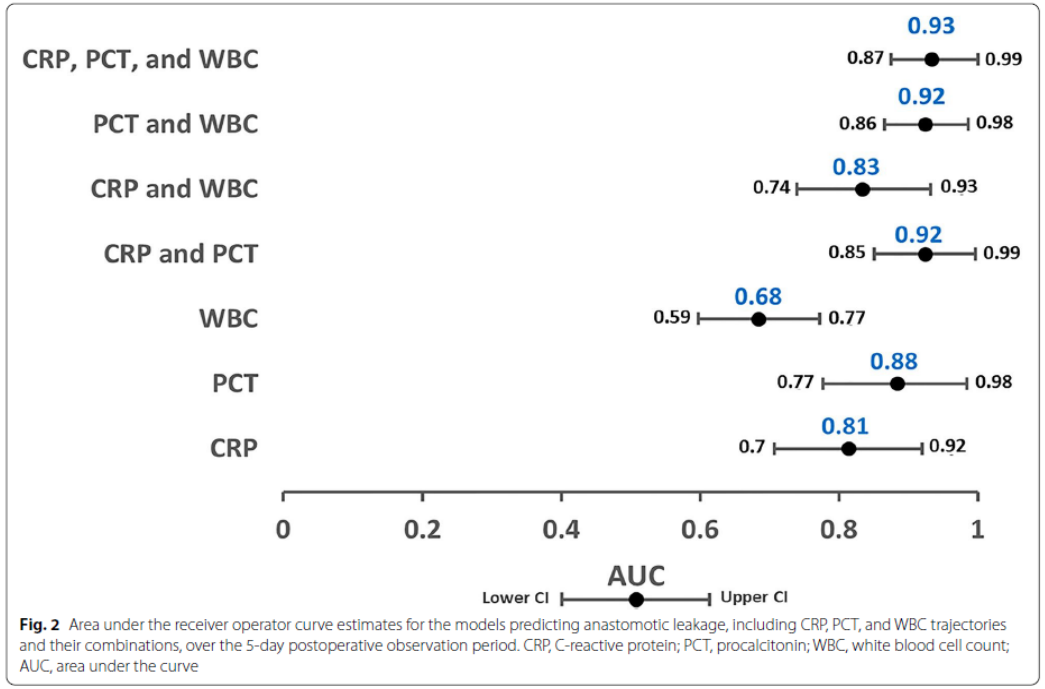



**Fig. 2** Area under the receiver operator curve estimates for the models predicting anastomotic leakage, including CRP, PCT, and WBC trajectories and their combinations, over the 5-day postoperative observation period. CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cell count; AUC, area under the curve

# PCT in assessing the severity and prognosis of acute pancreatitis

7

## Early elevation of PCT in patients suffering from AP is of great significance in predicting SAP

### Exploring the value of early laboratory indicators combined with pancreatitis activity scoring system in assessing the severity and prognosis of acute pancreatitis

*Fang Xu[1], Xin Hu[2], Shu-ling Li[3]*

**ABSTRACT**

***Objective***: To investigate the value of early laboratory indicators combined with the pancreatitis activity scoring system in assessing the severity and prognosis of acute pancreatitis (AP).

***Methods:*** This is a retrospective study. A total of 160 patients with AP admitted to the Affiliated Hospital of Hebei University from February 2021 to February 2023 were enrolled and classified into three categories: mild acute pancreatitis (MAP), moderate severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP), with 80 cases with MAP and MSAP as the control group and 80 cases with SAP as the experimental group. The differences of inflammatory markers, blood routine, biochemical markers, coagulation markers and PASS score within 24 hours after admission were compared between the two groups, and independent risk factors for predicting AP severity were analyzed. Moreover, the diagnostic efficacy and prognostic value of independent risk factors were evaluated.

***Results:*** The PASS score as well as CRP, PCT, IL-6, WBC, N, AST, DD and PT were higher in the experimental group than in the control group. Logistic regression analysis suggested that PASS, IL-6, PCT and WBC were independent risk factors for predicting severity of AP. In addition, PASS had the highest diagnostic efficacy.

***Conclusion:*** Early elevation of PASS, IL-6, PCT and WBC in patients suffering from AP is of great significance in predicting SAP. PASS score combined with IL-6, PCT and WBC has important value in evaluating the severity and prognosis of AP.

**KEYWORDS:** Acute pancreatitis, Early laboratory examination, Severity, PASS score.

**doi: https://doi.org/10.12669/pjms.39.5.7543**

***How to cite this:*** *Xu F, Hu X, Li S. Exploring the value of early laboratory indicators combined with pancreatitis activity scoring system in assessing the severity and prognosis of acute pancreatitis. Pak J Med Sci. 2023;39(5):---------. doi: https://doi.org/10.12669/pjms.39.5.7543*



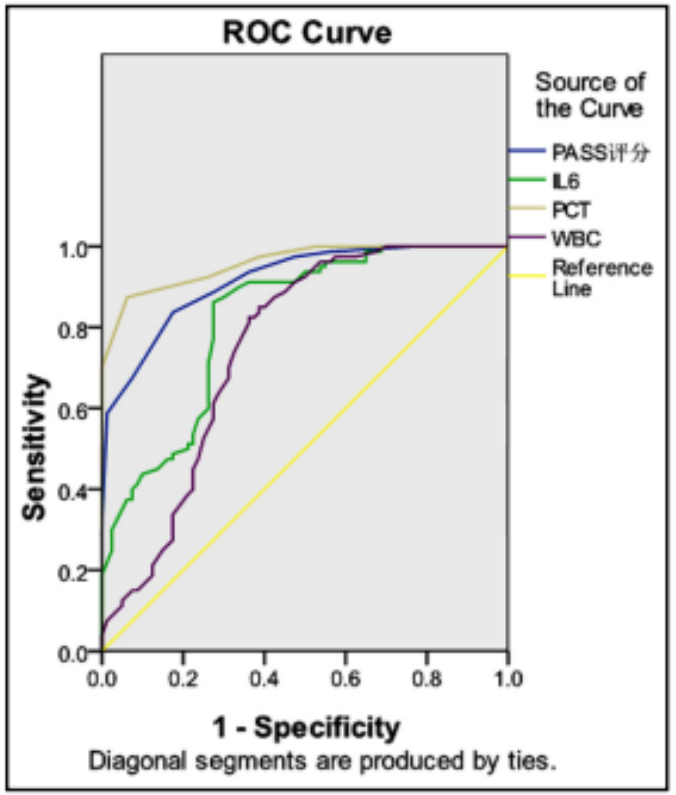
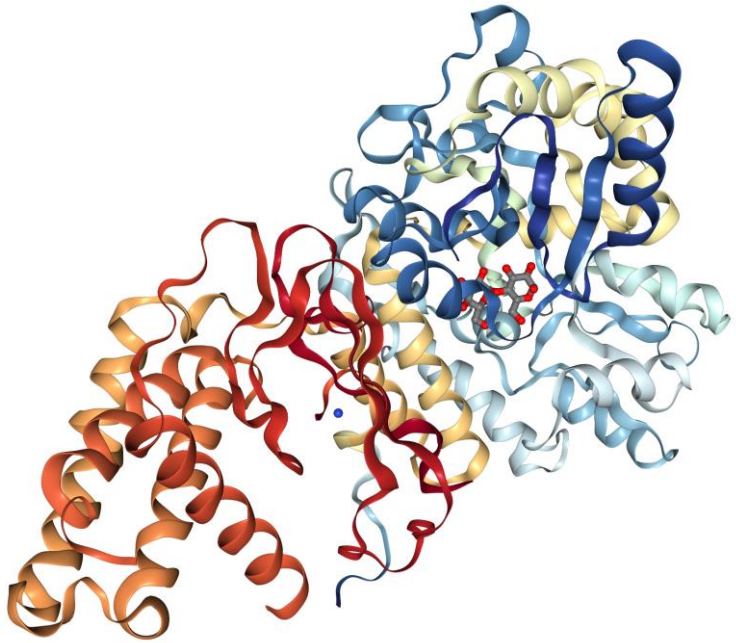
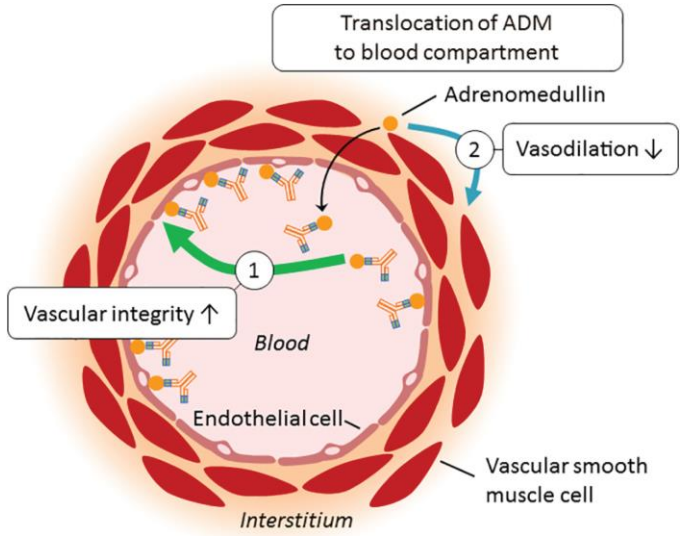



Fig.1: Diagnostic significance of PPASS score and independent risk factors in acute pancreatitis.

# Something new: adrenomedullin

- ✓ ADM = a hormone produced by a variety of different cell types and was first derived from pheochromocytoma nearly 3 decades ago. ADM has homeostatic and regulating effects on renal, immunological, endocrine and cardiovascular systems.
- ✓ The effects of ADM on blood vessels include vasodilation and **stabilization of the barrier function of endothelial cells maintaining adequate permeability**. ADM is typically elevated in pts with the metabolic syndrome, heart failure, chronic kidney failure as well as in unselected critically ill pts.






NEW!

# Something new: adrenomedullin

Several studies have reported a strong association between elevated ADM levels and mortality, severity of illness and need for organ support in sepsis pts, proposing ADM to be a predictive biomarker in sepsis.

PLOS ONE

RESEARCH ARTICLE

2022

Bioactive adrenomedullin in sepsis patients in the emergency department is associated with mortality, organ failure and admission to intensive care

Oscar H. M. Lundberg[1,2]*, Mari Rosenqvist[3,4], Kevin Bronton[3,5], Janin Schulte[6], Hans Friberg[1,2], Olle Melander[3,4,5]

1 Department of Clinical Sciences, Anaesthesiology and Intensive Care, Medical Faculty, Lund University, Lund, Sweden, 2 Department of Intensive and Perioperative Care, Skåne University Hospital, Malmö, Sweden, 3 Department of Clinical Sciences, Medical Faculty, Lund University, Malmö, Sweden, 4 Department of Infectious Diseases, Skåne University Hospital, Malmö, Sweden, 5 Department of Internal Medicine, Skåne University Hospital, Malmö, Sweden, 6 SphingoTec GmbH, Hennigsdorf, Germany

* oscar.lundberg@med.lu.se

Check for updates

*medicina*

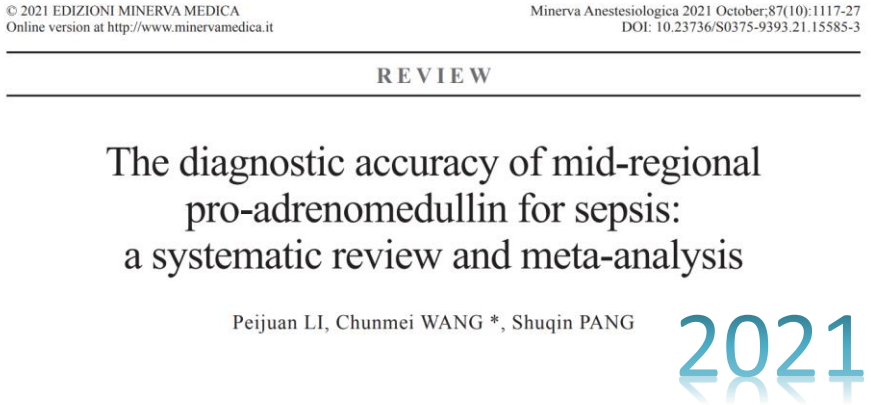
MDPI

*Review*

**Proadrenomedullin in Sepsis and Septic Shock: A Role in the Emergency Department**

Andrea Piccioni [1], Angela Saviano [1,*], Sara Cicchinelli [1], Federico Valletta [1], Michele Cosimo Santoro [1], Tommaso de Cunzo [1], Christian Zanza [1], Yaroslava Longhitano [2], Gianluca Tullo [1], Pietro Tilli [1], Marcello Candelli [1], Marcello Covino [1] and Francesco Franceschi [1]

2021



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Online version at http://www.minervamedica.it

Minerva Anestesiologica 2021 October;87(10):1117-27
DOI: 10.23736/S0375-9393.21.15585-3

REVIEW

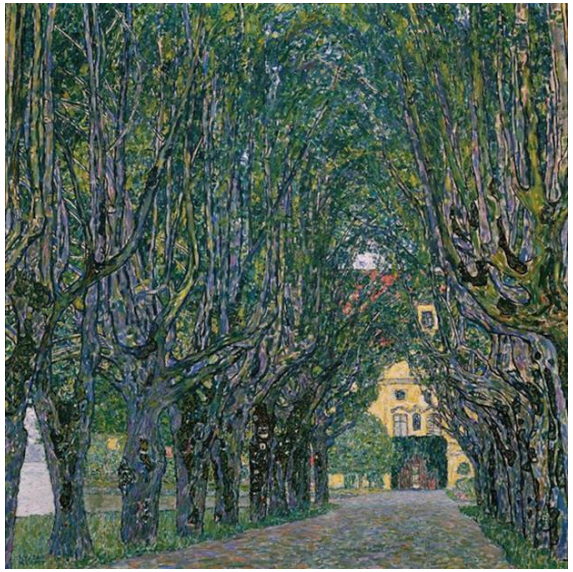
The diagnostic accuracy of mid-regional pro-adrenomedullin for sepsis: a systematic review and meta-analysis

Peijuan LI, Chunmei WANG *, Shuqin PANG

2021

# Something new: adrenomedullin

## …initial reports in surgical pathologies…



American Journal of Emergency Medicine xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

### Assessment of proadrenomedullin as diagnostic or prognostic biomarker of acute appendicitis in children with acute abdominal pain

2018

Niki Oikonomopoulou [a,*], Concepción Míguez-Navarro [a], Arístides Rivas-García [a], Mercedes García Gamiz [a], Rosario López-López [b], Paloma Oliver-Sáez [c], Bibiana Riaño-Méndez [d], Tamara Farfan-Orte [d], Zulema Lobato-Salinas [e], Júlia Rúbies-Olives [f], Priscila Llena-Isla [f], Encarnación María Lancho-Monreal [g], on behalf of the, group PROADM-DOLOR ABDOMINAL of the research net of the Spanish Society of Pediatric Emergencies (RISEUP-SPERG)

American Journal of Emergency Medicine xxx (xxxx) xxx–xxx

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### Relationship between serum Pentraxin 3 and pro-adrenomedullin levels with acute cholecystitis

2019

Abdullah Algin, MD [a], Umut Gulacti, MD [a,*], İbrahim Inan, MD [b], Mehmet Ozgur Erdogan, MD [c], Sahin Colak, MD [d], Mehmet Sariaydin, MD [e]

# Something new: adrenomedullin

- potential of modulating the ADM hormonal system has gained interest since exogenous infusion of ADM in animal models of sepsis has been shown to improve outcomes, which has led to the hypothesis that an increment of intravascular bio-ADM may be of therapeutic value in sepsis.
- non-neutralizing anti-ADM antibody (Adrecizumab) treatment in humans? Adrecizumab-ADM complexes generates elevated intravascular bio-ADM, exerting its endothelium-stabilizing effects: clinical implication of the use of Adrecizumab in sepsis is yet unanswered, but clinical trials to investigate this are planned.

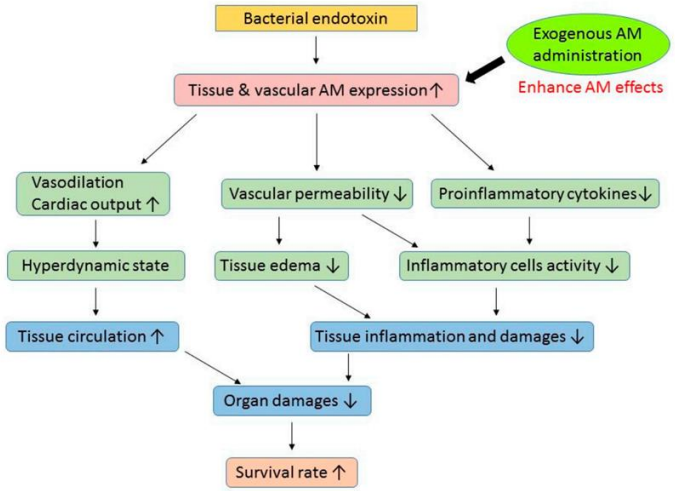



**Figure 3.** Simplified adrenomedullin cascade, an organ-protective factor against sepsis. AM: adrenomedullin.


2022

Kalvelage et al. Trials (2019) 20:156
https://doi.org/10.1186/s13063-019-3244-4

Trials

STUDY PROTOCOL Open Access

Personalized medicine with IgGAM compared with standard of care for treatment of peritonitis after infectious source control (the PEPPER trial): study protocol for a randomized controlled trial

Christina Kalvelage[1], Kai Zacharowski[2], Artur Bauhofer[3], Ulrich Gockel[4], Michael Adamzik[5], Axel Nierhaus[6], Peter Kujath[7], Christian Eckmann[8], Mathias W. Pletz[9], Hendrik Bracht[10], Tim-Philipp Simon[11], Michael Winkler[12], Detlef Kindgen-Milles[13], Markus Albertsmeier[14], Markus Weigand[15], Björn Ellger[16], Maximilian Ragaller[17], Roman Ullrich[18] and Gernot Marx[11*]

biomedicines

MDPI

*Review*

**Adrenomedullin Therapy in Moderate to Severe COVID-19**

**Toshihiro Kita * and Kazuo Kitamura**

# Something new: adrenomedullin

- PTX3 = an acute-phase protein belonging to the long-chain pentameric protein superfamily. As a key component of the human innate immune system, it plays an important role in the regulation of inflammation.
- In recent years, PTX3 has emerged as a promising biomarker for sepsis diagnosis and prognosis.

## Therapeutic implications….

**NEW!**

Wang et al. Critical Care (2022) 26:167
https://doi.org/10.1186/s13054-022-04032-x

Critical Care

RESEARCH Open Access

### Pentraxin-3 as a predictive marker of mortality in sepsis: an updated systematic review and meta-analysis

Guobin Wang, Chunyan Jiang, Junjun Fang, Zhitao Li and Hongliu Cai*

**Abstract**

**Background:** The purpose of this study was to clarify the prognostic value of Pentraxin-3 (PTX3) on the mortality of patients with sepsis.

**Methods:** Publications published up to January 2021 were retrieved from PubMed, EMBASE, and the Cochrane library. Data from eligible cohort and case–control studies were extracted for the meta-analysis. Multivariate regression analysis was used to evaluate the correlation of the outcomes with sample size and male proportion.

**Results:** A total of 17 studies covering 3658 sepsis patients were included. PTX3 level was significantly higher in non-survivor compared to survivor patients (SMD (95% CI): −1.06 (−1.43, −0.69), $P < 0.001$). Increased PTX3 level was significantly associated with mortality (HR (95% CI): 2.09 (1.55, 2.81), $P < 0.001$). PTX3 showed good predictive capability for mortality (AUC:ES (95% CI): 0.73 (0.70, 0.77), $P < 0.001$). The outcome comparing PTX3 level in non-survivors vs. survivors and the outcome of the association between PTX3 and mortality were associated with sample size but not male proportion. AUC was associated with both sample size and male proportion.

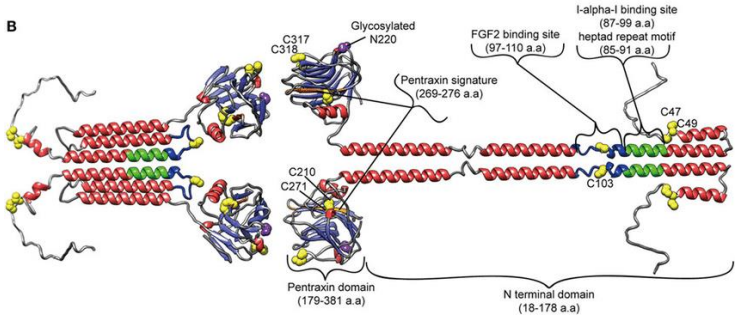
**Conclusions:** PTX3 level was significantly higher in non-survivor compared to survivor patients with sepsis. Elevated PTX3 level was significantly associated with mortality. Furthermore, the level of PTX3 might predict patient mortality.

**Keywords:** Pentraxin-3, Sepsis, Mortality, AUC, Meta-analysis

A

```
PTX3 N-terminal domain
      1  MHLLAILFCALWSAVLAENSDDYDLMYVNLDNEIDNGLHPTEDPTPCDCGQEHSEWDKLF 60
PSIPRED                  CCCCHHHHHHCCCCCCCCCCCCCCCCCCCCCCCCCCHHHHHH
SPIDER2                  CCCCCHCHHEEECCCCCCCCCCCCCCCCCCCCCCCCCHHHHHH
     61  IMLENSQMRERMLLQATDDVLRGELQRLREELGRLAESLARPCAPGAPAEARLTSALDEL 120
PSIPRED  HHHHCHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHCCCCCCCCCCHHHHHHHHHH
SPIDER2  HHHCCCHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHCCCCCCCCCCHHHHHHHHHH
    121  LQATRDAGRRLARMEGAEAQRPEEAGRALAAVLEELRQTRADLHAVQGWAARSWLPAG 178
PSIPRED  HHHHHHHHHHHHHHHHHCCCHHHHHHHHHHHHHHHHHHHHHHHHHHHHCCCCCC
SPIDER2  HHHHHHHHHHHHHCCCCCCCCHHHHHHHHHHHHHHHHHHHHHHHHHHHHCCCCC
```

B



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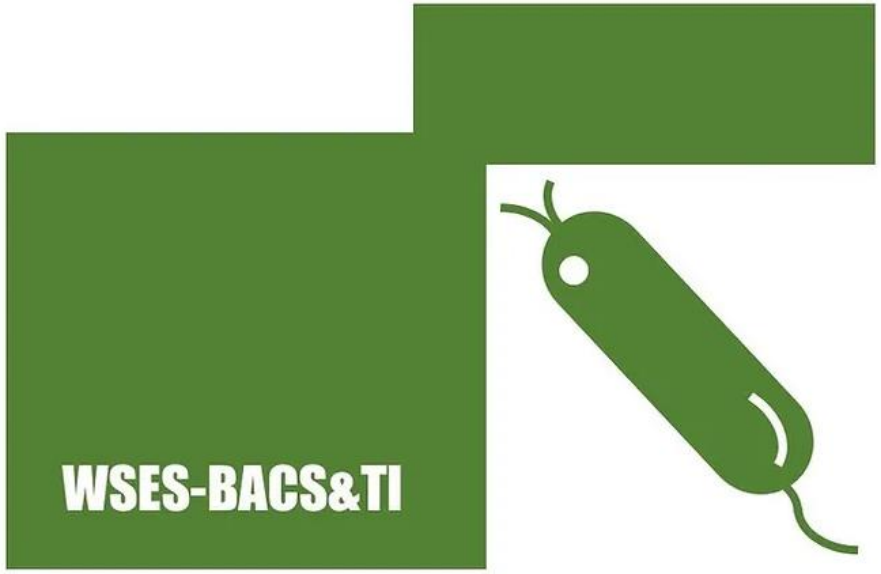


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Biomarkers in Acute Care Surgery & Trauma Initiative

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# THM station

- PCT better than CRP
- (1) PCT-appendicitis: diagnosis+ (with scores), complicated+++
- (2) PCT-cholecystitis: complicated+++ (difficult lap chole & postop complications) [CholepossumPro]
- (3) PCT-diverticulitis: complicated+++ (with CT)
- (4) PTC-guided abx therapy in critically «surgical» pts: reduces (improves) abx use & increases survival (?!)
- (5) PTC-guided abx therapy in pts with secondary peritonitis reduces (improves) abx use
- (6) PTC identifies pts at risk of complications after major abdominal (colorectal…) surgery: ERAS
- (7) PCT in patients suffering from AP is of great significance in predicting SAP
- New: ADM diagnosis+ prognosis+ therapy!!!
- New: PTX3 diagnosis+ prognosis+ therapy!!!

… I hope I have not bored you…


# THM station

- Different "PTC paradigms" for different pathological conditions of ACS&T…
- Need for studies to find appropriate paradigm for each condition
- WSES-BACS&TI

… I hope I have not bored you…

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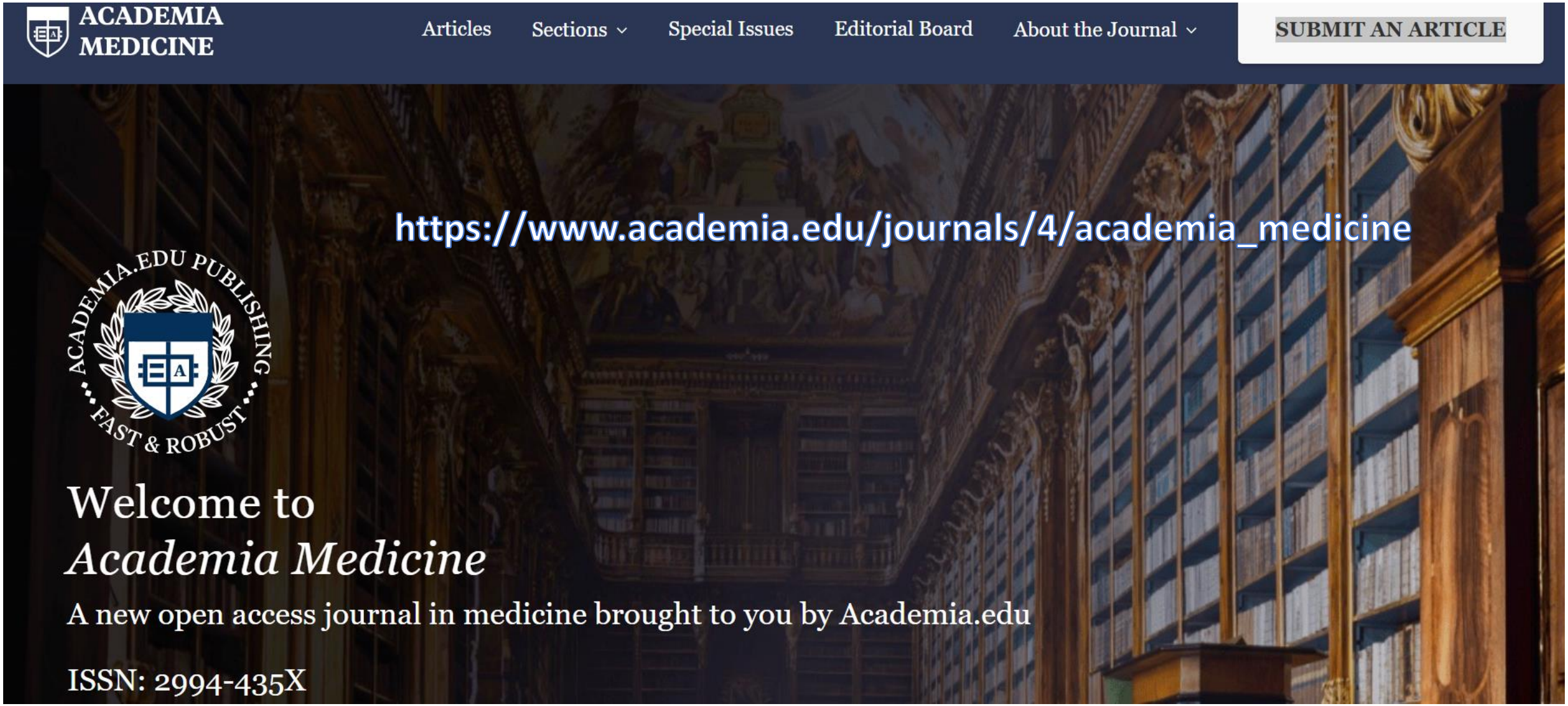

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# ...marketing... WSES 2024 CONGRESS


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# thank you for the attention!


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