


İnfektif Endokardit
TANIDA
Aklımıza Takılanlar

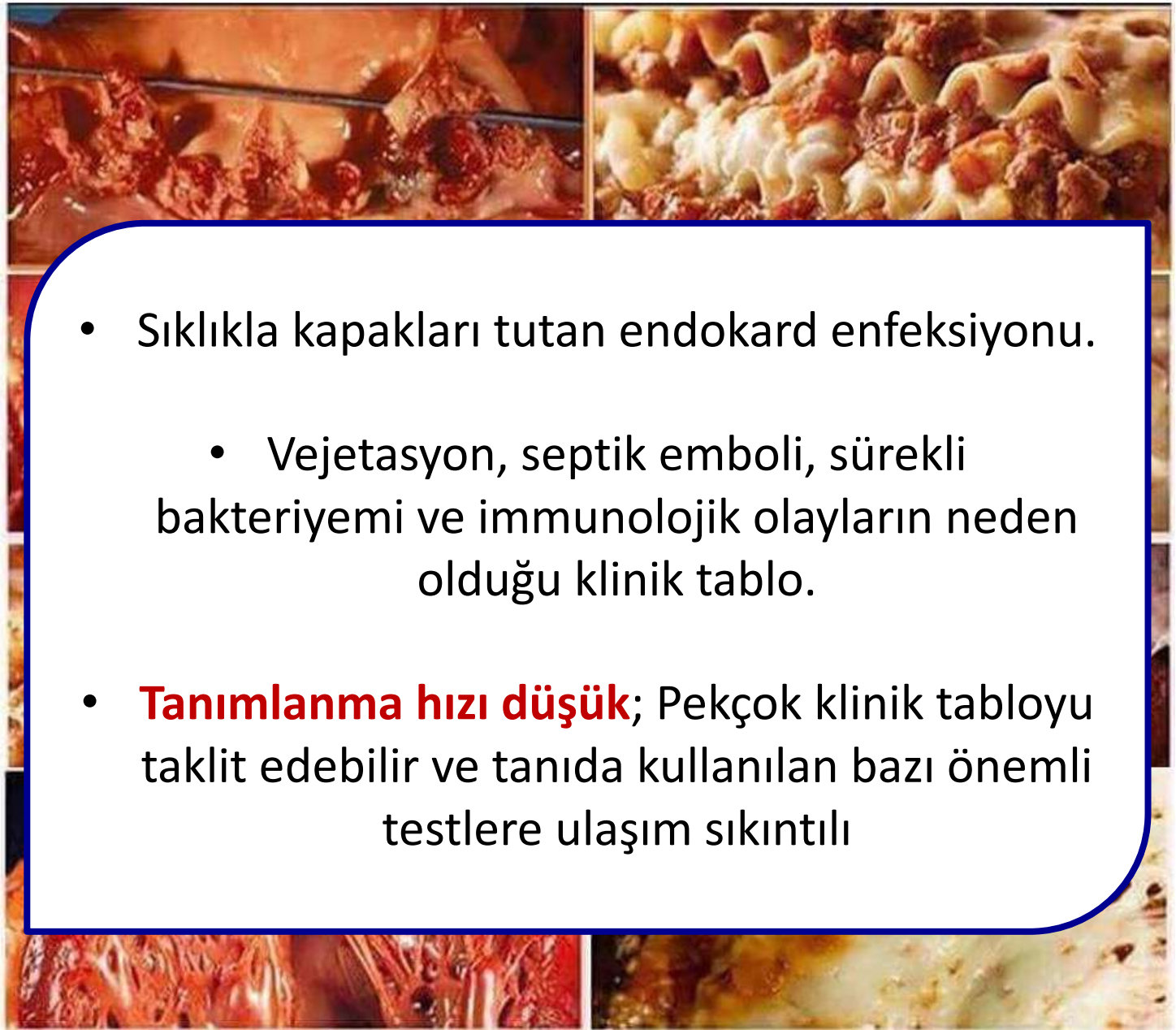
Yasemin TEZER TEKÇE

Sunumda İE tanısı ile ilgili

- Hatırlatma soru ve cevapları (Uzlaşı raporumuzdan)
- Klinikte karşılaşılan güçlüklerle ilgili soru ve cevaplar
- Çözüm bekleyen sorular ve olası cevapları

¿Lasagna o Endocarditis?

LALEO.COM



- Sıklıkla kapakları tutan endokard enfeksiyonu.

- Vejetasyon, septik emboli, sürekli bakteriyemi ve immunolojik olayların neden olduğu klinik tablo.

- **Tanımlanma hızı düşük**; Pekçok klinik tabloyu taklit edebilir ve tanıda kullanılan bazı önemli testlere ulaşım sıkıntılı

Hangi hastalarda İE'den kuşkulanacağız?

İnfektif Endokarditi Akla Getirecek Durumlar

1. Ateşli bir hastalığı olan hastada yeni gelişen kapak yetersizliği
2. İE eğilimi yaratan kardiyak durumu olan hastada başka bir odağın bulunamadığı ateşli hastalık
3. İE eğilimi yaratan kardiyak durumu olan hastada uzun süreli terleme, kilo kaybı, iştahsızlık veya yorgunluk
4. Ateşi olan hastada aşağıdakilerden herhangi birinin olması:
   - İE'ye eğilim yaratan kardiyak durum ve yakın geçmişte bakteriyemiye neden olabilecek işlem öyküsü
   - Yeni inme
   - Yeni başlayan konjestif kalp yetmezliği
   - Yeni ritim ve ileti bozukluğu
   - Vasküler veya immünolojik fenomen (embolik olaylar, Roth lekeleri, kıymıksı kanamalar, Janeway lezyonları, Osler nodülleri)
   - Nedeni bilinmeyen periferik apse (böbrek, dalak, beyin, vertebra)
5. Başka bir nedenle açıklanamayan yeni bir embolik olay (örneğin serebral veya ekstremiteyi ilgilendiren iskemi)
6. Başka bir nedenle açıklanamayan persistan kan kültürü pozitifliği
7. Kateter çekildikten 72 saat sonra da süren persistan kan kültürü pozitifliğinin belirlendiği damar içi kateter infeksiyonu

KLİNİK KUŞKU KATSAYISININ YÜKSEK, ARAŞTIRMA EŞİĞİNİN DÜŞÜK OLMASI GEREKİR!!!

İE eğilim yaratan durumlar nelerdir??

- Geçirilmiş endokardit
- Kalp kapak hastalığı
- Konjenital kalp hastalığı
- İntrakardiyak yabancı cisim varlığı
- Damar içi ilaç kullanıcısı
- Kronik hemodiyaliz hastaları
- Solid organ ve kök hücre alıcıları

İE’de tanı için hangi parametreler değerlendirilmelidir?

- Klinik bulgular
- Laboratuar bulguları
- Görüntüleme yöntemleri
- Mikrobiyolojik inceleme
- Patolojik inceleme

‘İE düşünülmesi gereken klinik ve laboratuvar özelliklerinin iyi bilinmesi; İE düşünülen hastalarda, tanıda kullanılabilecek tüm görüntüleme ve mikrobiyoloji yöntemlerinin sonuç alınıncaya kadar etkili bir şekilde kullanılması gereklidir. ’

İE tanıya yardımcı klinik tablo nasıldır?

- Devamlı bakteriyemiye bağlı sistemik bulgular
- Endokard
- Embolik
- Sürekli
  immünolojik olaylar

Klinik tablo; hastanın yaşına, etken m.o.'ya, altta yatan kardiyak hastalığa, yabancı cisim varlığına ve diğer komorbiditelere bağlı olarak DEĞİŞKENLİK GÖSTEREBİLİR!

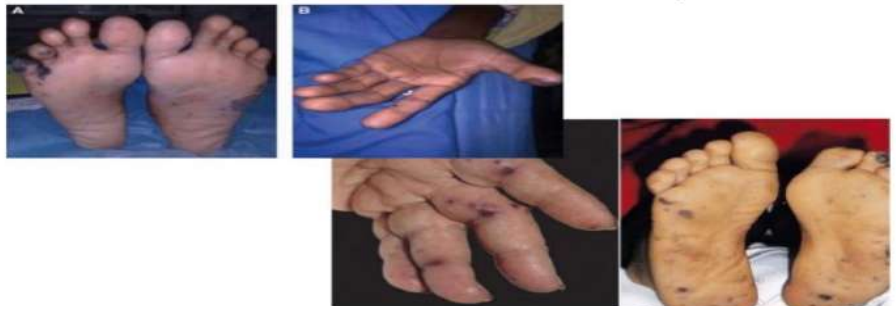
KLİNİK BULGULAR

Table 1. Clinical Signs and Complications of Infective Endocarditis

Sign	Patients, %
Fever	86-96
New murmur	48
Worsening of old murmur	20
Hematuria	26
Vascular embolic event	17
Splenomegaly	11
Splinter hemorrhages	8
Osler nodes	3
Janeway lesions	5
Roth spots	2
Complication	
Stroke	17-20
Nonstroke embolization	23-33
Heart failure	14-33
Intracardiac abscess	14-20
New conduction abnormality	8

Adapted from Murdoch et al[1] and Selton-Suty et al.[2]

Lesión de Janeway



Nódulos de Osler

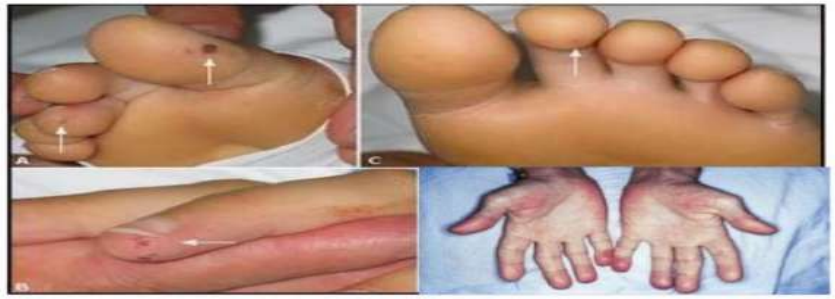
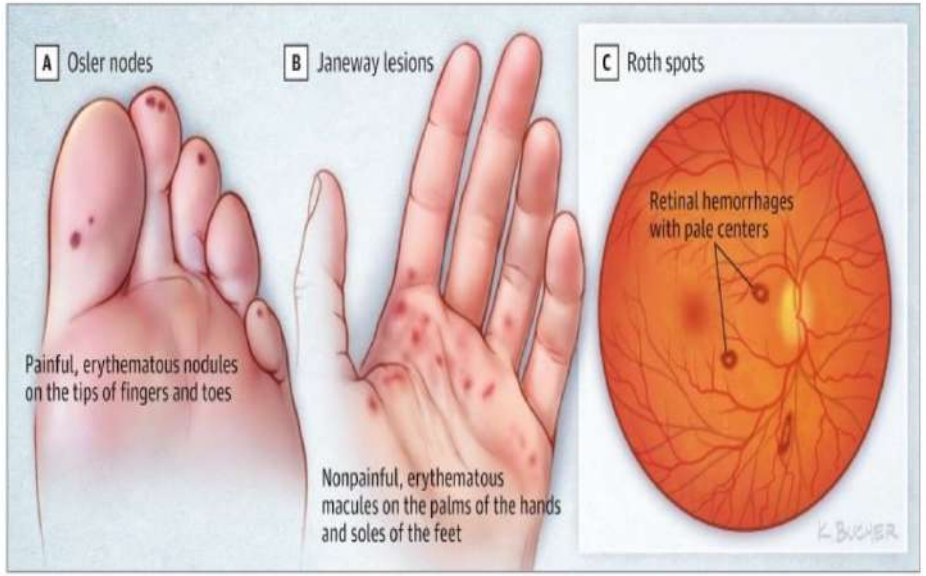


Figure 1. Classic, but Uncommon, Signs of Infective Endocarditis



A, Osler nodes (shown on the foot) present as painful, erythematous nodules on the tips of the fingers and toes.

B, Janeway lesions (shown on the hand) present as nonpainful, erythematous macules on the palms of the hands and soles of the feet.

C, Roth spots are hemorrhages with pale centers that are found on the retina.

İE tanısında laboratuar bulguları nasıldır?

- Sürekli antijenik uyarıya bağlı akut faz reaktanlarında↑
- Humorol ve hücresel immun yanıt uyarılmasına bağlı; dolaşımda çeşitli antikor ve immun kompleksler , hipergamaglobulunemi, RF, ANA, ANCA, antifosfolipid antikor ve antikardiyolipin antikor +
- Sepsis ve doku hasarına bağlı laktat bazı kan değerlerinde ↑,↓
- Kardiyak hasara bağlı, NT- pro BNP ve Troponin ↑

İE Tanısı için kullanılan kriterler nelerdir?

- Modifiye Duke Kriterleri
- 2015 ESC Modifikasyonuna göre İE Tanı Kriterleri
- Yeni 2019 Uluslararası CIED İnfeksiyon Kriterleri

KESİN İE : 2 majör;1 majör 3 minör;5 minör

OLASI İE: 1 major 1 minör; 3 minör

2015 ESC ve Modifiye Duke Kriterlerine göre Kesin İE, Major Patolojik/Klinik/Görüntüleme Bulguları

Kesin İnfektif Endokardit Tanısı Koydurur

Patolojik ölçütler

- Vejetasyonda, embolize o intrakardiyak bir apsede n histopatolojik incelemede

veya

- Histopatolojik incelemed endokardit gösteren lezy

Klinik ölçütler

- 2 majör ölçüt

veya

- 1 majör + 3 minor ölçüt

veya

- 5 minör ölçüt

Majör Ölçütler

1. **İnfektif endokarditle uyumlu pozitif kan kültürü**

a. İki ayrı kan kültüründe İE ile uyumlu tipik mikroorganizmaların üremesi (viridans streptokoklar, *Streptococcus bovis*, HACEK grubu, *Staphylococcus aureus*; ya da başka bir odak odak olmaması koşuluyla, toplumdan edinilmiş enterokoklar

ya da

b. İE ile uyumlu mikroorganiz sürekli üremesi >12 saat ar kültüründe pozitif sonuç alı kültürünün hepsinde ya da çoğunda (birinci ve son örn olması koşuluyla) pozitif so

ya da

c. *Coxiella burnetii* için tek şiş I antijenlerine karşı IgG anti

2. **Endokard tutulumunun kanıtları**

a. İE düşündüren ekokardiyografi bulguları*

- Vejetasyon
- Apse, psödoanevrizma, intrakardiyak fistül
- Kapak perforasyonu veya anevrizması
- Yapay kapakta ortaya çıkan yeni kısmi ayrışma

b. Yapay kapak çevresinde ^{18}F-FDG PET/BT'de (sadece kapağı >3 ay önce implante edilmiş hastalar için) veya SPECT/BT ile birlikte işaretli lökosit sintigrafisinde anormal aktivite belirlenmesi

c. Kardiyak BT'de kesin paravalvüler lezyonlar

2015 ESC ve Modifiye Duke Kriterlerine Göre Minör Kriterler

Minör Ölçütler†

1. **Yatkınlık:** İE'ye yatkınlık oluşturan kalp hastalığı, IVDU olma
2. **Ateş:** vücut sıcaklığının >38°C olması
3. **Vasküler olaylar** (sadece görüntülemeyle saptananlar dahil): majör arteriyel embolizm, septik pulmoner infarktlar, mikotik anevrizma, intrakraniyal kanama; konjunktival kanamalar ve Janeway lezyonları
4. **İmmünolojik olaylar:** glomerülonefrit, Osler nodülleri, Roth lekeleri, romatoid faktör pozitifliği
5. **Mikrobiyolojik kanıtlar:** majör ölçütleri karşılamayan kan kültürü pozitiflikleri ya da İE ile uyumlu bir mikroorganizmayla aktif infeksiyonu gösteren serolojik kanıtlar

Modifiye Duke Kriterlerine Göre İE Tanısından UZAKLAŞTIRIR

- Başka bir tanının konulmuş olması

veya

- ≤4 günlük antibiyotik tedavisiyle İE düşündüren belirtilerin ortadan kaybolması

veya

- ≤4 günlük antibiyotik tedavisi altında yapılan cerrahi girişim veya otopsi sırasında çıkarılan örnekte İE düşündürecek patolojik kanıtların olmaması

veya

- Klinik ölçütlerle olası İE olarak sınıflandırılamaması

mDK için güncelleme gerekiyor mu?

- Epidemiyolojik verilere göre?
- Yaşlılar, immunsüpresif hastalarda endokardit tanısı için eşik düşüren kriterler eklenebilir mi?
- Enterokokal İE (kaynağı belli olan ??) majör kriterler arasına??
- KNİE' lerde, *M chimera* gibi daha kolay, ulaşılabilir örneklem yapmak (microbial cell free DNA??) mümkün mü?
- Kapak ve kandan yapılan moleküler testler majör kriter arasına alınmalı mı?

İE tanısında mikrobiyolojik tanı neden önemlidir?

- Etken m.o.nın belirlenmesi, tanının konulması ve antimikrobik tedavinin yönlendirilmesi açısından kritiktir.

- Etken belirlenemeyenlerde mortalite X1.8↑ (komorbidite-)
- Gelişmiş ülkelerde %90 etken belirlenebilirken, gelişmekte %41-67
- Hospitalizasyonları sırasında %17 septik şok gelişebilmekte

Murashita et al. EurJ CardiothoracSurg2004; 26: 1104-1111

Díez-VillanuevaInt P. J Cardiol 2016; 220: 162-165.

Cuerve et al. Frontiers in Medicine February 2021 | Volume 8

İE mikrobiyolojik tanıda kullanılan yöntemler nelerdir?

- Kültür

Kan kültürü

Kapak doku kültürü

- Seroloji
- Moleküler tanı

Kandan, kültürden, kapakçık dokusundan

Geniş spektrumlu, etkene özgül PCR

Prob hibridizasyon…

Hangi mikroorganizmaların KK pozitifliği İE akla getirmelidir?

- Stafilokoklar (*S. aureus*, Co N Stafilokoklar, *S lugduniensis*)
- Streptokoklar (viridans streptokoklar, D grubu streptokoklar, nütrisyonel olarak varyant streptokoklar (NVS), *Gemella* spp.
- En sık tanımlanan streptokoklar, *S. sanguinis, S. bovis, S. mutans, S. mitis, S. anginosus, S .bovis (SGG)*
- Enterokoklar *(sıklıkla E faecalis)*
- *Brucella spp*
- *HACEK* grubu
- *HACEK* dışı *GNB ve diğer bakteriler (Cutibacterium vs….)*
- *Candida spp*

Hangi mikroorganizma KK pozitifliği sonrası ekokardiyografi ileri tetkik olarak istenmelidir?

- ***S. aureus*** (Başka nedenlerle *S. aureus* bakteriyemisi olan hastaların toplamda **%10-12'sinde**, altta yatan kapak hastalığı olanların ise %50'sinde İE gelişir)
- Odak belirlenememiş persistan üremesi devam eden ***E. faecalis***
- Odağı belli olmayan, persistan ***Candida spp*** üremeleri

Unutmamalı ki;

- Kan kültüründe üretilen ***S. mutans*** suşlarından İE etkeni olanların olmayanlara oranı 14/1 iken bu oran ***S. sanguinus*** için 3/1, ***Enterococcus faecalis*** için ise 1/1.2'dir.
- ***S. lugdiniensis*** bakteriyemisi %6.3-27 İE ile ilişkili

Journal of Infection (2017) 74, 179e186

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3237–3244
doi:10.1093/eurheartj/ehz327

CLINICAL RESEARCH
Valvular heart disease

Prevalence of infective endocarditis in patients with positive blood cultures: a Danish nationwide study

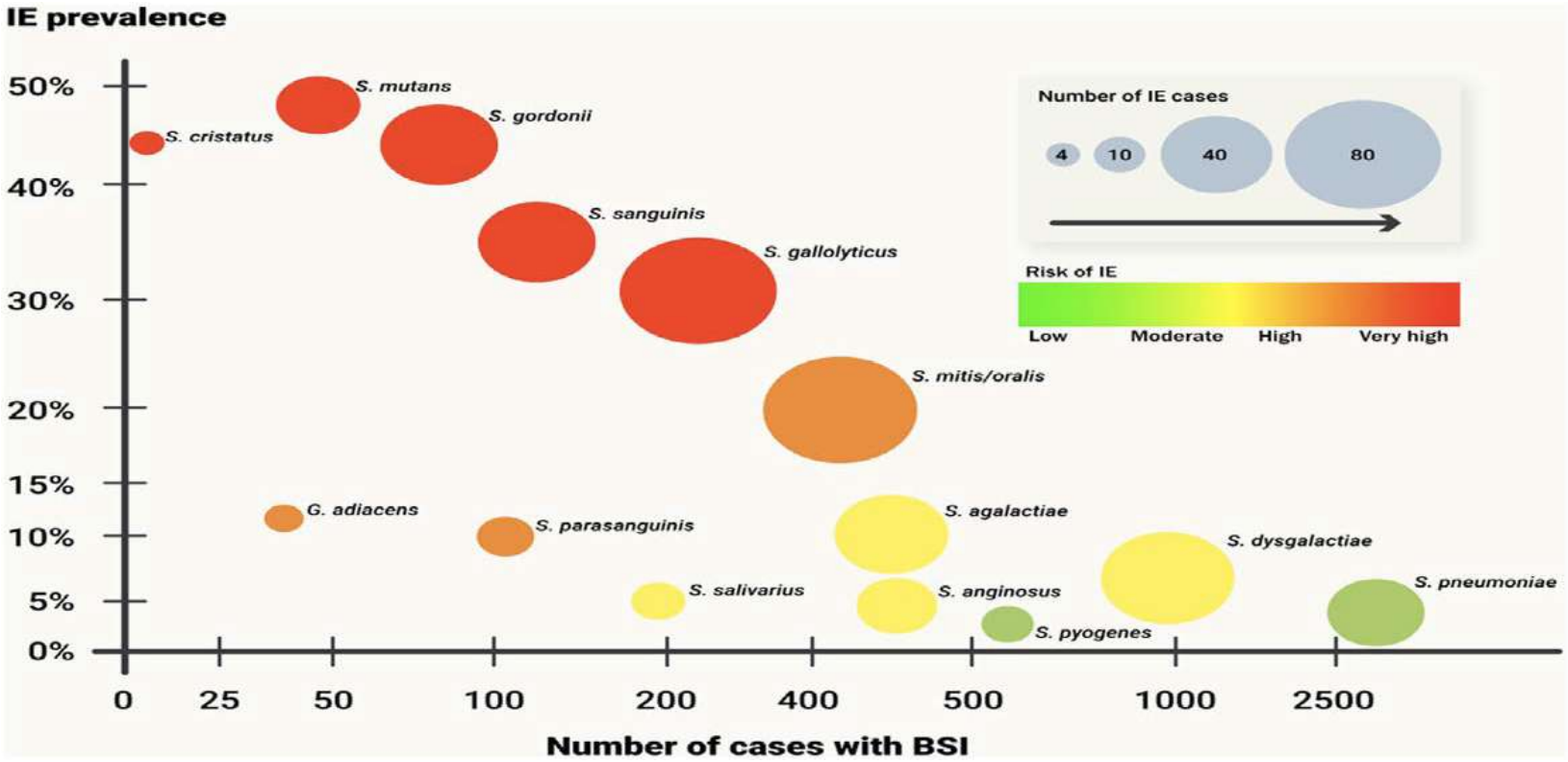
Aims Increasing attention has been given to the risk of infective endocarditis (IE) in patients with certain blood stream infections (BSIs). Previous studies have been conducted on selected patient cohorts, yet unselected data are sparse. We aimed to investigate the prevalence of IE in BSIs with bacteria typically associated with IE.

Methods and results By crosslinking nationwide registries from 2010 to 2017, we identified patients with BSIs typically associated with IE: *Enterococcus faecalis* (*E. faecalis*), *Staphylococcus aureus* (*S. aureus*), *Streptococcus* spp., and coagulase negative staphylococci (CoNS) and examined the concurrent IE prevalence. A trend test was used to examine temporal changes in the prevalence of IE. In total 69 021, distributed with 15 350, 16 726, 19 251, and 17 694 BSIs were identified in the periods of 2010–2011, 2012–2013, 2014–2015, and 2016–2017, respectively. Patients with *E. faecalis* had the highest prevalence of IE (16.7%) followed by *S. aureus* (10.1%), *Streptococcus* spp. (7.3%), and CoNS (1.6%). Throughout the study period, the prevalence of IE among patients with *E. faecalis* and *Streptococcus* spp. increased significantly ($P = 0.0005$ and $P = 0.03$, respectively). Male patients had a higher prevalence of IE for *E. faecalis*, *Streptococcus* spp., and CoNS compared with females. A significant increase in the prevalence of IE was seen for *E. faecalis*, *Streptococcus* spp., and CoNS with increasing age.

Conclusion For *E. faecalis* BSI, 1 in 6 had IE, for *S. aureus* BSI 1 in 10 had IE, and for *Streptococcus* spp. 1 in 14 had IE. Our results suggest that screening for IE seems reasonable in patients with *E. faecalis* BSI, *S. aureus* BSI, or *Streptococcus* spp. BSI.

ORIGINAL RESEARCH ARTICLE

Prevalence of Infective Endocarditis in Streptococcal Bloodstream Infections Is Dependent on Streptococcal Species



En yüksek endokardit prevelansı;

S mutans, S gordonii, S sanguinis, S gallolyticus, ve S mitis/oralis

Circulation. 2020;142:720–730. DOI: 10.1161/CIRCULATIONAHA.120.046723

Kan kültürü nelere dikkat edilmeli?

- S
- A
- A
- D

-B device)

-K

-U

-A a AB do

-1

1.Set		2.Set		Değerlendirme
Aerobik	Anaerobik	Aerobik	Anaerobik	
				Negatif
				Kontaminasyon
				Kontaminasyon
				Etken
				Etken
				Etken
				Etken
				Etken
				Etken
				Etken

Kan Kültürlerinde inkübasyon süresi uzatılmalı mı?

- Otomatize sistemlerde 5 günlük inkübasyon HACEK, Candida, *Abiotrophia*, *Granulicatella* gibi NVS için yeterli
- Kan K. pozitif hastadan, **negatifleşinceye kadar 48 saatte kontrol kültürleri 2 set olarak alınmalı!!**
- Tek istisna *C. acne*. (14 gün gerekmekte); 5 gün sonunda sinyal- şişeler çikolata agara kör pasaj yapılmalı.
- Uygun KK alımı ile BCNİE oranları %30'dan %5 düşer.
- Son 10 yılda kalp cerrahisi geçirenlerde *M. chimaera* unutulmamalı!

Kan kültür pozitiflik zamanı İE için gösterge olabilir mi ?

European Journal of Clinical Microbiology & Infectious Diseases (2021) 40:1657–1664
https://doi.org/10.1007/s10096-021-04210-9

ORIGINAL ARTICLE

Short time to blood culture positivity in *Enterococcus faecalis* infective endocarditis

Abstract

Time to blood culture positivity (TTP) is an indirect measure of bacterial concentration in blood. A short TTP has been linked to the presence of infective endocarditis (IE) and to poor prognosis in *Staphylococcus aureus* bacteremia. We analyze factors influencing TTP in bacteremia with *Enterococcus faecalis*. This retrospective observational study of medical records included adults diagnosed with monomicrobial *E. faecalis* bacteremia between 2015 and 2018 in the Skåne region (Sweden). For each episode, the shortest TTP was recorded. Median TTP was compared between patients grouped based on age, sex, comorbidity, site of acquisition, and focus of infection. Using a dichotomized TTP (shorter or longer than 12 h), a multivariable logistic regression for factors associated to TTP was performed. The association between TTP and IE or mortality was evaluated. Three hundred sixty-seven episodes with monomicrobial *E. faecalis* bacteremia with the corresponding TTP were identified. Median TTP for the entire cohort was 11.6 (IQR 9.9–14.1) h and a significantly shorter TTP was noted for episodes which represented IE (n = 55, 9.4 (IQR 6.4–10.6) h). Only IE remained associated with a short TTP (≤ 12 h) in binary logistic regression analysis. Factors associated with IE were investigated and TTP was associated with IE also when adjusted for age, gender, comorbidity, and nosocomial acquisition. There was no association between TTP and mortality. A low TTP is associated with IE in *E. faecalis* bacteremia and could be used as a help in determining the need for echocardiography in patients with this condition.

Clinical Microbiology and Infection 25 (2019) 481–488

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journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Time to blood culture positivity: An independent predictor of infective endocarditis and mortality in patients with *Staphylococcus aureus* bacteraemia

ABSTRACT

Objectives: Time to blood culture positivity (TTP), a routinely available parameter in automated blood culture systems, may be a proxy for infectious burden in patients with bloodstream infections. We aimed to study the association between TTP and infective endocarditis (IE), or death, in patients with *Staphylococcus aureus* bacteraemia.

Methods: VIRSTA is a multicentre prospective cohort study that included all adult patients with *S. aureus* bacteraemia in eight university hospitals in France (2009–2011). We analysed data from four centres which collected data on TTP. Regression models were used to study the association between TTP and definite IE (Duke-Li criteria), and 30 day-mortality.

Results: We included 587 patients with *S. aureus* bacteraemia: mean age was 65.3 ± 16.3 years, 420 out of 587 patients (71.6%) were male, 121 out of 587 (20.6%) died, and 42 out of 587 (7.2%) had definite IE. Median TTP of first positive blood culture was 13.7 h (interquartile range 9.9–18). On multivariate analysis, 30-day mortality was associated with TTP ≤13.7 h (74/295 (25.1%) vs. 47/292 (16.1%), p 0.02), as well as old age, McCabe score, methicillin resistance, stroke, pneumonia, and C-reactive protein. TTP was also independently associated with IE, but with a U-shape curve: IE was more common in the first (TTP <10 h, 17/148, 11.5%), and the last (TTP ≥18 h, 8/146, 5.5%) quartiles of TTP, p 0.002.

Conclusions: TTP provides reliable information in patients with *S. aureus* bacteraemia, on the risk of IE, and prognosis, with short TTP being an independent predictor of death. These data, readily available at no cost, may be used to identify patients who require specific attention. **S. Siméon, Clin Microbiol Infect 2019;25:481**

Kan kültür pozitiflik zamanı İE için gösterge olabilir mi ?

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Official journal of the Spanish Society of Chemotherapy

Review

Revista Española de Quimioterapia
doi:10.37201/req/066.2022

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Patricia Muñoz[1,2,3,4]
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Unresolved issues in the epidemiology and diagnosis of bacteremia: an opinion paper

Rev Esp Quimioter 2022;35(6): 519-537

Table 7 Representation of the heterogeneity of results and methodology of a selection of recent studies on the usefulness of time to blood culture positivity as a predictor of severity.

Reference	Country	Type of study	Result	Comment
Hsieh [131]	Multinational	Meta-analysis	A short TTP was associated with higher mortality and septic shock in some bacterial species, but not in *Candida* spp.	- Notable biases, presence of heterogeneity, mixing of pediatric and adult populations, important confounding factors not assessed, meta-regression analysis not significant.
Hamilton [138]	United Kingdom	Prospective multicenter cohort study.	TTP not associated with mortality except in *Candida* spp. (elevated TTP) and possibly in streptococci.	- More methodological soundness than most studies (includes time to incubation). - Limitations: does not assess time to effective treatment, small samples in some groups.
Siméon [143],	France	Prospective multicenter cohort study.	A short TTP is related to mortality and to the presence of endocarditis in *S. aureus* bacteremia.	- Some limitations: small sample, blood culture systems used, does not analyze blood culture volume.
Kim [139]	Canada	Retrospective study	Elevated TTP is associated with mortality in *S. aureus* bacteremia.	- Some limitations: retrospective, does not have detailed clinical information, does not analyze foci of infection, does not analyze antibiotic treatment.
Oldberg [144]	Sweden	Retrospective observational study	No association was observed between TTP with mortality or the presence of endocarditis in *E. faecalis* bacteremia.	- Some limitations: retrospective study, transesophageal echocardiogram not performed in all patients, does not include patients under treatment, does not analyze blood culture volume.

Tek kan kültür negatifliği yeterli midir?

Open Forum Infectious Diseases

MAJOR ARTICLE

Intermittent Negative Blood Cultures in *Staphylococcus aureus* Bacteremia; a Retrospective Study of 1071 Episodes

Background. Recommended management of *Staphylococcus aureus* bacteremia (SAB) includes follow-up blood culture sets (BCs) to determine the duration of bacteremia. Duration of bacteremia is an important prognostic factor in SAB, and follow-up BCs have a critical role in differentiation of uncomplicated and complicated SAB. However, intermittent negative BCs occur in SAB. Clinical guidelines for SAB management do not specify an approach to follow-up BCs' collection or define the number of negative BCs required to demonstrate resolution of bacteremia. This study assessed the frequency of intermittent negative BCs in SAB and used these findings to formulate a recommendation for collection of follow-up BCs.

Methods. This retrospective study reviewed 1071 episodes of SAB. Clinical and microbiological data including the duration of bacteremia and the occurrence of intermittent negative BCs (those preceded and followed by positive cultures) were considered.

Results. Intermittent bacteremia occurred in 13% (140/1071) of episodes. A single negative BC on days 1–3 had a predictive value of 87%–93% for resolution of bacteremia, although this was improved if all BCs collected within the same day were considered.

Conclusions. Intermittent negative BCs are common in SAB. Given this, we would not recommend accepting a single negative BC as demonstrating resolution of the bacteremia. This is particularly important if a patient is to be classified as having uncomplicated SAB.

Infection (2019) 47:1047–1053
https://doi.org/10.1007/s15010-019-01339-w

BRIEF REPORT

Is a single set of negative blood cultures sufficient to ensure clearance of bloodstream infection in patients with *Staphylococcus aureus* bacteremia? The skip phenomenon

Abstract

Background The most recent version of the Infectious Diseases Society of America guidelines for the treatment of methicillin-resistant *Staphylococcus aureus* infections states that a single set of negative blood cultures is sufficient to demonstrate clearance of bacteremia. However, *S. aureus* might exhibit fluctuating blood culture positivity, labeled as "the skip phenomenon". Our objectives were to determine the prevalence of the skip phenomenon in a cohort of hospitalized patients with *S. aureus* bacteremia and to determine the associated clinical variables.

Methods We conducted a nested case–control study, using a previous cohort of 757 adult inpatients between July 2006 and June 2011 with ≥ 3 days of *S. aureus* bacteremia. Each case of *S. aureus* bacteremia with the skip phenomenon was matched to 2 to 4 controls based on age, gender, and duration of bacteremia. The association of clinical characteristics with the skip phenomenon was analyzed via conditional logistic regression.

Results Of the 757 patients in the cohort, 29 (4%) had the skip phenomenon. 26 (90%) patients in the cases group were male. The median age was 69.4 years (interquartile range [IQR] 58.7 to 80.3). Although an attempt to match for the duration of bacteremia was done, there was a statistically longer duration in patients with cases as compared to that in controls (median [IQR], 10 [7–12] days, vs 8 [6–10] days; $P = 0.015$). Accordingly, duration of bacteremia was adjusted for in regression models. Notably, 26 (90%) patients in the case group were receiving chronic immunosuppressive therapy, as compared to 69 (79%) patients in the control group ($P = 0.427$).

Conclusion Our findings prompt consideration of a practice chance to obtain serial negative blood cultures to ensure clearance of bacteremia among patients with *S. aureus* bacteremia.

İyi planlanmış çalışmalara ihtiyaç olmakla birlikte ???

Kontrol kan kültürlerinin 48 saatte bir ve 2 set olarak alınması gereklidir.

Uzlaşı raporu

Kan kültürü negatif İE tanısında hangi mikrobiyolojik yöntemler kullanılır?

- 3 önemli neden

1. Öncesinde AB kullanımı
2. Zor üreyen bakteri
3. Hücre içi yerleşen ve kültürlerde üretilemeyen bakteri (*M. chimaera, Bartonella, T whipplei)*

Ek inkübasyon ve pasajlarla da üreme saptanmayan olgular BCNIE olarak değerlendirilmelidir. Bu hastalarda, hem söz konusu üretilemeyen etkenlere yönelik olarak yapılacak ***serolojik*** *testler, hem de özellikle daha önce antibiyotik kullanmış hastalar için olmak üzere, değerlendirmeye* ***moleküler testlerle*** *devam edilmelidir*

İE tanısında serolojik testler hangi m.o. İçin kullanılmaktadır?

IFA testi ile Ig G sınıfı antikorlar

- *Brucella* spp (1/160; Negatifse Coombs ya da Brucellacapt>1/320)
- *C. burnetti* (faz I Ag yönelik >1/800)
- *B. henselae* (Bartonella spp >1/800)
- *B. quintana*
- *L. pneumophilia* (1/216)
- *Chlamydia* spp (1/512)

Clinical Infectious Diseases
MAJOR ARTICLE

Microbial Cell-Free DNA Identifies Etiology of Bloodstream Infections, Persists Longer Than Conventional Blood Cultures, and Its Duration of Detection Is Associated With Metastatic Infection in Patients With *Staphylococcus aureus* and Gram-Negative Bacteremia

Background. Microbial cell-free DNA (mcfDNA) sequencing of plasma can identify the presence of a pathogen in a host. In this study, we evaluated the duration of pathogen detection by mcfDNA sequencing vs conventional blood culture in patients with bacteremia.

Methods. Blood samples from patients with culture-confirmed bloodstream infection were collected within 24 hours of the index positive blood culture and 48 to 72 hours thereafter. mcfDNA was extracted from plasma, and next-generation sequencing was applied. Reads were aligned against a curated pathogen database. Statistical significance was defined with Bonferroni adjustment for multiple comparisons ($P < .0033$).

Results. A total of 175 patients with *Staphylococcus aureus* bacteremia (n = 66), gram-negative bacteremia (n = 74), or noninfected controls (n = 35) were enrolled. The overall sensitivity of mcfDNA sequencing compared with index blood culture was 89.3% (125 of 140), and the specificity was 74.3%. Among patients with bacteremia, pathogen-specific mcfDNA remained detectable for significantly longer than conventional blood cultures (median 15 days vs 2 days; $P < .0001$). Each additional day of mcfDNA detection significantly increased the odds of metastatic infection (odds ratio, 2.89; 95% confidence interval, 1.53–5.46; $P = .0011$).

Conclusions. Pathogen mcfDNA identified the bacterial etiology of bloodstream infection for a significantly longer interval than conventional cultures, and its duration of detection was associated with increased risk for metastatic infection. mcfDNA could play a role in the diagnosis of partially treated endovascular infections.

Kültür negatif İE'de bir seçenek olabilir mi?

Kapak incelemesi nasıl olmalıdır?

- Histopatolojik
- Mikrobiyolojik –Kültür
- Mikrobiyolojik- Moleküler

Kapak kültürü mü kan kültürü pozitifliği mi? Hangisinin pozitifliği daha kıymetlidir?

- %6-26'sında pozitif, kontaminasyon oranları çok yüksek (%28-36)

Duyarlılık (%8-33) ve özgüllüğü (%56-94) düşük

- Endokardit dışı vakalarda kapak kültürü ÖNERİLMEZ!
- Kan kültürü ile uyumsuz sonuçlarda KAN KÜLTÜRÜ sonuçları dikkate alınmalı!

Kapak Kültürü için ameliyathanede neler planlanmalı?

- 3 tane steril vidalı kapaklı plastik kapak ayarlanmalı.
- Kapak ya da embeloktomi gibi operasyon materyalleri
- Kan ve kapak kültüründe üreyen m,o tür düzeyinde tanımlanmalı!
- Gram boyama, kültür ve histopatolojik inceleme
- DDX arasında İE olmayan hastalarda kapak kültürü önerilmez!
- Makroskopik inceleme-doku homojenizatörü gram-giemsa boyama- kanlı, katı ve sıvı by'de aerop ve anaerob ekim yapılmalı; 7 gün inkübasyon
- Klasik tanımlamanın yanısıra direk koloniden MALDI-TOF, 16 SrRNA dizileme
- M.o.'nın MİC belirlenmeli!
- Suşlar ek inceleme ve rekürrens için 1 yıl süre ile saklanmalı!

Moleküler Testler hangileri olmalı?

- Kan ve kapakta
- Geniş kapsamlı PCR ve patojene özgü gerçek zamanlı PCR
- Özgül bir klinik şüphe olmadığında tüm bakterilerde bulunabilen 16SrRNA, 23SrRNA, rpoB hedefleyen primerlerin kullanıldığı geniş kapsamlı PCR
- Etken öngörülebiliyorsa, patojene özgü gerçek zamanlı PCR testleri
- AB almış KK(-) hastalarda, tam kandan multiplex PCR(SetptiFast, SepsiTest..)
- AB(-)+ KK(-) + kapakta 16SrRNA gen analizi ve *T whipplei* için PCR

İE'de Etkene Yönelik Mikrobiyolojik İncelemede Algoritma Nasıl Olmalı?

İE tanısında histopatolojik yöntemlerde algoritma nasıldır?

- Altın standart
- KK pozitif hastalarda aktivasyonu; KK negatif olgularda hücre içi yerleşen m.o

KK negatif olgularda, kapakta moleküler testler

İnfektif endokarditli hastadan çıkarılmış kalp kapağ

ası ve kültürü

Kapağın histopa

(Moleküler testler, sadece kan kültürü
bulgulara göre aşağıda verildiği şekilde yapılmalıdır)

Akut inflamasyon±mikroorganizma

16s rRNA geni için PCR/dizileme

Pozitif

Negatif

Coxiella burnetii PCR
Bartonella spp. PCR
Tropheryma whipplei PCR
Diğer mikroorganizmalar için özgül PCR‡

Kronik inflamasyon ve makrofajların baskın olması

PAS-D histopatolojik boyama†
Tropheryma whipplei PCR

Pozitif

Negatif

16S rRNA geni için PCR/dizileme
Coxiella burnetii PCR
Bartonella spp. PCR
Diğer mikroorganizmalar için özgül PCR‡

İnflamasyon veya mikroorganizma olmaması

İnfeksiyon dışı nedenleri araştır

İE tanısında kullanılan görüntüleme yöntemleri nelerdir?

- Ekokardiyografi

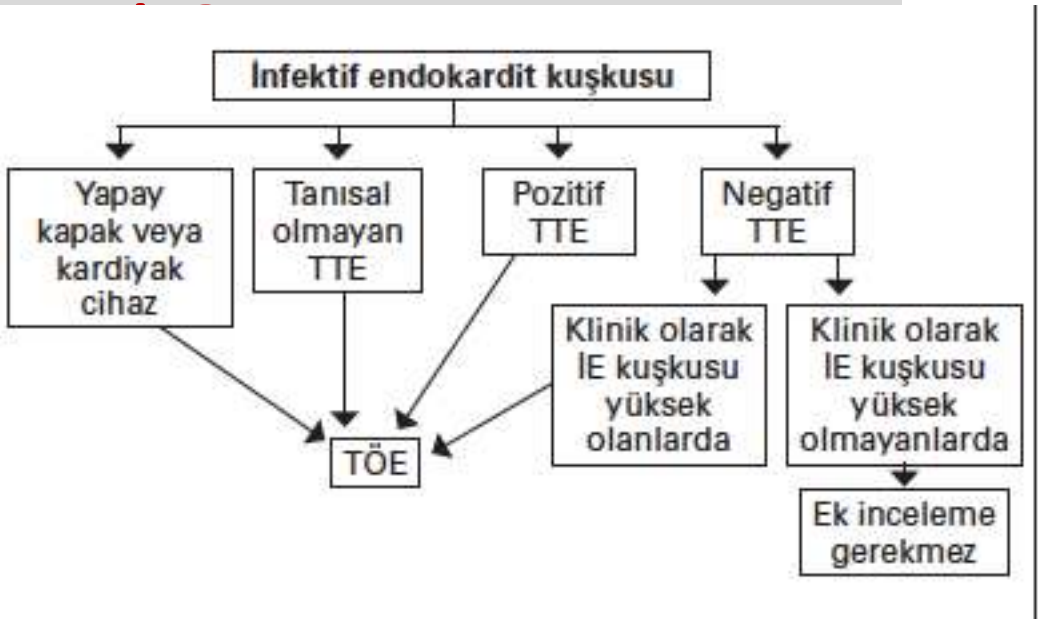
-TTE

-TÖE

- Çok kesitli bilgisayarlı tomografi
- Serebral/ Kardiyak MRI
- PET/BT
- Lökosit İşaretli sintigrafi

Ekokardiyografi kimlere yapılı
TÖE gerekmeyen İE hangisidi

- **TTE;** İE şüphesi olan tüm hastalar,
- **TÖE;** TTE'de görüntü kalitesi kötü olan, klinik olarak negatif olduğu, yapay kapağı veya kardiyak cihazı o düşünülen hastalarda,



*TTE'si pozitif olan, **sağ kalp İE'li** ve negatif TTE sonrası İE kuşkusu olmayan hastalar **dışında tüm İE** düşünülen hastalarda TÖE yapılmalıdır.*

Majör ölçüt olarak kabul edilen ekokardiyografik bulgular: [1] vejetasyon, [2] apse, psödoanevrizma veya intrakardiyak fistül, [3] kapakta anevrizma ve perforasyon, [4] yapay kapakta yeni kısmi ayrışma varlığı, [5] ekokardiyografik olarak belirlenmiş, yeni veya belirgin olarak artış gösteren bir kapak yetersizliğinin ortaya çıkması

Ekokardiyografi ile tanı konamaz ise ne yapılmalı?

- İE olgularının yaklaşık %15'inde, intrakardiyak yabancı cismi olan hastaların ise %30'unda ne TTE ne de TÖE ile sonuç alınamayabilir.
- Doğal kapak endokarditlerinde kardiyak BT,
- Yapay kapak endokarditlerinde ise kapak ameliyatından sonraki ilk 1-3 ayda kardiyak BT ve SPECT/BT ile birlikte işaretli lökosit sintigrafisi,
- 3 aydan uzun süre geçmiş ise, kardiyak BT ve PET/ BT yapılması öncelikle düşünülmelidir.

Çok kesitli bilgisayarlı tomografi

- TÖE ile karşılaştırıldığında, doğal kapaktaki duyarlılığı %97, özgüllüğü %88, yapay kapaktaki duyarlılığı %93'tür. Standard tanı yöntemleriyle birlikte kullanıldığında ise ÇK-BT'nin duyarlılığı %100, özgüllüğü %91'dir
- ÇK-BT, İE'nin perivalvüler yayılımın gösterilmesinde TÖE'ye daha üstünken, vejetasyonların gösterilmesinde TÖE'ye göre daha az doğruluk oranlarına sahiptir.
- ÇK-BT, psödoanevrizma, apse, fistül anatomisi ve perivalvüler yayılım hakkında daha ayrıntılı bilgi verebilir .
- Yapay kapak varlığında TÖE ile endokardın görülmesi zorlaşabilir; bu durumda metalik artefaktlara karşın ÇK-BT daha iyi görüntü sağlayabilir

Tek foton emisyon tomografisi/bilgisayarlı tomografiyle birlikte işaretli lökosit sintigrafisi:

- Kapak ameliyatının ilk 1-3 ayında İE gelişmiş yapay kapak endokarditlerinde

- İE belirlemedeki özgüllüğü yüksek olmakla birlikte, duyarlılığının düşük olması en önemli zayıflığıdır.

Ne zaman PET CT?

- İE tanısı net olarak ortaya konulamayan kardiyak cihazlı hastalar,
- Nedeni bilinmeyen ateş veya bakteriyemi bulunan kardiyak cihazlı hastalar,
- Klinik olarak İE tanısı olasılığı yüksek olan ancak ekokardiyografi ve/veya kan kültüründe tanı konulamayan hastalar,
- İnfeksiyon yaygınlığının araştırılması, olası embolizasyon odaklarının saptanması, antibiyotik tedavisine yanıtın değerlendirilmesi

- *Doğal kapak İE'sinde PET/BT ve işaretli lökosit sintigrafisiyle yapılan çalışmalarda duyarlılık düşüktür (%6-14).*

Nativ kapakta PET/BT'nin yeri nedir ?

- Doğal kapak İE'sinde PET/BT ve işaretli lökosit sintigrafisiyle duyarlılık düşüktür (%6-14).
- Bu nedenle nükleer tıp yöntemleri öncelikli değildir. Ancak özellikle PET/BT'nin **metastatik infeksiyonu, gizli infeksiyon odaklarını** ve **septik embolizasyonu** göstermedeki üstünlüğü nedeniyle tanı basamaklarında yer alması önerilir.
- Doğal kapaklı olgulardaki potansiyel infeksiyon odaklarının varlığı, PET/BT ile %15-32 oranında daha fazla ortaya konabilir.
- PET/BT bu hastaların %35'inde tedavi değişikliğine neden olabilmektedir.

Şimşek-Yavuz S et al. *İnfektif Endokardit Ulusal Uzlaşı Raporu*

Klimik Derg. 2019; 32(Suppl. 1): 2-116

^{18}F-FDG PET/CT improves diagnostic certainty in native and prosthetic valve Infective Endocarditis over the modified Duke Criteria

Background. International guidance recognizes the shortcomings of the modified Duke Criteria (mDC) in diagnosing infective endocarditis (IE) when transoesophageal echocardiography (TOE) is equivocal. ^{18}F-FDG PET/CT (PET) has proven benefit in prosthetic valve endocarditis (PVE), but is restricted to extracardiac manifestations in native disease (NVE). We investigated the incremental benefit of PET over the mDC in NVE.

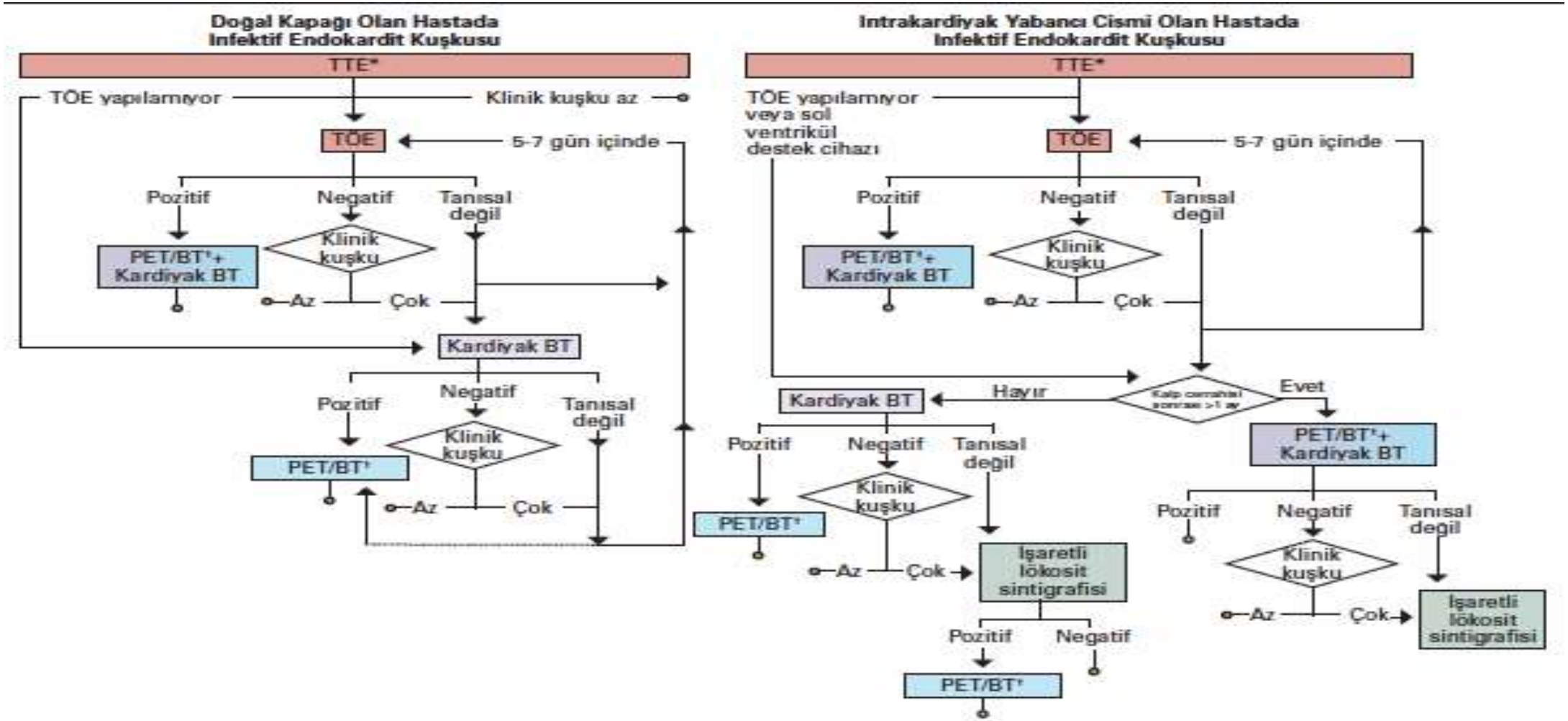
Methods. Dual-center retrospective study (2010-2018) of patients undergoing myocardial suppression PET for NVE and PVE. Cases were classified by mDC pre- and post-PET, and evaluated against discharge diagnosis. Receiver Operating Characteristic (ROC) analysis and net reclassification index (NRI) assessed diagnostic performance. Valve standardized uptake value (SUV) was recorded.

Results. 69/88 PET studies were evaluated across 668 patients. At discharge, 20/32 had confirmed NVE, 22/37 PVE, and 19/69 patients required surgery. PET accurately re-classified patients from possible, to definite or rejected (NRI: NVE 0.89; PVE 0.90), with significant incremental benefit in both NVE (AUC 0.883 vs 0.750) and PVE (0.877 vs 0.633). Sensitivity and specificity were 75% and 92% in NVE; 87% and 86% in PVE. Duration of antibiotics and C-reactive Protein level did not impact performance. No diagnostic SUV cut-off was identified.

Conclusion. PET improves diagnostic certainty when combined with mDC in NVE and PVE. (J Nucl Cardiol 2022;29:2119–28.)

	Native valve endocarditis			Prosthetic valve endocarditis		
	Pre-PET	Post-PET	Discharge diagnosis	Pre-PET	Post-PET	Discharge diagnosis
Modified Duke Criteria						
Definite	14	16	20	14	21	22
Possible	12	2	–	19	3	–
Rejected	6	14	12	4	13	15
Net Reclassification Index						
Overall			0.89			0.90
Positive			0.44			0.50
Negative			0.45			0.40

İE Tanısında Görüntüleme Yöntemleri



Imaging Modality	Strengths	Limitations
Transthoracic echocardiography (TTE)	Widely available, first-line modality, safe with no radiation exposure, portable, high temporal resolution, assesses hemodynamics, valve function, endocarditis features, and chamber function.	Operator and patient dependent on imaging windows, creates artifacts, lower sensitivity than more advanced modalities in identifying most endocarditis features including small vegetations, periannular complications, prosthetic valve, and device-related endocarditis.
Transesophageal echocardiography (TEE)	Portable, higher sensitivity than TTE for most endocarditis features, preferred modality for vegetations, valve perforation, prosthetic valve dehiscence and paravalvular leak, identifies fistula, high spatial and temporal resolution.	Invasive imaging modality, may still have artifact and lower sensitivity for some prosthetic valves and cardiac devices, avoid in contraindications such as prior gastroesophageal disease and surgery, active bleeding, patient intolerance.
Cardiac CT	Short study, excellent for detection of perivalvular complications (pseudoaneurysm, abscess, and fistula) in all types of endocarditis, can also identify other endocarditis features, detect extracardiac complications, high spatial resolution, use for pre-operative workup, and assesses coronaries and major vessels.	Non-portable, lower sensitivity than echocardiography for smaller vegetations, perforations, and paravalvular leaks. Inferior temporal resolution to echocardiography, radiation exposure, iodinated contrast administration (avoid in chronic renal impairment, especially when creatinine clearance below 30).
Cardiac Magnetic Resonance	Can identify endocarditis complications in some scenarios, such as using its high sensitivity for cerebral lesions. Reference standard for chamber quantification and can also quantify valve disease and shunts (such as for fistula).	Long study, non-portable, can cause claustrophobia, cost, non-compatible devices, lower temporal resolution than echocardiography, only for stable patients who can lie flat and follow instructions.
^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT)	Improved sensitivity for prosthetic valve and device-related endocarditis in some scenarios.	Non-portable, low sensitivity for native valve endocarditis, no functional cine imaging, radiation exposure, special pre-test preparation, cost, false-positive results within 3 months after cardiac surgery, false-negative results in patients treated with antimicrobials.

MSS harici embolik olayları incelemek için rutin tüm vücut taraması gerekir mi?

- MSS dışındaki embolik olayların görüntüleme yöntemleri ile rutin olarak araştırılması önerilmemektedir.

- Dalak, böbrek vs bu gibi görüntülemelerin sadece belirti veya bulgu olması halinde yapılması gerekmektedir.

(USG; ateş devam eden hastalarda ek ölçüt için)

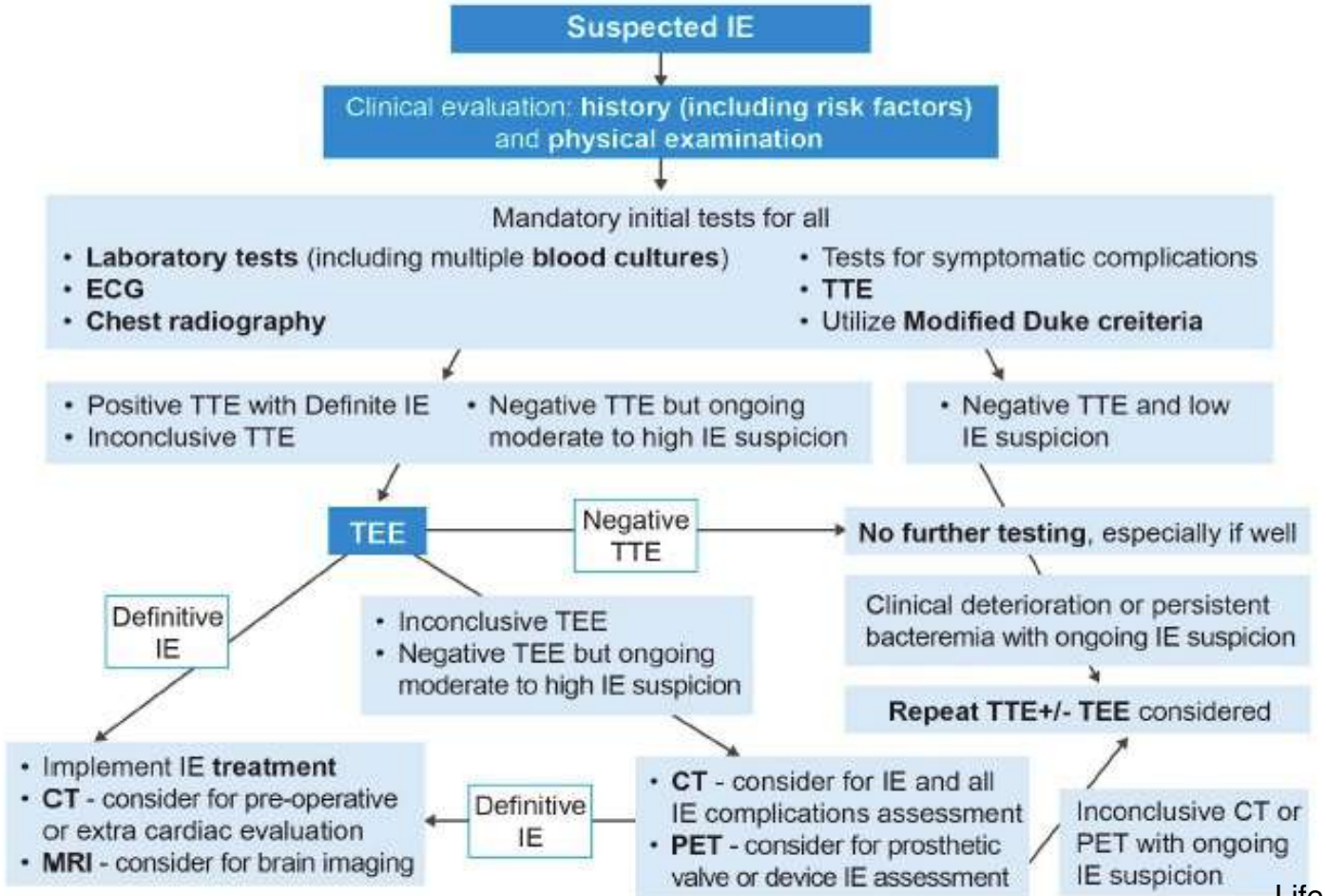
- Ancak özellikle dalak apsesi ve infarktlarının ayırıcı tanısında USG'nin BT'den daha az duyarlı olduğu bilinmeli ve dalakta USG ile lezyon belirlenen hastalarda mümkünse BT çekilerek apse mi infarkt mı olduğu ayırt edilmelidir

life

MDPI

Review

Contemporary Review of Multi-Modality Cardiac Imaging Evaluation of Infective Endocarditis



Life 2023, 13, 639. https://doi.org/10.3390/life13030639

Bakteri spesifik skorlama sistemleri gerçekten ‘EKO/SUZ’ İE tanısını koymakta etkin mi?

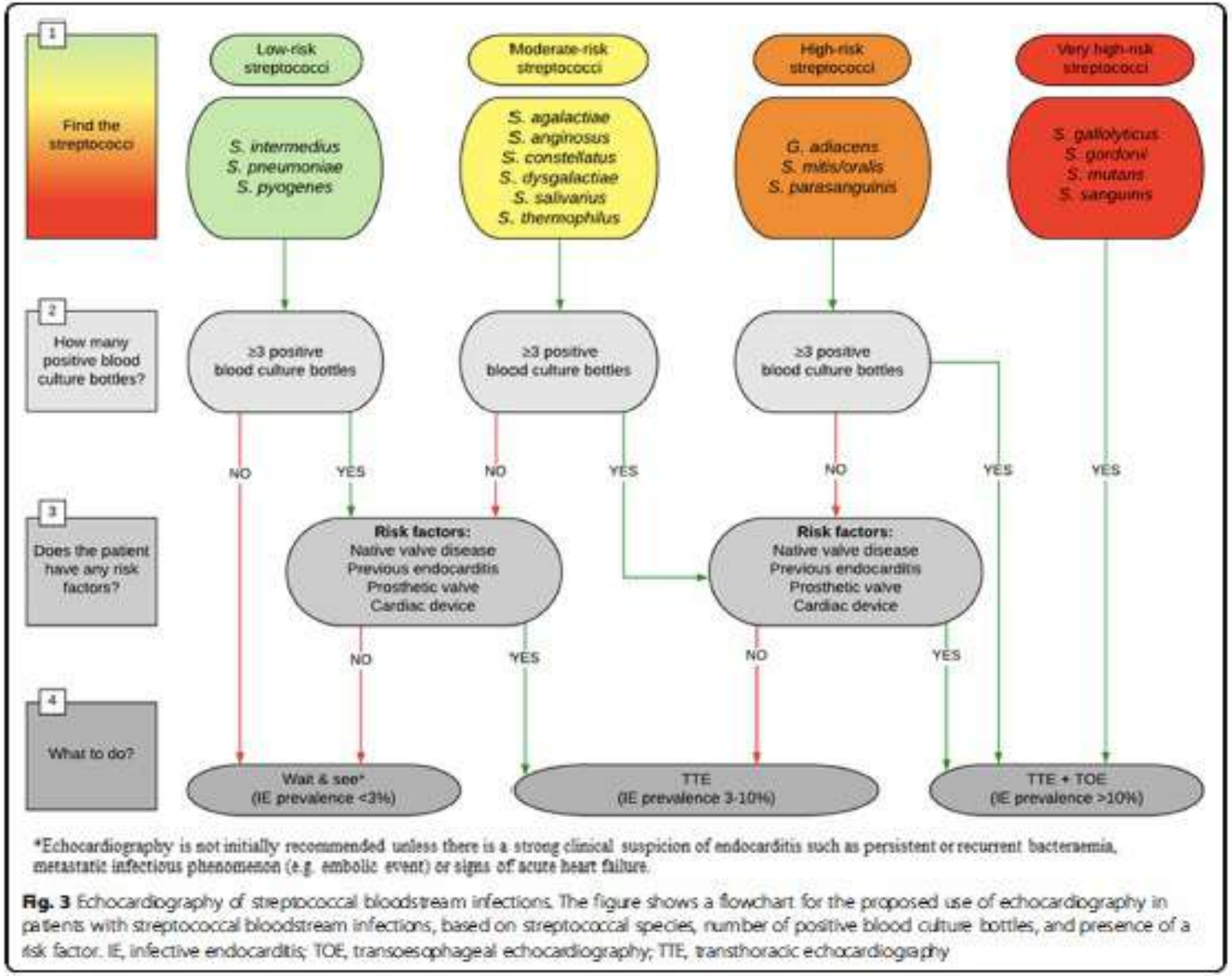
Chamat-Hedemand et al. BMC Infectious Diseases (2021) 21:689
https://doi.org/10.1186/s12879-021-06391-2

BMC Infectious Diseases

RESEARCH Open Access

Proposal for the use of echocardiography in bloodstream infections due to different streptococcal species

Modifiye Duke/2015
ESC 'ye tamamlayıcı !!



*Echocardiography is not initially recommended unless there is a strong clinical suspicion of endocarditis such as persistent or recurrent bacteraemia, metastatic infectious phenomenon (e.g. embolic event) or signs of acute heart failure.

Fig. 3 Echocardiography of streptococcal bloodstream infections. The figure shows a flowchart for the proposed use of echocardiography in patients with streptococcal bloodstream infections, based on streptococcal species, number of positive blood culture bottles, and presence of a risk factor. IE, infective endocarditis; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

The NOVA Score: A Proposal to Reduce the Need for Transesophageal Echocardiography in Patients With Enterococcal Bacteremia

Background. Frequency of enterococcal bloodstream infection (E-BSI) is increasing, and the number of episodes complicated by infective endocarditis (IE) varies. Performing transesophageal echocardiography (TEE) in all patients with E-BSI is costly and time-consuming. Our objectives were to identify patients with E-BSI who are at very low risk of enterococcal IE (and therefore do not require TEE) and to compare the outcome of E-BSI in patients with/without IE.

Methods. Between September 2003 and October 2012, we performed a prospective cohort study (all patients with E-BSI) and a case-control study (patients with/without enterococcal IE) in our center.

Results. We detected 1515 patients with E-BSI and 65 with enterococcal IE (4.29% of all episodes of E-BSI, 16.7% of patients with E-BSI who underwent transthoracic echocardiography, and 35.5% of all patients with E-BSI who underwent TEE). We developed a bedside predictive score for enterococcal IE—Number of positive blood cultures, Origin of the bacteremia, previous Valve disease, Auscultation of heart murmur (NOVA) score—based on the following variables: Number of positive blood cultures (3/3 blood cultures or the majority if more than 3), 5 points; unknown Origin of bacteremia, 4 points; prior heart Valve disease, 2 points; Auscultation of a heart murmur, 1 point (receiver operating characteristic = 0.83). The best cutoff corresponded to a score ≥4 (sensitivity, 100%; specificity, 29%). A score <4 points suggested a very low risk for enterococcal IE and that TEE could be obviated.

Conclusions. Enterococcal IE may be more frequent than generally thought. Depending on local prevalence of endocarditis, application of the NOVA score may safely obviate echocardiography in 14%–27% of patients with E-BSI.

Table 4. Score for Assessing the Risk of Infective Endocarditis in Patients With Enterococcal Bloodstream Infections

Variable	Points	Odds Ratio (95% Confidence Interval)
Number of positive blood cultures (N)	5	9.9 (2.2–40.6)
Unknown origin of bacteremia (O)	4	7.7 (2.5–23.8)
Prior valve disease (V)	2	3.7 (1.6–8.7)
Auscultation of a heart murmur (A)	1	1.8 (.77–4.3)
Total	12	

CID 2015:60 (15 February) • Bouza et al

Skorlama sistemleri İE tanısı için destekleyici

Infection (2019) 47:45–50
https://doi.org/10.1007/s15010-018-1208-3

ORIGINAL PAPER

The DENOVA score efficiently identifies patients with monomicrobial *Enterococcus faecalis* bacteremia where echocardiography is not necessary

Table 2 Variables of the DENOVA score, each giving 1 point, and their association with IE in multivariate analyses

	Odds ratio (95% CI)	*p* value
Duration of symptoms ≥ 7 days	9.7 (3.6–26)	<0.001
Embolization	50 (6.2–400)	<0.001
Number of positive cultures ≥ 2	6.8 (1.5–32)	0.01
Origin of infection unknown	7.3 (2.0–26)	0.003
Valve disease	1.7 (0.57–4.9)	0.35
Auscultation of murmur	13 (4.7–36)	<0.001

Abstract

Objectives Enterococcal bacteremia can be complicated by infective endocarditis (IE) and when suspected, transesophageal echocardiography (TEE) should be performed. The previously published NOVA score can identify patients with enterococcal bacteremia at risk for IE and we aimed to improve the score.

Methods Factors associated with IE were studied retrospectively in a population-based cohort of patients with monomicrobial *Enterococcus faecalis* bacteremia (MEFsB). Factors associated with IE in multivariable analysis were included in a new score system which was compared to the NOVA score and validated in a cohort of patients with MEFsB from another region.

Results Among 397 episodes of MEFsB, 44 episodes with IE were compared to those without IE. Long Duration of symptoms (≥ 7 days) and Embolization were associated with IE in the multivariate analysis and hence were added to the NOVA variables (Number of positive cultures, Origin of infection unknown, Valve disease, and Auscultation of murmur) to generate a novel score; DENOVA. The area under the curve in ROC analyses was higher for DENOVA (0.95) compared to NOVA (0.91) ($p=0.001$). With a cutoff at ≥ 3 positive variables the DENOVA score has a sensitivity of 100% and specificity of 83% which is superior to the NOVA score (specificity 29%). The DENOVA score was applied to the validation cohort (26 IE episodes and 256 non-IE episodes) and the resulting sensitivity was 100% and the specificity was 85% compared to 35% for NOVA.

Conclusions The DENOVA score is a useful tool to identify patients with MEFsB where TEE is not needed.

Taylor & Francis
Taylor & Francis Group

INFECTIOUS DISEASES,
2020; VOL. 52,
NO. 1, 54–57

https://doi.org/10.1080/23744235.2019.1679388

ORIGINAL ARTICLE

OPEN ACCESS Check for updates

External validation of the HANDOC score – high sensitivity to identify patients with non-beta-haemolytic streptococcal endocarditis

ABSTRACT

Background: Invasive infections with non-beta-haemolytic streptococci (NBHS) is quite common and presents the clinicians with difficulties regarding which patients are at risk for infective endocarditis (IE). The HANDOC score was developed to identify patients with NBHS bacteraemia who are at low risk of IE. This study was conducted to validate HANDOC in an external cohort.

Methods: Patients with NBHS in blood cultures between March and September 2016 in a Danish centre were included as part of an on-going study. Patient characteristics were collected to classify bacteria according to Dukés criteria and the components of the HANDOC score were collected retrospectively from the patients' medical records.

Results: 68 patients were included in the cohort, of which 16 fulfilled Dukés criteria for IE. All patients with IE (16 of 16) had a HANDOC score above the predefined cut-off. Cases of IE were found in patients with. *Streptococcus mitis*, *Streptococcus bovis*, *Streptococcus mutans*, *Streptococcus anginosus*, and *Streptococcus sanguinis* group streptococci. The HANDOC score thus had a sensitivity of 100% and a specificity of 62% in this cohort.

Conclusions: HANDOC has a sensitivity of 100% and a relatively high specificity (62%) also in a prospectively enrolled cohort of patients from another country than its origin. This indicates that HANDOC can be implemented in clinical practice to identify patients with a low risk of IE in whom echocardiography can be omitted.

Table 1. Components of the HANDOC-score [6].

Variable	Components of score	Points given or subtracted
Heart murmur or valvular disease		1
Aetiology	*S. bovis* group	1
	S. mutans group	1
	S. sanguinis group	1
	S. anginosus group	−1
	S. mitis group	0
	S. salivarius group	0
Number of positive blood cultures ≥ 2		1
Duration of symptoms ≥ 7 days		1
Only one species in blood cultures		1
Community acquired infection		1

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association

HANDOC: A Handy Score to Determine the Need for Echocardiography in Non-β-Hemolytic Streptococcal Bacteremia

Background. Non-β-hemolytic streptococci (NBHS) can cause infective endocarditis (IE). Echocardiography is used to diagnose IE, but it is not known which patients with NBHS bacteremia should undergo echocardiography.

Method. Medical records of patients with NBHS bacteremia in southern Sweden from 2012 to 2014 were studied retrospectively. The patients were divided into 2 cohorts. In the first, correlations between the reported data and IE were studied. These variables were used to construct the HANDOC score, which was then validated in the second cohort.

Results. Three hundred thirty-nine patients with NBHS bacteremia were included in the first cohort, of whom 26 fulfilled the criteria for IE. Several factors differed significantly between the patients with IE and those without. Among these variables, the presence of Heart murmur or valve disease; Aetiology with the groups of *Streptococcus mutans*, *Streptococcus bovis*, *Streptococcus sanguinis*, or *Streptococcus anginosus*; Number of positive blood cultures ≥2; Duration of symptoms of 7 days or more; Only 1 species growing in blood cultures; and Community-acquired infection were chosen to form the HANDOC score. With a cutoff between 2 and 3 points, HANDOC had a sensitivity of 100% and specificity of 73% in the first cohort. When tested in the validation cohort (n = 399), the sensitivity was 100% and the specificity 76%.

Conclusions. HANDOC can be used in to identify patients with NBHS bacteremia who have a risk of IE so low that echocardiography can be omitted; therefore, its implementation might reduce the use of echocardiography.

Keywords. endocarditis; streptococcus; bacteremia; echocardiography; prognostic score.

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ORIGINAL ARTICLE

Epidemiology, bacteriology, and clinical characteristics of HACEK bacteremia and endocarditis: a population-based retrospective study

Abstract

The objective was to describe the epidemiology, bacteriology, clinical presentation, risk factors for endocarditis (IE), diagnostic workup, and outcome of patients with bacteremia caused by the non-*influenzae Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella* genera (HACEK). A retrospective population-based cohort of patients with bacteremia collected from 2012 to 2017 was identified. Clinical data from identified patients were collected from medical records to classify patients, calculate incidences, analyze risk factors of IE, and describe the management and outcome of the cohort. A total of 118 episodes of HACEK bacteremia were identified, of which 27 were definite IE. The incidence of HACEK bacteremia was 5.2 and of HACEK IE 1.2 episodes per 1,000,000 inhabitants per year. Other focal infections were identified in 55 of 118 of the episodes, most commonly within the abdomen (26 episodes). The propensity to cause IE ranged from 62 in *Aggregatibacter actinomycetemcomitans* to 6% in *Eikenella*. Risk factors for IE were cardiac implantable electronical device, predisposing cardiac conditions, community acquisition, long duration of symptoms, multiple positive blood cultures, fever, heart murmur, embolization, and unknown origin of infection. The scoring system DENOVA developed to predict IE in bacteremia with *Enterococcus faecalis* also had a high sensitivity and specificity for predicting IE in HACEK bacteremia. The 30-day mortality was 4% in IE and 15% in non-IE bacteremia, and only one case of relapse was found. IE is common in bacteremia with *Aggregatibacter*, *Cardiobacterium*, and *Kingella* but relatively rare in *Haemophilus* and *Eikenella*. Treatment failures are very rare, and DENOVA can be used to evaluate the need for transesophageal echocardiography.

Scoring system	Sensitivity (%)	Specificity (%)	PPV* (%)	NNS*	NPV* (%)
NOVA	100	23	28	3.6	100
DENOVA	93	79	57	1.8	98
HANDOC	96	49	36	2.8	99

*Positive predicted value (PPV), numbers needed to screen (NNS), and negative predictive value (NPV). The cutoff values set in the corresponding reports were used, NOVA ≥ 4, DENOVA ≥ 3, and HANDOC ≥ 3 [2, 3, 5]

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MDPI

Article

Unreliability of Clinical Prediction Rules to Exclude without Echocardiography Infective Endocarditis in *Staphylococcus aureus* Bacteremia

Abstract: Background: It is unclear whether the use of clinical prediction rules is sufficient to rule out infective endocarditis (IE) in patients with *Staphylococcus aureus* bacteremia (SAB) without an echocardiogram evaluation, either transthoracic (TTE) and/or transesophageal (TEE). Our primary purpose was to test the usefulness of PREDICT, POSITIVE, and VIRSTA scores to rule out IE without echocardiography. Our secondary purpose was to evaluate whether not performing an echocardiogram evaluation is associated with higher mortality. Methods: We conducted a unicentric retrospective cohort including all patients with a first SAB episode from January 2015 to December 2020. IE was defined according to modified Duke criteria. We predefined threshold cutoff points to consider that IE was ruled out by means of the mentioned scores. To assess 30-day mortality, we used a multivariable regression model considering performing an echocardiogram as covariate. Results: Out of 404 patients, IE was diagnosed in 50 (12.4%). Prevalence of IE within patients with negative PREDICT, POSITIVE, and VIRSTA scores was: 3.6% (95% CI 0.1–6.9%), 4.9% (95% CI 2.2–7.7%), and 2.2% (95% CI 0.2–4.3%), respectively. Patients with negative VIRSTA and negative TTE had an IE prevalence of 0.9% (95% CI 0–2.8%). Performing an echocardiogram was independently associated with lower 30-day mortality (OR 0.24 95% CI 0.10–0.54, $p = 0.001$). Conclusion: PREDICT and POSITIVE scores were not sufficient to rule out IE without TEE. In patients with negative VIRSTA score, it was doubtful if IE could be discarded with a negative TTE. Not performing an echocardiogram was associated with worse outcomes, which might be related to presence of occult IE. Further studies are needed to assess the usefulness of clinical prediction rules in avoiding echocardiographic evaluation in SAB patients.

	Cut-Off	Sens.	Spec.	PPV	NPV	PLR	NLR	AUC
PREDICT (5-day model)	>1 point	90%	37.1%	16.7%	96.4%	1.43	0.27	0.70
POSITIVE	>4 points	76%	65.5%	23.6%	95.1%	2.17	0.37	0.78
VIRSTA	>2 points	92.0%	50.8%	20.8%	97.8%	1.84	0.16	0.85

YAPILACAKLAR	ZAMANLAMA
CBC; BK;CRP; Sedim;PRC,BNP	HEMEN
3 set KK	İlk 1 saat içinde (0-30ve 60 dakika)
3 düz ve 1 EDTA tüp Kan örneği	
1. Düz tüp; RF ; ANA ; Wright Agg.	İlk 24 saat
2. Düz tüp; Coxiella burnetti faz I Ig G	72 saatlik KK negatifliği sonrası
3. Düz tüp ve EDTA'lı tüp; Moleküler ve serolojik testler için (-20 derecede)	72 saatlik KK negatifliğinden sonra
EKG	HEMEN
TTE	HEMEN
TEE	Komp. şüphe ise HEMEN; diğer durumlarda ilk 4
Gözdibi muayene	İlk 48 saat
Son 10 gün AB ise; KK zamanı	AB siz geçen 72 saat sonra
Abdominal USG (Ateş düşmeyenlerde ve ek ölçüt için	İlk 5 gün
Modifiye Duke ölçütlerine göre tanı konması	İlk 5 gün
Kardiyak BT; MRI,PET/BT,SPECT/BT	İlk hafta (hasta bazında kompl ve ekstrakardiyak

Teşekkürler…