Sepsis Biyobelirteci; Prokalsitonin(PCT)

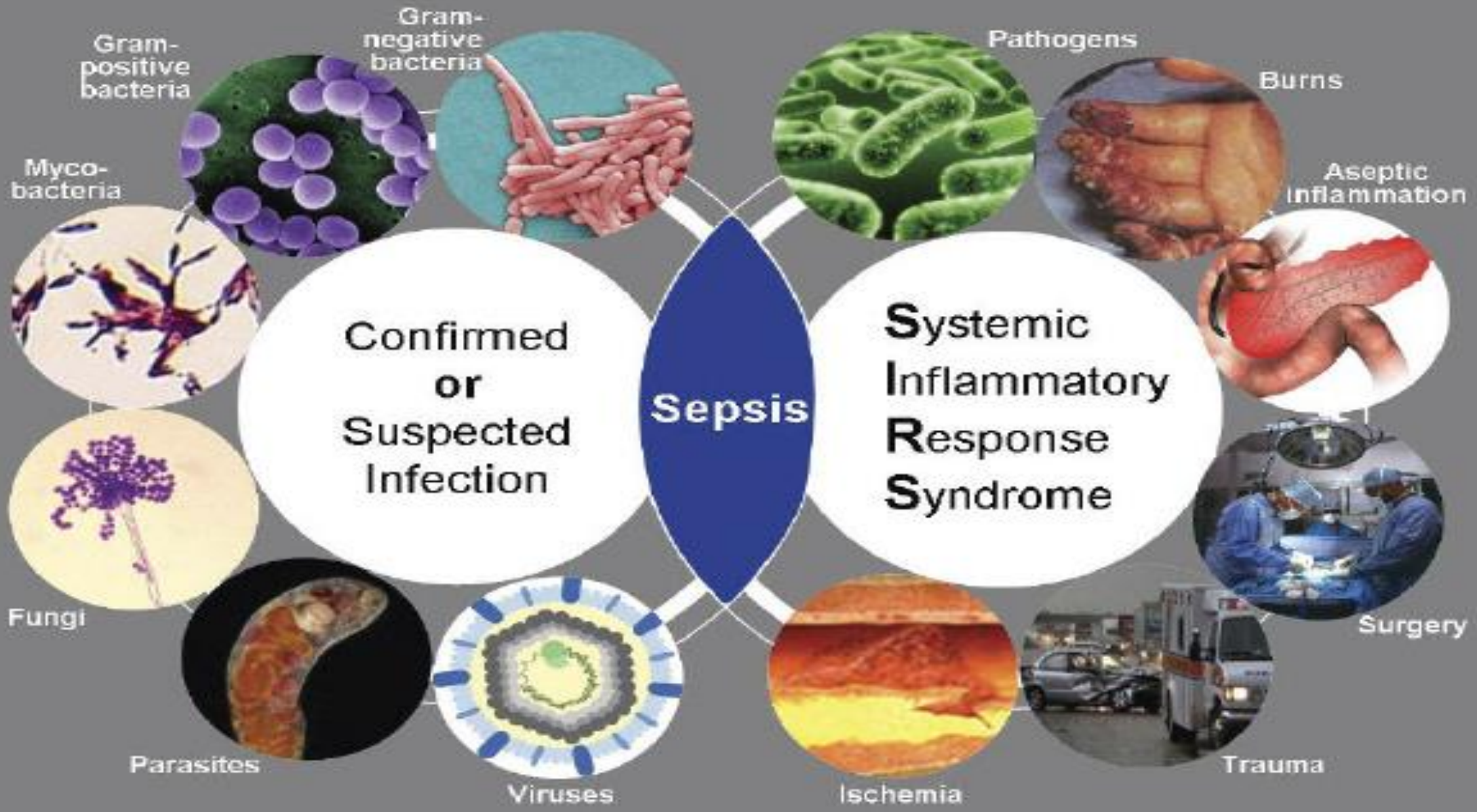
Dr. Bilge SÜMBÜL GÜLTEPE

Bezmialem Vakıf Üniversitesi Tıp Fakültesi,

Tıbbi Mikrobiyoloji Anabilim Dalı

Sunu Planı

- Sepsisin tanımı
- Sepsis biyobelirteçleri
- PCT'nin moleküler yapısı, kaynağı, seviyesi, salınım evreleri
- PCT'nin klinik mikrobiyolololojideki önemi
- PCT'nin avantajları ve klinik kısıtlamaları
- Sonuç


Gram-positive bacteria
Gram-negative bacteria
Pathogens
Burns
Myco-bacteria
Aseptic Inflammation
Confirmed or Suspected Infection
Sepsis
Systemic Inflammatory Response Syndrome
Fungi
Surgery
Parasites
Viruses
Ischemia
Trauma

Sepsisin tanımı

- **SIRS kriterleri:**
  - -Vücut sıcaklığı >38 ^{O}C veya <36 ^{O}C
  - -Kalp atımı >90 atım/dk
  - -Solunum hızı >20 nefes/dk (veya pCO_2 <32 mmHg)
  - -WBC >12000/mm^3 veya <4000/mm^3
  - -Periferik yaymada %10'dan fazla band formunun görülmesidir.

Sepsis= İnfeksiyon+SIRS
Şiddetli sepsis= Sepsis+ organ disfonksiyonu

Crit Rev Clin Lab Sci, 2013; 50(1): 23-36.

Sepsiste Biyobelirteç Neden Gerekli?

- Non-spesifik kriterler.
- Kültür zaman alır.
- Erken tedavi mortaliteyi azaltır
- Tedavi ne zaman başlanmalı ve sonlandırılmalı.
- Antibiyotiklerin yüksek doz kullanılması toksisite, süperinfeksiyon ve dirence neden olur.

Sepsis Biyobelirteçleri

- Sepsisli hastaların serumlarında çok sayıda biyobelirteç bulunmaktadır.
- **Sitokinler ve kemokinler** (IL-1, IL1β, IL-6, IL-8, IL-10, TNF, MIF,vb…)
- **Hücre belirteçleri** (CD10, CD14, CD18, vb…)
- **Reseptörler** (TNF reseptör, Toll-like reseptör,vb…)
- **Koagülasyon biyobelirteçleri** (Antitrombin, aPTT, D-dimer, Fibrin,vb…)
- **Akut faz proteinleri** (Serum amiloid A protein, Seruloplazmin, CRP, Ferritin, Alfa1-asit glikoprotein, Lipopolisakkarit binding protein, Prokalsitonin, vb…)

CritCare. 2010;14(1):R15. Epub2010 Feb9. Review.

İdeal Biyobelirtecin Özellikleri

- Biyokimyasal olarak stabil olmalı
- Az kan volümünde çalışılmalı
- Örnekleme zamanı geniş olmalı
- Hızlı, ucuz, basit ve otomatize sistemle saptanabilmeli
- Duyarlılığı %100 ve özgüllüğü >%85 olmalı.

Ann Intensive Care. 2013; 3(1): 22.

Ann Intern Med. 2003; 138(1): W1-12.

Int J Epidemiol. 2005; 34(4): 953-5.

İdeal Biyobelirtecin Özellikleri

- Bakteriyel ve viral patojeni ayırt edebilmeli,
- Sepsis ve nonenfeksiyöz SIRS durumlarını ayırt edebilmeli,
- İnflamatuar yanıt ve organ disfonksiyonuyla bağıntısı olmalı,
- Prognoz tayininde komplikasyonlu gidişi öngördürebilmelidir,
- Tedavinin etkinliğini gösterebilen özelliklere sahip olmalıdır.

Curr Opin Crit Care. 2005; 11(5): 473-80.

Crit Care Med. 2003; 31(5): 1560-7.

Infect Chemother. 2014; 46(1): 1-12.

Crit Care. 2010; 14(1): R15.

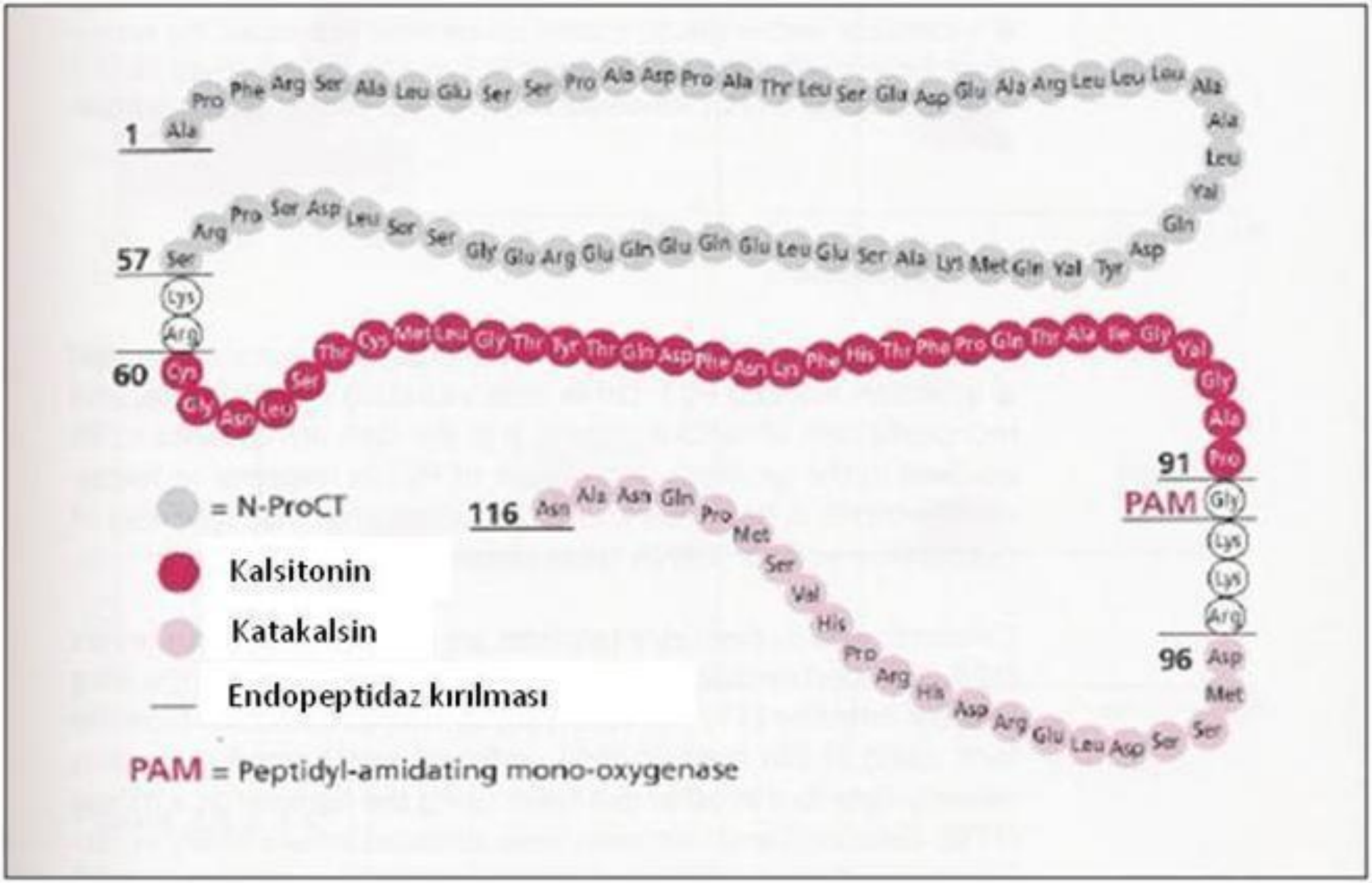
Prokalsitonin (PCT)

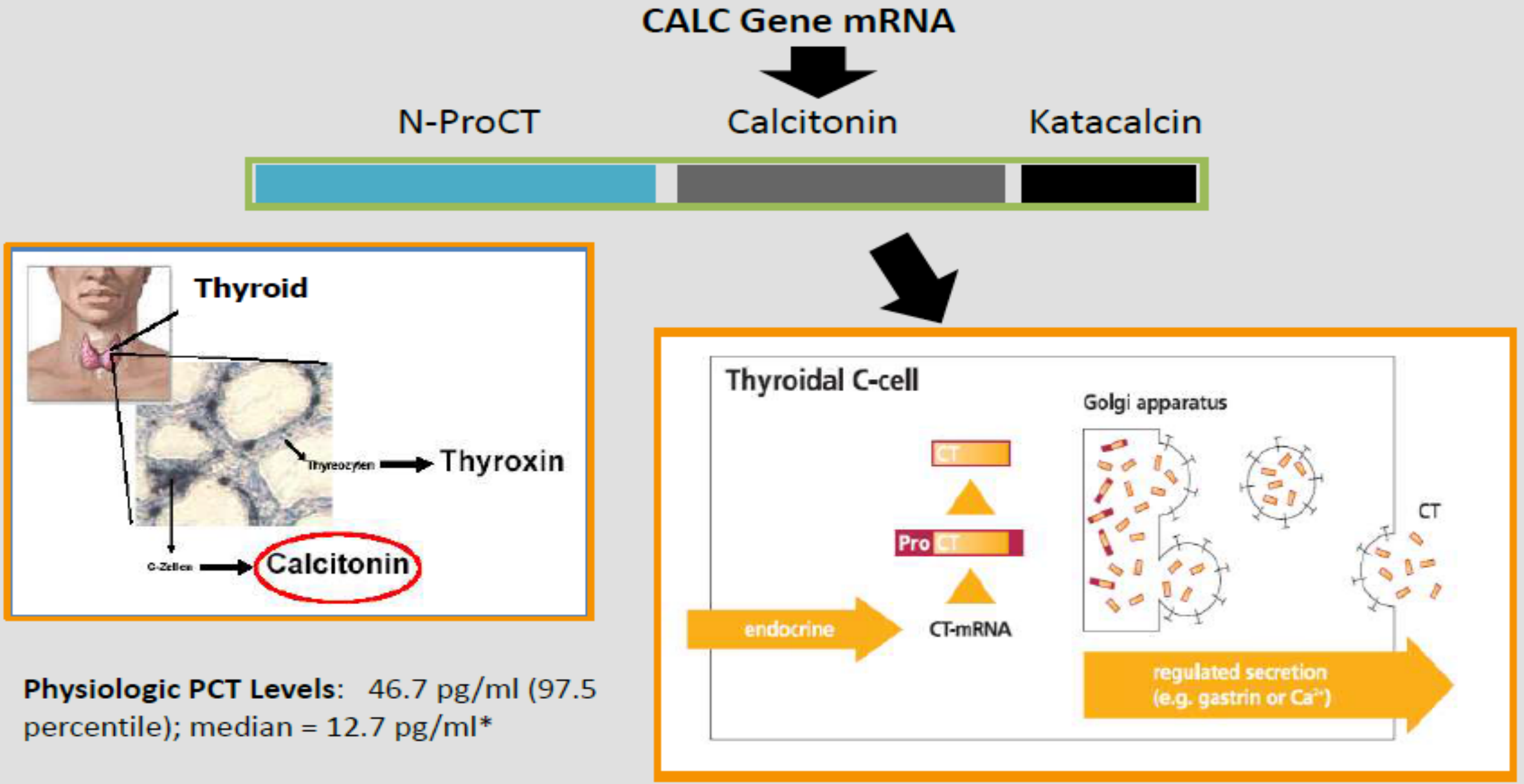
- PCT ilk kez 1983 yılında *Staphylococcus aureus* tarafından oluşan toksik şok sendromunda seviyesinin yükseldiği görülmüştür.
- PCT ilk kez 1993 yılında infeksiyon için yeni bir belirteç olarak tanımlanmıştır.

Crit Care Med 2000; 28: 586-7.

Clin Chim Acta. 2005 Jan;351(1-2):17-29.2.

Clin Infect Dis. 2004 Jul 15;39(2):206-17. Epub2004 Jul 2.

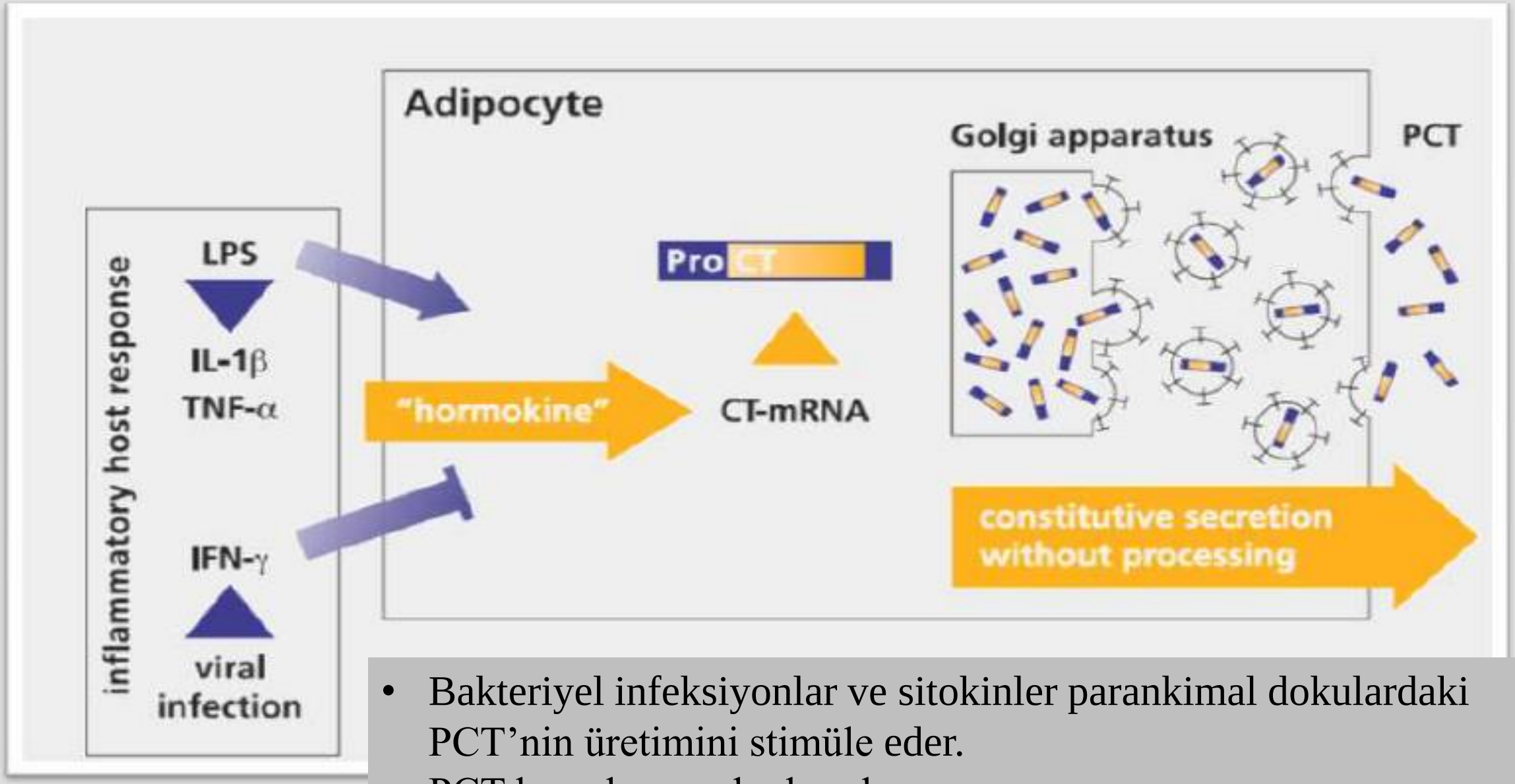

1 Ala Pro Phe Arg Ser Ala Leu Glu Ser Ser Pro Ala Asp Pro Ala Thr Leu Ser Glu Asp Glu Ala Arg Leu Leu Leu Ala Ala Leu Val Gln Asp Tyr Val Glu Ala Met Gln Ser Ala Glu Leu Glu Gln Glu Gln Glu Gly Ser Ser Leu Asp Pro Ser Arg
57 Ser
Lys
Arg
60 Cys Gly Asn Leu Ser Thr Cys Met Leu Gly Thr Tyr Thr Gln Asp Phe Asn Lys Phe His Thr Phe Pro Gln Thr Ala Ile Gly Val Gly Ala Pro
91
PAM Gly
Lys
Lys
Arg
96 Asp Met Ser Ser Leu Asp Glu Arg Asp His Pro Arg Pro His Val Met Ser Pro Gln Asn Ala Asn
116 Asn
= N-ProCT
Kalsitonin
Katakalsin
Endopeptidaz kırılması
PAM = Peptidyl-amidating mono-oxygenase



Physiologic PCT Levels: 46.7 pg/ml (97.5 percentile); median = 12.7 pg/ml*

Morgenthaler N. et al., *Clin Lab.* 2002, 48: 263-270

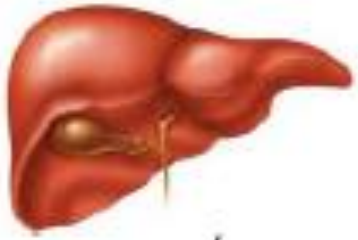
After P. Linscheid, Endocrinology 2003

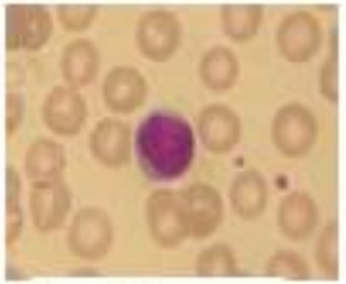


- Bakteriyel infeksiyonlar ve sitokinler parankimal dokulardaki PCT'nin üretimini stimüle eder.
- PCT kan akımına hızla salınır.
- Viral infeksiyonlar tarafından üretilen sitokinler bu yolu inhibe eder.

PCT'nin Kaynağı

C hücreleri





Lenfosit

Adiposit

Prokalsitonin

Nöroendokrin Tümörler

Medüller Tiroid Ca
Küçük Hücreli AC CA
Karsinoid Sendrom

Non-İnfeksiyöz Sistemik İnflamasyonlar

İnhalasyon Hasarı
Pankreatit
Sıcak Çarpması
Mezenterik İskemi-İnfarkt

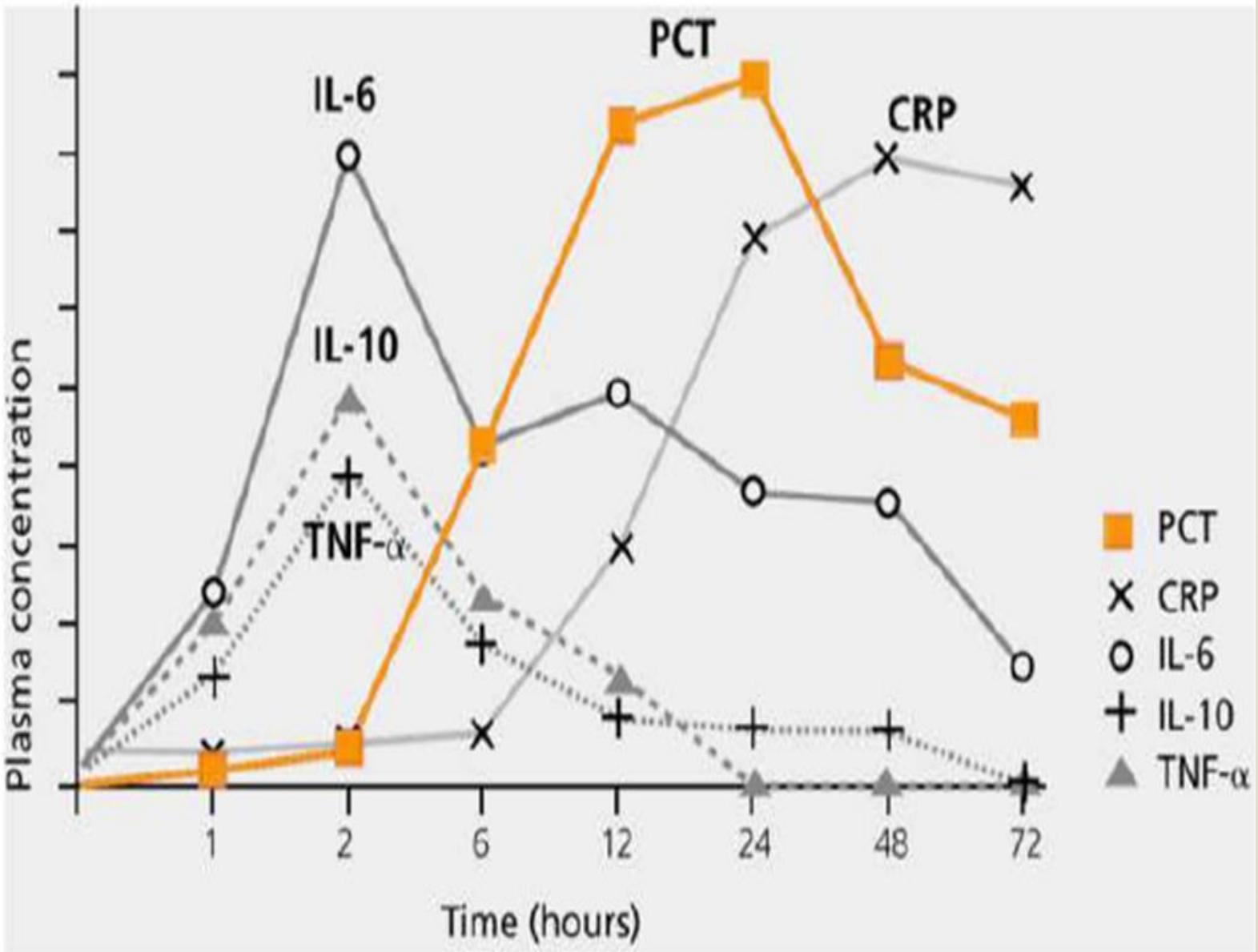
Ağır İnfeksiyon-Sepsis

Bakteriyel
Sistemik fungal
Paraziter

Malarya

Travma

Mekanik hasar
Yanık
Cerrahi



PCT yükselişi infeksiyon başladıktan 2-6 saat

6-12 saate pik

Yarılanma ömrü 24 saat

Brunkhorst FM et al., *Intens. Care Med* 1998;24: 888-892.

Prokalsitonin (PCT)

- Prokalsitonin konak cevabını gösteren bir parametredir.
- Prokalsitonin üretimini tetikleyen majör neden enfeksiyonlar olmakla birlikte, doku inflamasyonuna yol açan her şey PCT üretiminin artmasına neden olur.

Clin Chim Acta 2005 Jan;351(1-2):17-29.

Prokalsitonin Seviyesi

- Sağlıklı erişkinlerde serum düzeyi **0.1 ng/ml**'nin altındadır.
- Sepsis için sınır değer **2 ng/ml**, septik şok için ise **11.6 ng/ml** olarak belirlenmiştir.
- Şok tablosunda olduğu kesinleşmiş hastalarda PCT>5 ng/ml ise etyolojinin infeksiyon olduğunu düşünmek gerekir.

ClinChimActa. 2005 Jan;351(1-2):17-29.

ClinInfect Dis. 2004 Jul 15;39(2):206-17. Epub2004 Jul 2.

IntJ AntimicrobAgents. 2002 Jul;20(1):1-9. Review.

PCT'nin Klinik Kullanımı

- PCT bakteriyel sepsis vakalarını gösteren bir biyobelirteçtir ve mikrobiyal infeksiyonun şiddeti ile korelasyon gösterir.
- PCT seviyesi ile bakteriyel yük arasında mükemmel ilişki vardır.
- PCT'nin 0.1 ng/ml cutoff değeri bakteriyemiyi ekarte etmek için yüksek bir sensitiviteye sahiptir.
- Sepsiste PCT seyri prognostik bir göstergedir.
- PCT bakteriyel ve viral infeksiyon arasındaki ayırımı yapabilir, viral infeksiyonlu hastalarda bakteriyel süperinfeksiyon varlığını gösterebilir.

Infection 2007a;35(5):352-5.

Clinical Microbiology Newsletter 33:22,2011.

Clinical Mikrobiolgy Reviers p. 609-634.

Infection 39: 411-417.

INFECTIOUS DISEASE/ORIGINAL RESEARCH

Procalcitonin Test in the Diagnosis of Bacteremia: A Meta-analysis

Alan E. Jones, MD
James F. Fiechtl, MD
Michael D. Brown, MD
Jason J. Ballew, MD
Jeffrey A. Kline, MD

From the Department of Emergency Medicine, Carolinas Medical Center, Charlotte, NC (Jones, Fiechtl, Ballew, Kline); and the Grand Rapids Medical Education and Research Center/Michigan State University Program in Emergency Medicine, Grand Rapids, MI (Brown).

Dr. Fiechtl is currently affiliated with the Department of Emergency Medicine, Vanderbilt University, Nashville, TN.

Study objective: We seek to evaluate the diagnostic performance of the procalcitonin test for the diagnosis of bacteremia in the emergency department (ED) population.

Table 2. Summary of included studies.

Study by First Author	Year	N	Sensitivity, %	Specificity, %	Prevalence, %	Procalcitonin Cutoff, ng/mL	Population	Patient Spectrum	Patient Setting*	Patient Disposition†
Han	1999	105	66.7 (30.0–90.3)	97.0 (91.5–99.0)	5.7	0.5	Pediatric	B	ED	Unclear
Fleischhack	2000	110	56.3 (33.2–76.9)	87.2 (79.0–92.5)	14.5	0.5	Pediatric	A	ED	Admission
van Langevelde	2000	381	81.8 (70.9–89.3)	51.4 (45.9–56.9)	17.3	0.5	Adult	A	Hospital	Admission
Lacour	2001	91	100.0 (51.0–100.0)	60.9 (50.4–70.5)	4.4	0.9	Pediatric	A	ED	Mixed
Guven	2002	34	100.0 (77.2–100.0)	81.0 (60.0–92.3)	38.2	2.0	Adult	B	ED	Mixed
Chirouze	2002	163	95.5 (78.2–99.2)	57.4 (49.2–65.3)	13.5	0.4	Adult	A	Hospital	Admission
Delevaux	2003	168	81.0 (60.0–92.3)	81.0 (73.8–86.5)	12.5	0.5	Adult	A	Hospital	Admission
Han	2003	90	87.1 (71.1–94.9)	49.2 (36.8–61.6)	34.4	0.5	Pediatric	A	Hospital	Admission
Scott	2003	24	100.0 (20.7–100.0)	69.6 (49.1–84.4)	4.2	0.5	Adult	B	ED	Mixed
Lacour	2003	88	75.0 (30.1–95.4)	52.4 (41.8–62.7)	4.5	0.5	Pediatric	B	ED	Mixed
Prat	2004	65	100.0 (81.6–100.0)	83.3 (70.4–91.3)	26.2	2.0	Pediatric	B	ED	Unclear
Ciaccio	2004	54	89.7 (73.6–96.4)	16.0 (6.4–34.7)	53.7	0.5	Pediatric	B	Hospital	Admission
Caterino	2004	108	53.8 (29.1–76.8)	71.6 (61.8–79.7)	12.0	0.5	Adult	B	ED	Unclear
Giamarellou	2004	158	48.1 (35.1–61.3)	65.1 (55.6–73.5)	32.9	1.0	Adult	B	Hospital	Admission
Bugden	2004	183	88.9 (56.5–98.0)	89.1 (83.6–92.9)	4.9	0.5	Mixed	A	ED	Mixed
Persson	2004	94	54.3 (38.2–69.5)	81.4 (69.6–89.3)	37.2	0.5	Adult	B	Hospital	Admission
Aalto	2004	92	92.3 (66.7–98.6)	68.4 (57.5–77.6)	14.1	0.4	Adult	A	ED	Admission

*Patient setting refers to the setting from which patients were identified (ED, ED only; Hospital) at the time of admission to the hospital.
†Patient disposition refers to the ultimate disposition of included patients (admitted; discharged; mixed, admitted and discharged patients; or unclear).

Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis

Christina Wacker, Anna Prkno, Frank M Brunkhorst*, Peter Schlattmann*

Lancet Infect Dis 2013; 13: 426–35

Published Online February 1, 2013 http://dx.doi.org/10.1016/S1473-3099(12)70323-7

See Comment page 382

*Contributed equally

Department of Medical Statistics, Computer Sciences and Documentation (C Wacker Cand Med, A Prkno Cand Med, Prof P Schlattmann PhD), and Department of Anaesthesiology and Intensive Care Medicine (Prof F M Brunkhorst MD), Centre for Sepsis Control and Care, Jena University Hospital, Jena, Germany

Summary

Background Procalcitonin is a promising marker for identification of bacterial infections. We assessed the accuracy and clinical value of procalcitonin for diagnosis of sepsis in critically ill patients.

Methods We searched Medline, Embase, ISI Web of Knowledge, the Cochrane Library, Scopus, BioMed Central, and Science Direct, from inception to Feb 21, 2012, and reference lists of identified primary studies. We included articles written in English, German, or French that investigated procalcitonin for differentiation of septic patients—those with sepsis, severe sepsis, or septic shock—from those with a systemic inflammatory response syndrome of non-infectious origin. Studies of healthy people, patients without probable infection, and children younger than 28 days were excluded. Two independent investigators extracted patient and study characteristics; discrepancies were resolved by consensus. We calculated individual and pooled sensitivities and specificities. We used I^2 to test heterogeneity and investigated the source of heterogeneity by metaregression.

Findings Our search returned 3487 reports, of which 30 fulfilled the inclusion criteria, accounting for 3244 patients. Bivariate analysis yielded a mean sensitivity of 0·77 (95% CI 0·72–0·81) and specificity of 0·79 (95% CI 0·74–0·84). The area under the receiver operating characteristic curve was 0·85 (95% CI 0·81–0·88). The studies had substantial heterogeneity (I^2=96%, 95% CI 94–99). None of the subgroups investigated—population, admission category, assay used, severity of disease, and description and masking of the reference standard—could account for the heterogeneity.

PCT’nin Klinik Kullanımı

- PCT neonatal dönemde bakteriyel infeksiyonların erken döneminde tespit edilmesinde faydalıdır.
- Çocuklarda sepsis ve menenjit gibi invaziv bakteriyel infeksiyonlarda PCT seviyesi CRP ye oranla daha önemli derecede yükselir.

Pediatr Infect Dis J 2007;26:672-7.

J Global Health 2011;1:201-9.

Intensive Care Med (2011) 37:747–762
DOI 10.1007/s00134-011-2174-8

REVIEW

Evridiki K. Vouloumanou
Eleni Plessa
Drosos E. Karageorgopoulos
Elpis Mantadakis
Matthew E. Falagas

Serum procalcitonin as a diagnostic marker for neonatal sepsis: a systematic review and meta-analysis

Received: 23 June 2010
Accepted: 9 December 2010
Published online: 5 March 2011

E. K. Vouloumanou · E. Plessa · D. E. Karageorgopoulos · M. E. Falagas (✉)
Alfa Institute of Biomedical Sciences (AIBS), 9 Neapoleos Street, 151 23 Marousi, Athens, Greece
e-mail: m.falagas@aibs.gr
Tel.: +30-210-6839604
Fax: +30-210-6839605

E. Mantadakis
Department of Pediatrics, Democritus University of Thrace and University General Hospital of Alexandroupolis, Thrace, Greece

M. E. Falagas
Department of Medicine, Henry Dunant Hospital, Athens, Greece

M. E. Falagas
Department of Medicine, Tufts University School of Medicine, Boston, MA, USA

Abstract *Purpose:* To assess the value of serum procalcitonin (PCT) for the differentiation between patients with and without neonatal sepsis. *Methods:* We systematically searched PubMed, Scopus, and the Cochrane Library for studies evaluating PCT in neonatal sepsis. PCT had to be measured in neonatal blood samples, at the initial presentation of patients with suspected sepsis, before the administration of antibiotics. We performed a bivariate meta-analysis of sensitivity and specificity, and constructed a hierarchical summary receiver-operating characteristic (HSROC) curve. *Results:* Overall, 29 studies eligible for inclusion were identified. We analyzed the 16 studies (involving 1,959 neonates) that evaluated PCT in neonates with culture-proven or clinically diagnosed sepsis in comparison with ill neonates with other conditions. The pooled (95% confidence interval) sensitivity and specificity were 81% (74–87%) and 79% (69–87%), respectively. The area under the HSROC curve (AUC) was 0.87. The diagnostic accuracy of PCT seemed higher for neonates with late-onset sepsis (>72 h of life) than for those with early onset sepsis; the AUC for these analyses was 0.95 and 0.78, respectively. However, fewer data were available for late-onset sepsis. High statistical heterogeneity was observed for all analyses. *Conclusion:* Our findings suggest that serum PCT at presentation has very good diagnostic accuracy (AUC = 0.87) for the diagnosis of neonatal sepsis. However, in view of the marked observed statistical heterogeneity, along with the lack of a uniform definition for neonatal sepsis, the interpretation of these findings should be done with appropriate caution.

Keywords Biological markers · Diagnostic tests · Inflammatory markers · Neonatal sepsis · Neonatal infections · Procalcitonin

PCT'nin Klinik Kullanımı

- Viral enfeksiyonların çoğunda PCT düzeyi <1 ng/ml'dir, genellikle de normal bulunur.
- Viral enfeksiyonu olan 236 hastanın değerlendirildiği bir çalışmada sadece 3 hastada PCT düzeyi >2ng/ml saptanmış ve en yüksek düzey 5.2 ng/ml bulunmuştur.
- Fungal enfeksiyon sırasında, bakteriyel enfeksiyondan daha düşük düzeyler gözlenir.

CritCare Med. 2008 Mar;36(3):941-52.

Infection. 2008 Oct;36(5):396-407. Epub2008 Aug 30.

PCT'nin Klinik Kullanımı

- Majör cerrahi girişim sonrası diğer inflamatuar biyobelirteçler 2 haftaya kadar yüksek kalabilir.
- PCT ise kısa süreli ve az miktarda yükselir ve nadiren 5ng/ml'yi aşar.
- Aseptik cerrahi girişimlerde daha az yükselme gözlenir.
- 2 gün veya daha uzun süre PCT düzeyinin 1.8 ng/ml üstünde olması infeksiyonu düşündürmelidir (duyarlılık %94, özgüllük %91) .

ClinChimActa. 2005 Jan;351(1-2):17-29.

IntJ Antimicrob Agents. 2002 Jul;20(1):1-9. Review.

CritCare Med. 2008 Mar;36(3):941-52.

PCT'nin Klinik Kullanımı

- PCT steril ve enfekte akut pankreatit ayırımında yararlıdır.
- PCT yüksekliğinin, ciddi akut pankreatiti göstermede CRP, APACHE II skoru ve Ranson skoruna göre çok daha anlamlı olduğu gösterilmiştir.

J Infect. 2010 Jun;60(6):409-16.

Crit Care Med. 2008 Mar;36(3):941-52.

The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: Systematic review

Reza Mofidi, MB, MCh,[a] Stuart A. Suttie, MB, BCh,[b] Pradeep V. Patil, MB, BS,[b] Simon Ogston, BA, MSc,[c] *and* **Rowan W. Parks, MD,[a]** *Edinburgh, United Kingdom*

Background. *Many studies have evaluated serum levels of procalcitonin (PCT) as a predictor in the development of severe acute pancreatitis (SAP) and infected pancreatic necrosis (IPN). This study assesses the value of PCT as a marker of development of SAP and IPN.*

Methods. *Medline, Web of Science, the Cochrane clinical trials register, and international conference proceedings were searched systematically for prospective studies, which evaluated the usefulness of PCT as a marker of SAP and IPN. The sensitivity, specificity, and diagnostic odds ratios (DORs) were calculated for each study, and the study quality and heterogeneity among the studies were evaluated.*

Results. *Twenty-four of 59 studies identified were included in data extraction. The sensitivity and specificity of PCT for development of SAP were 0.72 and 0.86, respectively (area under the curve [AUC] = 0.87; DOR = 14.9; 95% confidence interval [CI] = 5.6–39.8), albeit with a significant degree of heterogeneity (Q = 28.56, P < .01). The sensitivity and specificity of PCT for prediction of infected pancreatic necrosis were 0.80 and 0.91 (AUC = 0.91; DOR = 28.3; 95% CI = 13.8–58.3) with no significant heterogeneity (Q = 7.83, P = .18). No significant heterogeneity was observed among the studies when only higher quality studies (AUC = 0.91; DOR = 30.7; 95% CI = 10.7–87.8) or studies that used a cutoff PCT level >0.5 ng/mL (AUC = 0.88, 32.8; 95% CI = 10.1–106.6) were included.*

Conclusion. *Serum measurements of PCT may be valuable in predicting the severity of acute pancreatitis and the risk of developing infected pancreatic necrosis. (Surgery 2009;146:72-81.)*

PCT'nin Klinik Kullanımı

- Yanık sonrası PCT düzeylerinde belirgin yükselme olabildiği bildirilmiştir.
- Yeni yayınlarda PCT yarı ömrünün hemodializle uzamadığı bildirilmektedir.

J Infect. 2010 Jun;60(6):409-16.

Crit Care Med. 2008 Mar;36(3):941-52.

ANTICANCER RESEARCH *36*: 3803-3810 (2016)

Review

Procalcitonin: A New Biomarker for Medullary Thyroid Cancer? A Systematic Review

APOSTOLOS K.A. KARAGIANNIS[1], CONSTANTINE GIRIO-FRAGKOULAKIS[2] and THEODORA NAKOUTI[3]

[1]*Department of Endocrinology, Diabetes and Metabolism, Korgialeneio-Mpenakeio Hospital, Athens, Greece;*
[2]*Department of Clinical Radiology, Nottingham University Hospitals, Nottingham, U.K.;*
[3]*2nd Department of Internal Medicine, "Henry Dunant" Hospital Center, Athens, Greece*

Abstract. *Medullary thyroid cancer (MTC) is a rare but aggressive thyroid malignancy. The gold-standard biomarker for its diagnosis and follow-up is calcitonin (CT); however, it has a variable half-life dependent on its circadian variability. It has been suggested that a more stable hormone, procalcitonin (PCT), may overcome these problems and its introduction to routine practice may give more accurate results in the diagnosis and follow-up of MTC. We systematically reviewed Pubmed, Scopus, Biosis Previews and Embase databases up to March 2016. A total of 15 out of 184 articles were retrieved and analyzed. Of these 15 studies, 3 were case reports. In these 15 studies, the values of CT and PCT were assessed in both patients with MTC and patients that were either healthy volunteers or with benign/malignant thyroid nodular disease or with bacterial infection. Our search suggests that PCT seems to be a useful*

Medullary thyroid carcinoma (MTC) is a relatively rare malignancy, accounting for 2-5% of all thyroid cancers (1). It originates from thyroid neuroendocrine cells (C-cells) that secrete calcitonin (CT), currently, the gold standard biomarker used in the diagnosis, evaluation and follow-up of MTC (2, 3).

Calcitonin is a 32-amino-acid polypeptide hormone that is formed by the splitting of a larger protein precursor, which is a product of the *CALC1* gene (4, 5). In healthy individuals, CT is involved in calcium homeostasis and its release is stimulated by increased levels of serum calcium and by the hormones gastrin and pentagastrin (PG) (5-7). In disease, apart from MTC, an elevated CT may be seen in C-cell hyperplasia, non-thyroidal small cell or other malignancies, acute and chronic renal failure, hypercalcemia or

PCT'nin Klinik Kullanımı

- İnhalasyon yaralanmalarında,
- Ciddi cerrahi operasyonların ardından,
- Malarya enfeksiyonlarında tedaviye yanıtın takibinde de yararlıdır.
- PCT nötropenik hastalarda beklenenden bir miktar düşük saptanabilir.

Clin Chim Acta. 2005 Jan;351(1-2):17-29.5.

Int J Antimicrob Agents. 2002 Jul;20(1):1-9. Review.

Crit Care Med. 2008 Mar;36(3):941-52.

Infection. 2008 Oct;36(5):396-407. Epub2008 Aug 30.

PCT'nin Klinik Kullanımı

- Mezenter iskemide,
- Kardiyak cerrahi ve kardiyojenik şokta,
- Allojeneik kemik iliği nakli yapılan hastalarda ve graft rejeksiyonunda
- Sıcak çarpmasını takiben ciddi şekilde yükselebilir.
- Aerobik egzersizi takibeden 3-24 saat içinde ılımlı PCT yüksekliği saptanabilir.
- PCT, çoklu organ yetmezliğinde erken prognostik göstergesidir.

Clin Chim Acta. 2005 Jan;351(1-2):17-29.5.
Crit Care Med. 2008 Mar;36(3):941-52.
Int J Antimicrob Agents. 2002 Jul;20(1):1-9.
J Infect. 2010 Jun;60(6):409-16. Epub2010 Mar 27.

PCT'nin Avantajları

- Bakteriyel ve viral enfeksiyonların ayrımını yapabilir
- İnfeksiyöz ve non-infeksiyöz SIRS'ın ayrımını yapabilir.

Clin Chim Acta. 2005 Jan;351(1-2):17-29.

Int J Antimicrob Agents. 2002 Jul;20(1):1-9. Review.

Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: systematic review and meta-analysis

Benjamin M P Tang, Guy D Eslick, Jonathan C Craig, Anthony S McLean

Lancet Infect Dis 2007; 7: 210–17

Department of Intensive Care Medicine, Nepean Hospital, Penrith, New South Wales, Australia (B M P Tang MD, A S McLean MD); **School of Public Health, University of Sydney, Sydney, New South Wales** (B M P Tang, G D Eslick PhD, J C Craig MD); **and Department of Medicine, University of Sydney, Nepean Hospital, Penrith** (G D Eslick)

Correspondence to:

Procalcitonin is widely reported as a useful biochemical marker to differentiate sepsis from other non-infectious causes of systemic inflammatory response syndrome. In this systematic review, we estimated the diagnostic accuracy of procalcitonin in sepsis diagnosis in critically ill patients. 18 studies were included in the review. Overall, the diagnostic performance of procalcitonin was low, with mean values of both sensitivity and specificity being 71% (95% CI 67–76) and an area under the summary receiver operator characteristic curve of 0·78 (95% CI 0·73–0·83). Studies were grouped into phase 2 studies (n=14) and phase 3 studies (n=4) by use of Sackett and Haynes' classification. Phase 2 studies had a low pooled diagnostic odds ratio of 7·79 (95% CI 5·86–10·35). Phase 3 studies showed significant heterogeneity because of variability in sample size (meta-regression coefficient –0·592, p=0·017), with diagnostic performance upwardly biased in smaller studies, but moving towards a null effect in larger studies. Procalcitonin cannot reliably differentiate sepsis from other non-infectious causes of systemic inflammatory response syndrome in critically ill adult patients. The findings from this study do not lend support to the widespread use of the procalcitonin test in critical care settings.

PCT'nin Avantajları

- Sepsisin ciddiyetini ve prognozunu değerlendirmede PCT CRP'den belirgin derecede üstündür.
- Sepsisin seyri sırasında sitokin salınımına bağlı olarak PCT seviyeleri yükselişini sürdürürken CRP belli bir tavan düzeyde kalma eğilimindedir.
- PCT değeri septik şoklu hastalarda belirgin şekilde artar.

Clin Chim Acta. 2005 Jan;351(1-2):17-29.

Int J Antimicrob Agents. 2002 Jul;20(1):1-9.

Clinical Infectious Diseases 2004; 39:206–17

REVIEW ARTICLE

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

PCT'nin Klinik Mikrobiyolojide Önemi

- Gram negatif bakteriyemilerde, gram pozitif bakteriyemiye oranla daha yüksek PCT düzeyleri elde edilmiştir.
- Gerçek koagülaz negatif stafilokok infeksiyonlarıyla kontaminasyonları ayırmada PCT uygun bir belirteçtir.

Infection. 2008 Oct;36(5):396-407. Epub2008 Aug 30.

IntJ Antimicrob Agents. 2002 Jul;20(1):1-9. Review.

Crit Care Med. 2008 Mar;36(3):941-52.

Serum Procalcitonin for Discrimination of Blood Contamination from Bloodstream Infection due to Coagulase-Negative Staphylococci

P. Schuetz, B. Mueller, A. Trampuz

Abstract

The diagnostic value of serum procalcitonin (PCT) to distinguish blood contamination from bloodstream infection (BSI) due to coagulase-negative staphylococci was evaluated. Patients with BSI had higher PCT concentration than those with blood contamination at day −1, day 0 and day +1 with regard to blood culture collection ($p < 0.05$), whereas serum C-reactive protein values were significantly higher only on day +1. At a cutoff of 0.1 ng/dl, PCT had a sensitivity of 86% and 100%, and a specificity of 60% and 80% for the diagnosis of BSI on day −1 and 0, respectively. In addition to clinical and microbiological parameters, PCT may help discriminating blood contamination from BSI due coagulase-negative staphylococci.

Infection 2007; 35: 352–355
DOI 10.1007/s15010-007-7065-0

Patients and Methods

The study was conducted at the University Hospital Basel in Switzerland, a 950-bed tertiary healthcare center. We prospectively included consecutive patients ≥ 18 years of age admitted to our hospital between 1 April and 31 August 2005, from whom at least one blood culture grew coagulase-negative staphylococci. Patients with one or more positive blood cultures collected within 10 days were considered as one episode. Patients with positive blood cultures from outside hospitals and those obtained postmortem were excluded from the analysis. Blood cultures were processed using an automated colorimetric detection system (BacT/ALERT, bioMerieux, Durham, NC, USA) [10]. The time to positivity was defined as the time between the start of incubation and the instrument signal indicating growth in either the aerobic or anaerobic blood culture bottle, confirmed by Gram staining.

Patient records were reviewed with a standardized data-collection case report form to retrieve demographic, clinical,

PCT Düzey Takibi

- PCT tek bir kez ölçümü prognozu belirlemek için yeterli olmayabilir, takipler daha anlamlıdır. **6-24 saatlik** aralıklarla ölçüm yapılmalıdır.
- Yoğun bakımda yatan hastanın PCT seviyesinin monitorize edilmesi sepsisin daha erken dönemde tespit edilmesini ve daha etkili bir tedavi verilmesini sağlar.

Crit Care Med. 2008 Mar;36(3):941-52.

Int J Antimicrob Agent 2002 Jul;20(1):1-9.

Clim Chin Acta 2005 Jan;351(1-2):17-29.5.

Crit Rev Clin Lab Sci, 2013; 50(1): 23-36.

PCT Düzeyleri Takibi

- Bakteriyel infeksiyonu olan hastalarda antibakteriyel tedavinin başlanmasından sonra geçen **24 saat** içinde prokalsitonin düzeyinde **%30'dan fazla düşme** olması uygun antibiyotiğin başlanmış olduğunu ve infeksiyonun kontrol altına alınmış olduğunu gösterir.
- Prokalsitonin değerinde yükselme olması ise antibiyotik değişikliğine gidilmesini gerektirir.

.

Scientific World Journal. 2010 Oct1;10:1941-6.

Klinik Kısıtlamalar

- Artmış PCT seviyeleri her zaman bakteriyel infeksiyon ile ilişkili olmayabilir

  -Yenidoğan <48 saat fizyolojik yükseklik

  -Major travma, cerrahi, ciddi yanık, proinflamatuar sitokin tedavisi sonrası birinci gün

  -İnvaziv fungal infeksiyonlar, akut plasmodyum atağı

  -Uzamış veya ciddi kardiyojenik şok, organ perfüzyon anormallikleri

  -Vaskülitin bazı formları

  -Tiroid medüller kanseri ve akciğer küçük hücreli kanseri.

Klinik Kısıtlamalar

- Düşük PCT bakteriyel infeksiyon varlığını dışlamaz
  - -İnfeksiyonun erken evresinde,
  - -Lokal infeksiyonda
  - -İnfektif endokarditte düşük olabilir.

- Takip ve PCT tekrarları ile kontrol önemlidir.

Cihaz adı	Ölçüm prensibi	Numune türü	Örnek miktarı	İnkübasyon zamanı	Ölçüm aralığı	Rapor zamanı	Cihaz gereksinimi
Brahms PCT LIA	Immuno luminescence assay (sandwich)	Serum veya plazma	20 µL	1 saat	0.1-500 µg/L	2 saat	Luminometre
Brahms PCT Kryptor	Homogeneous immunoassay (sandwich)	Serum veya plazma (heparin, EDTA)	50 µL	19 dk	0.02-50 µg/L	19 dk	Immunoanalizer
Brahms PCT Q (semi-kan.)	Immunokromatografi	Serum veya plazma	200 µL	30 dk	<0.5 µg/L, 0.5-2µg/L, 2-10 µg/L, >10 µg/L	30 dk	-
Vidas Brahms PCT	Enzyme-linked fluorescent assay (ELFA)	Serum veya plazma	200 µL		0.05-200 µg/L	20 dk	VIDAS®
1. **2.** **3.** **4.**	Kemilümunoassay	Serum veya plazma	100 µL 30 µL 60 µL 100 µL		0.02-75.00 µg/L 0.02-100 µg/L 0.02 -100 µg/L 0.020 up to 100 µg/L	26 dk 18 dk 30 dk 16 dk	ADVIA Centaur Cobas e LUMIPULSE LIAISON®
Samgsung IB Brahms PCT	Point-of-care (POC)	EDTA (Plazma ve kan)	200 µL	30 dk	0.08-10.0 µg/L	20 dk	POC immunoassay

*** 1. Advia Centaur Brahms PCT, 2. Elecsys Brahms PCT, 3. Lumipulse G Brahms PCT, 4. Lıaıson Brahms PCT II Gen**

Sonuç

- PCT sepsisin tanısı, izlemi ve tedaviye yönlendirmede kullanışlı bir biyobelirteçtir.
- Hasta başı test sistemlerinden (POC), tam otomatize sistemlere kadar değişen farklı yöntemler mevcuttur.
- Klinik mikrobiyoloji test menüsü içinde giderek önemi artmaktadır.

Teşekkürler