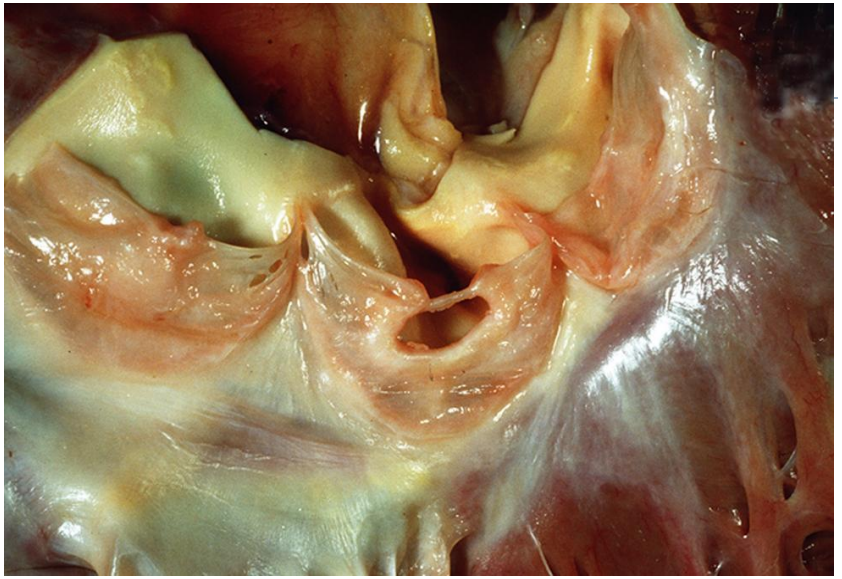
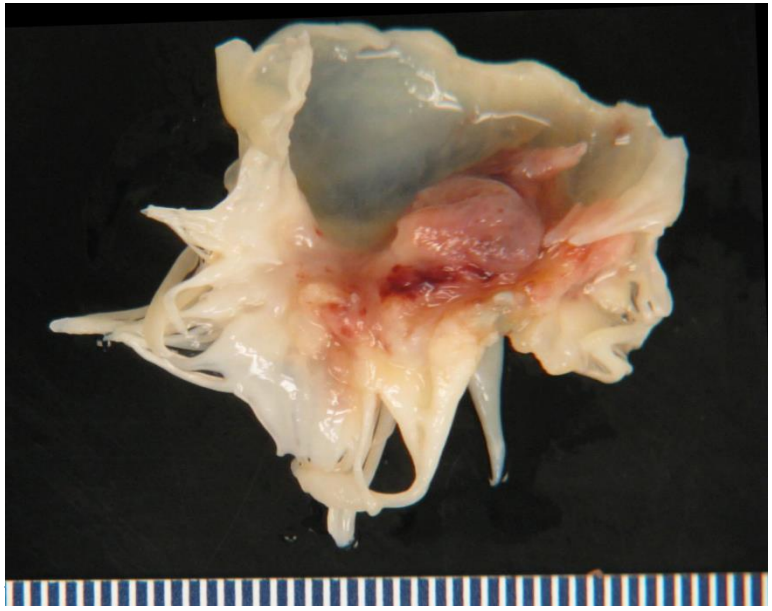
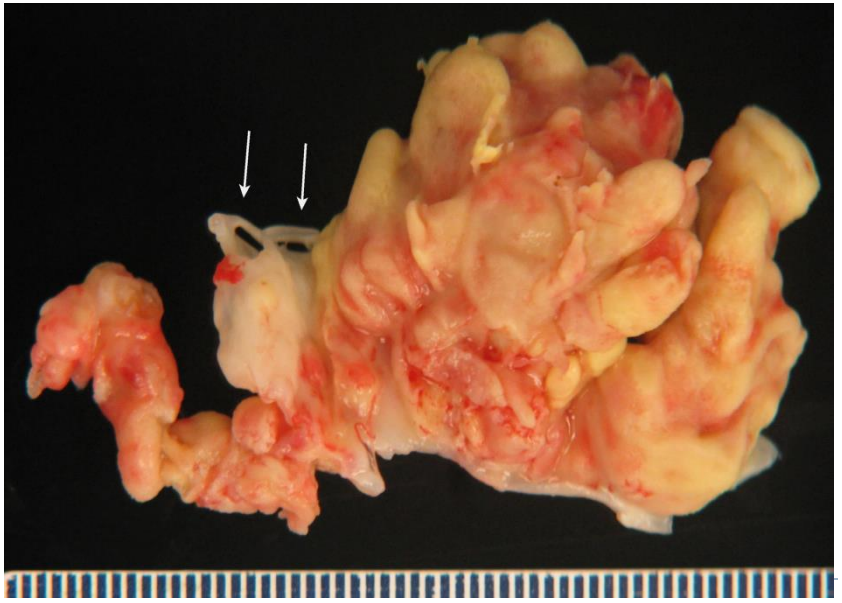
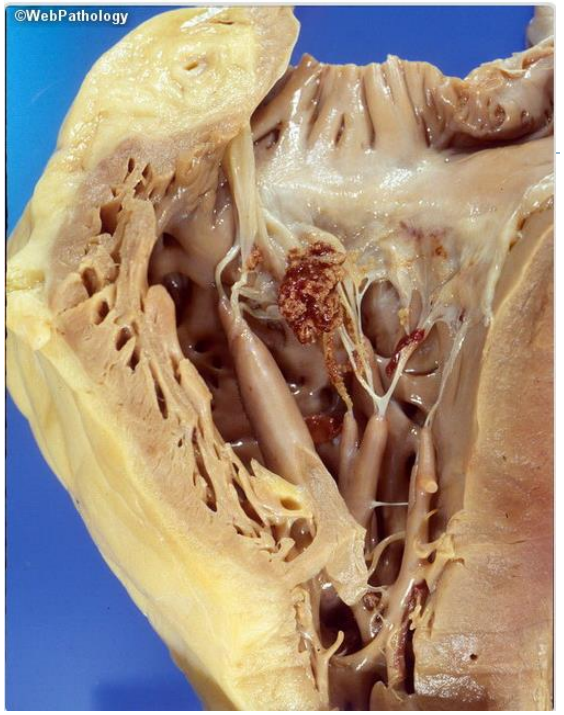
Enfektif Endokardit: Neler Değişiyor?

Dr. Cemal Bulut





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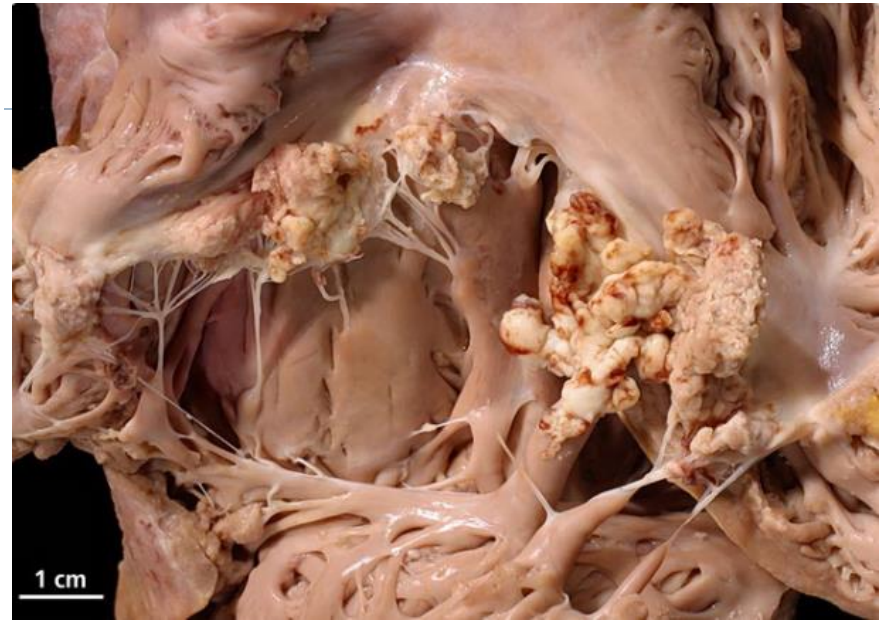
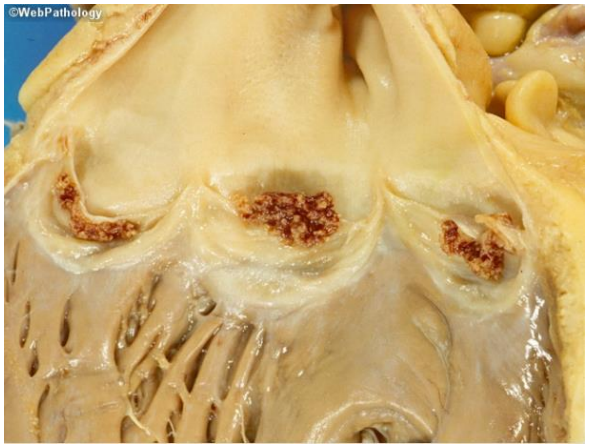

1 cm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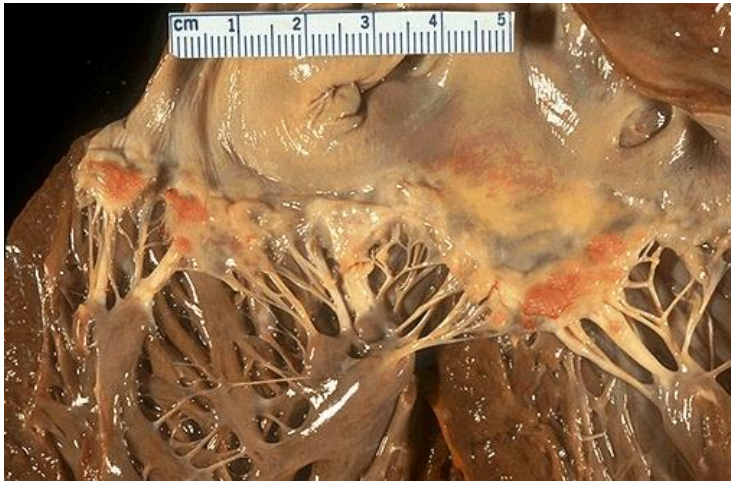
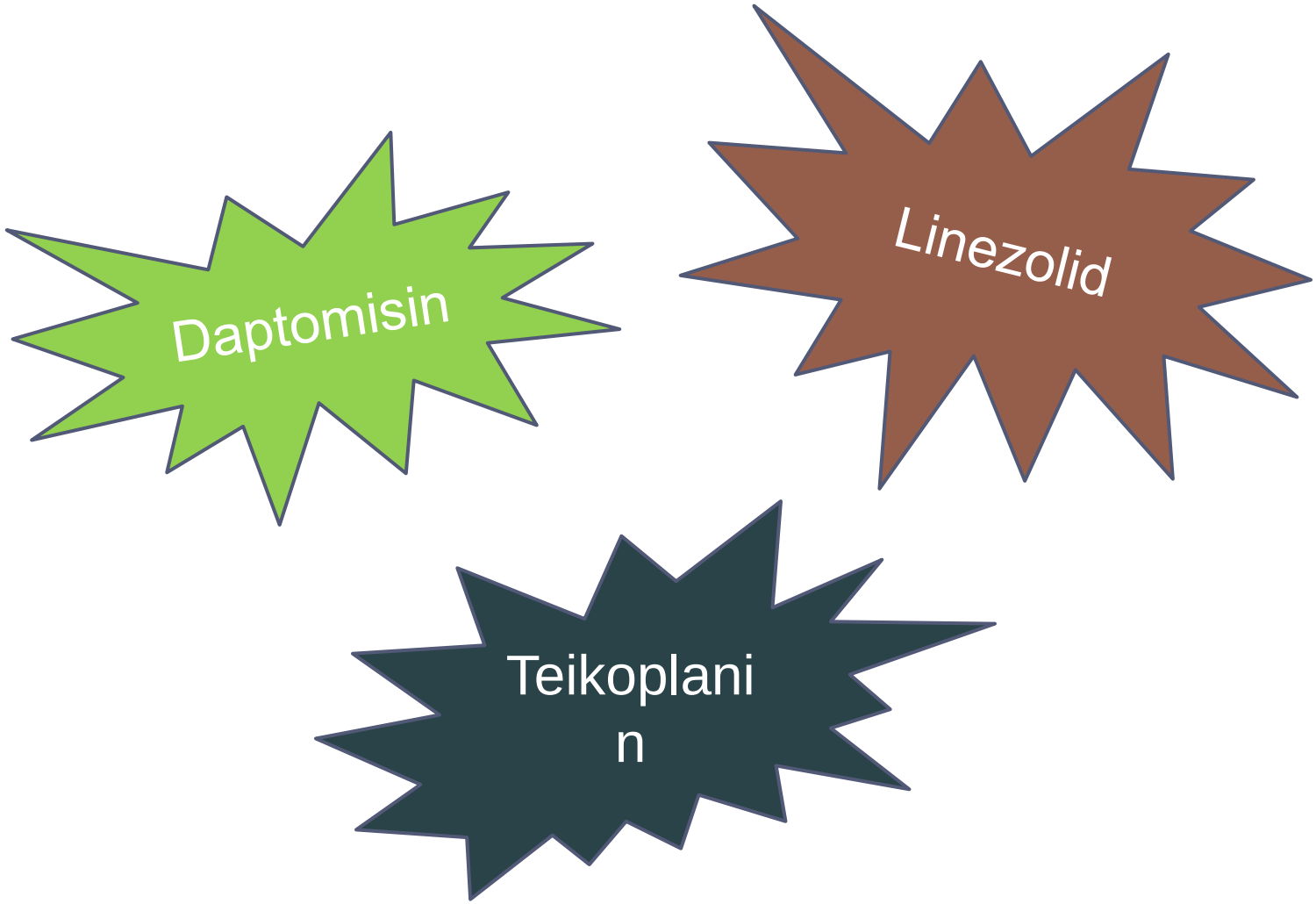
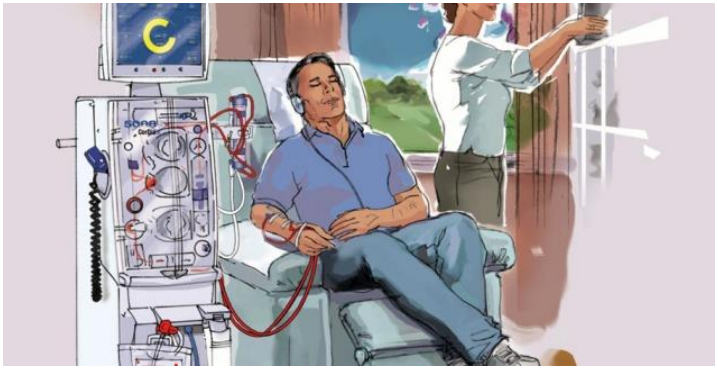

cm 1 2 3 4 5

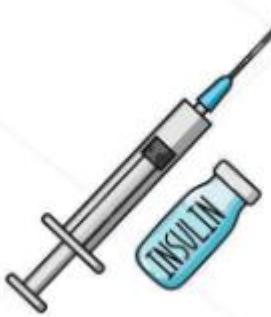
- 1938 sulfonamidlerin kullanımı
- 1944 penisilinlerin kullanımı
- 1956 vankomisin
- 1960'lar penisilinaza dirençli penisilinler

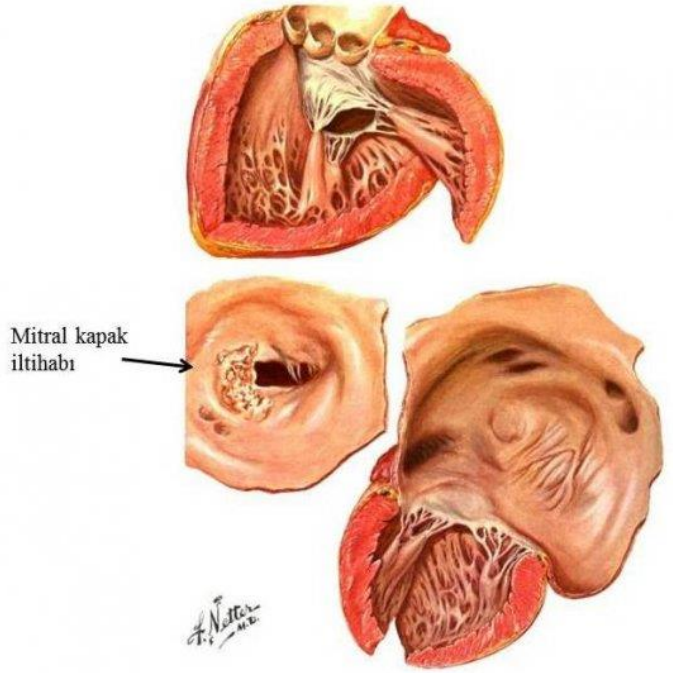
Sinerjistik anti[illegible] kombinasyon!


Daptomisin
Linezolid
Teikoplani
n

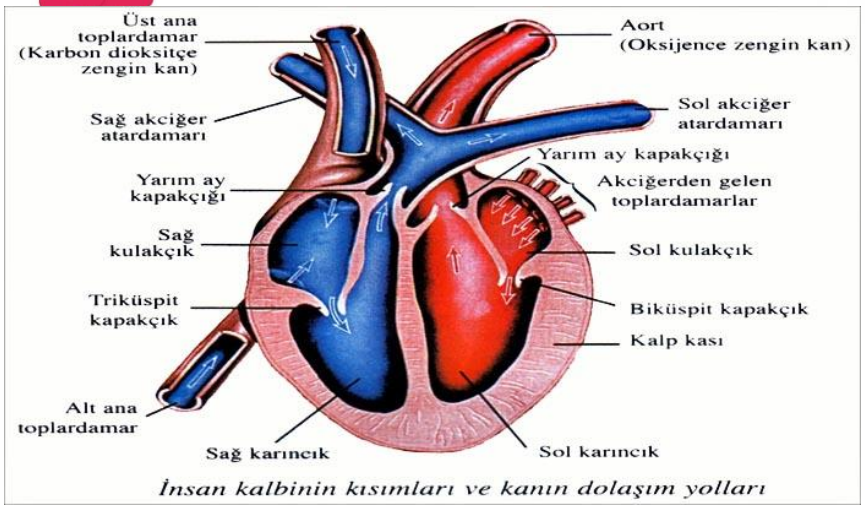
- Hastaların yaş ortalaması daha yüksek
- Sağlık bakım ilişkili endokarditler artıyor
- Etkenler daha agresif patojenler
  - Stafilokoklar
  - Dirençli –enterokoklar
  - Mantarlar
- hemodiyaliz, diabetes mellitus ve intravasküler aletler en sık risk faktörleri
- Eskiden genç hastalar
- Predispoze kardiyak patolojisi olanlar romatizmal kalp hastalıkları, konjenital kalp anomalileri
- Moreover, access to new diagnostic technologies and surgical facilities remains
- diffi cult in developing countries,53 thus aff ecting prognosis of these patients.




INSULIN



Kalp romatizması



İnsan kalbinin kısımları ve kanın dolaşım yolları

- Kan kültürü altın standart
- 3 set kan kültürü
  - Farklı damarlardan,
  - Bir saat arayla
  - Bir aerob, bir anaerob
  - 5 gün inkübasyon

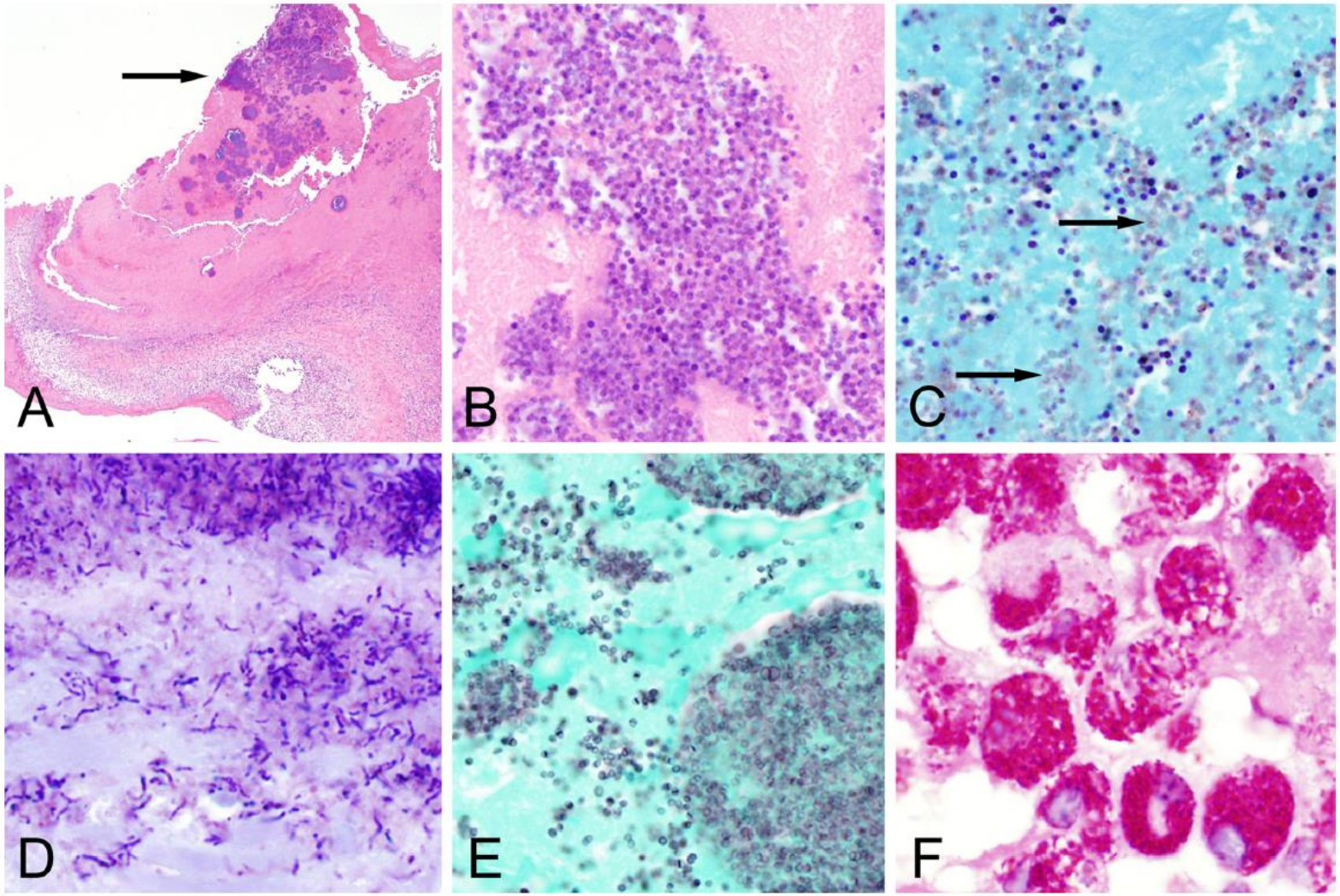
Mikrobiyolojik Tanıda Yenilikler

- Kan kültürü negatif olabilir (%2-40)
  - Antibiyotik kullanımı
  - Yavaş üreyen patojenler
  - Mantarlar
- Serolojik testler
  - *C.burnetii, Bartonella* türleri
- Dokudan PCR ile patojen saptanması

Doku incelemesi

- Histopatoloji inceleme
- Dokudan bakteri izolasyonu
  - Cerrahi müdahale %25-53
- %6-26 pozitiflik
  - Yanlış pozitiflik yüksel
- Moleküler teknikler
  - Organizma spesifik PCR
  - 16 sRNA

Liesman RM, Pritt BS, Maleszewski JJ, Patel R. 2017. Laboratory diagnosis of infective endocarditis. J Clin Microbiol 55:2599–2608.


A
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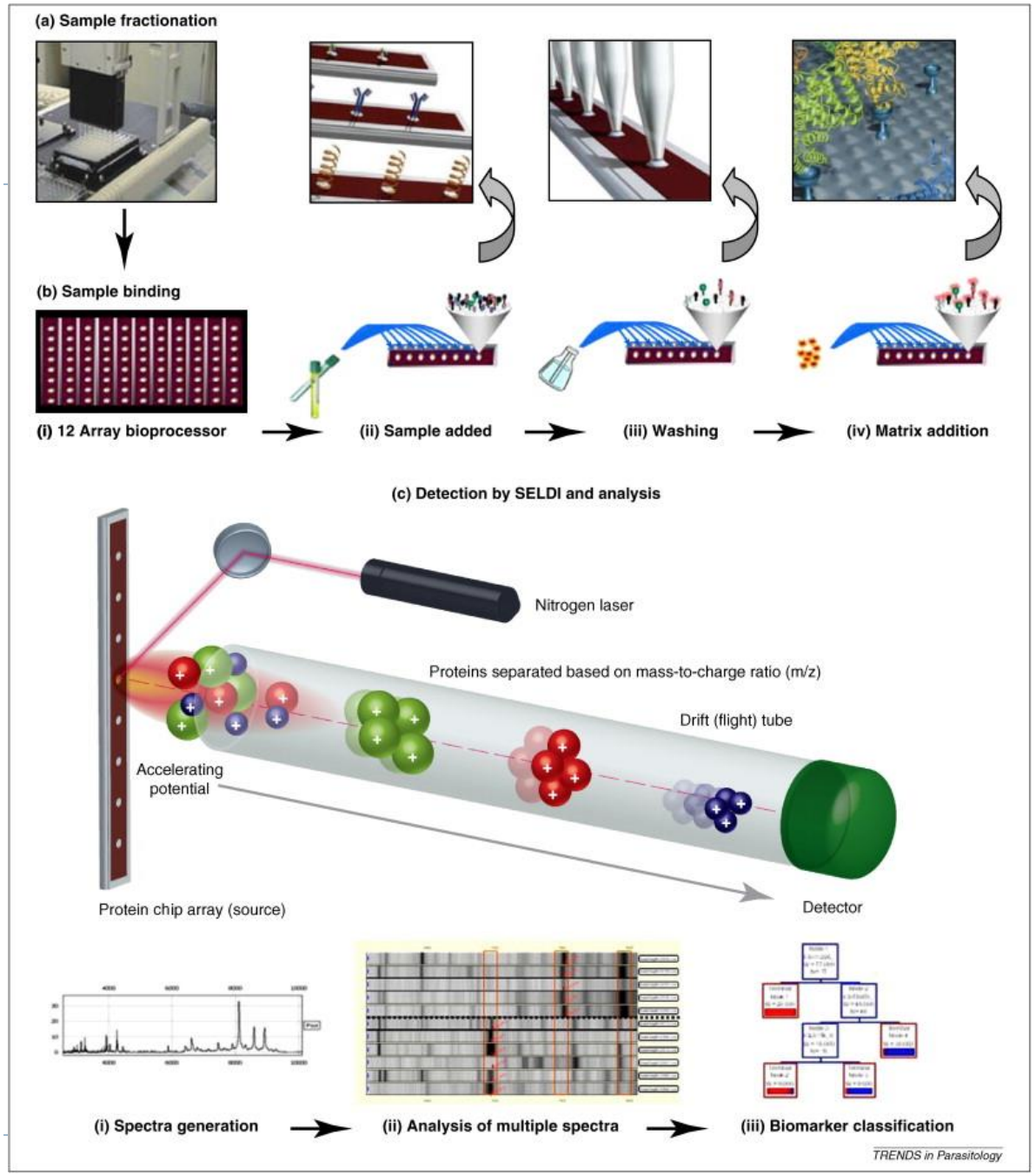
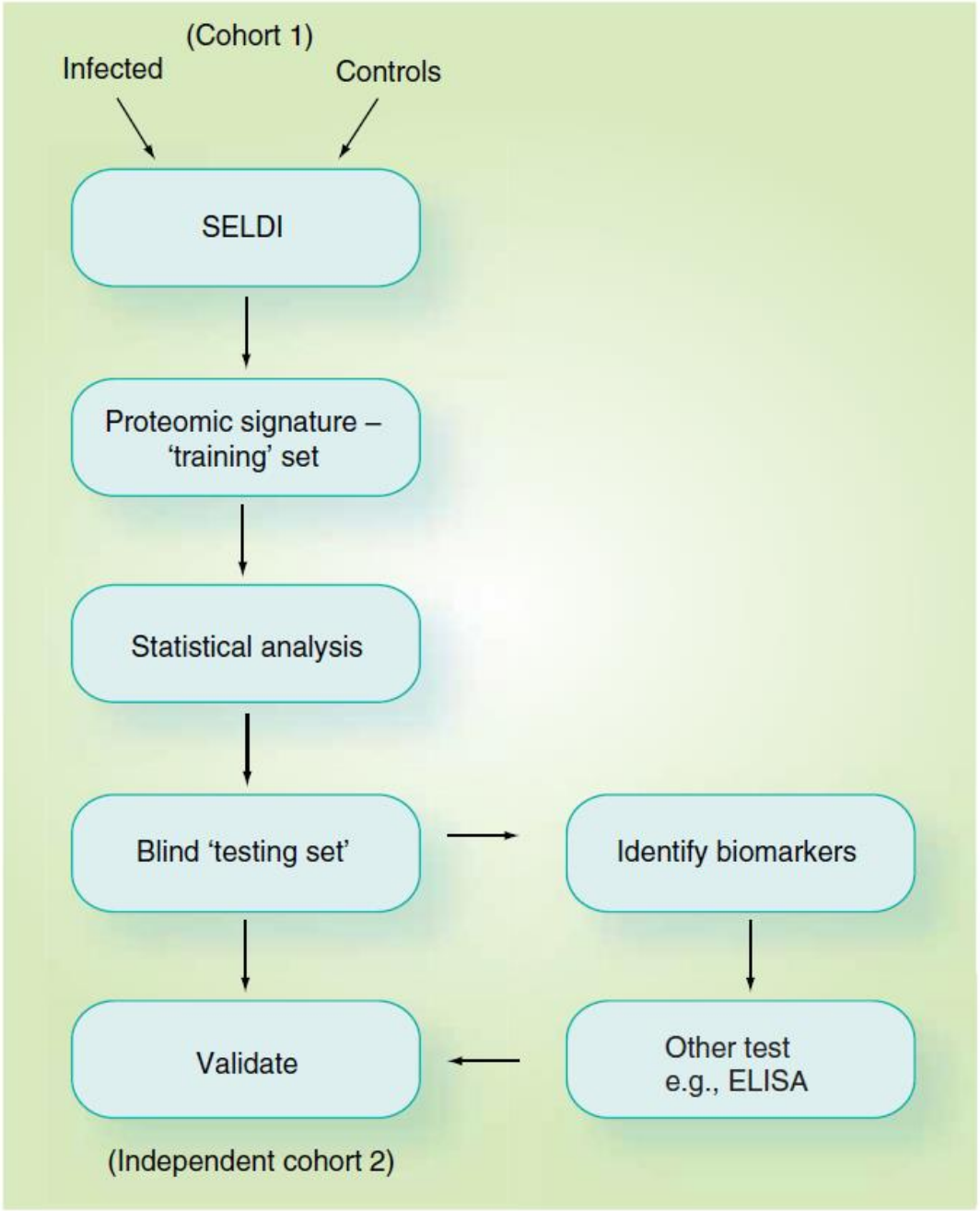
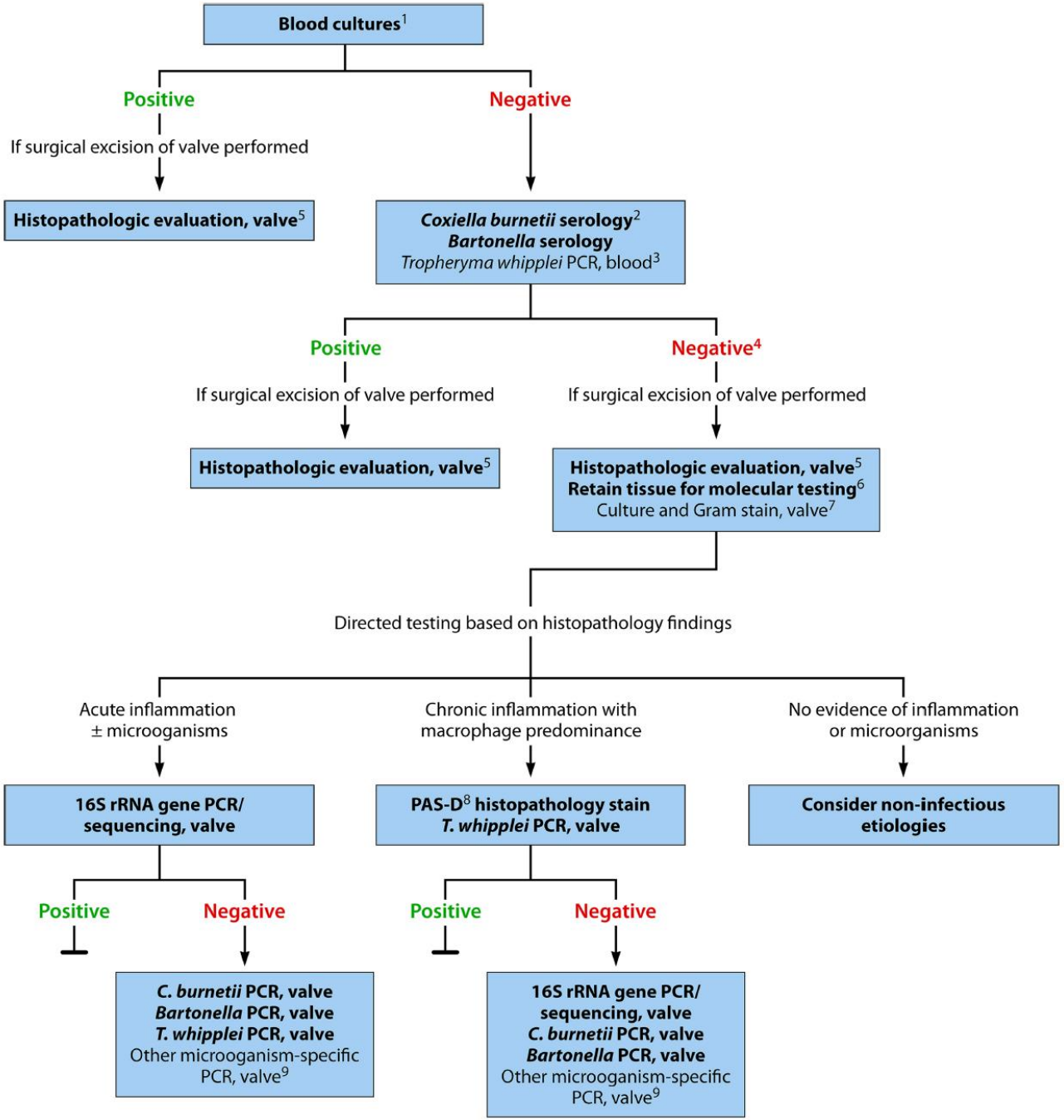
SELDİ-TOF


(a) Sample fractionation
(b) Sample binding
(i) 12 Array bioprocessor
(ii) Sample added
(iii) Washing
(iv) Matrix addition
(c) Detection by SELDI and analysis
Nitrogen laser
Proteins separated based on mass-to-charge ratio (m/z)
Drift (flight) tube
Accelerating potential
Protein chip array (source)
Detector
(i) Spectra generation
(ii) Analysis of multiple spectra
(iii) Biomarker classification
TRENDS in Parasitology

- Serumda özel proteomik imzalar bulunmaktadır
- Etyolojik ajan birden fazla olsa bile bu yapılar değişmemektedir.



Hodgetts A. Biomarkers discovery in infectious diseases usin SELDI. Future Microbiol 2007


Blood cultures[1]
Positive
Negative
If surgical excision of valve performed
Histopathologic evaluation, valve[5]
Coxiella burnetii serology[2]
Bartonella serology
Tropheryma whipplei PCR, blood[3]
Positive
Negative[4]
If surgical excision of valve performed
If surgical excision of valve performed
Histopathologic evaluation, valve[5]
Histopathologic evaluation, valve[5]
Retain tissue for molecular testing[6]
Culture and Gram stain, valve[7]
Directed testing based on histopathology findings
Acute inflammation
± microoganisms
Chronic inflammation with
macrophage predominance
No evidence of inflammation
or microorganisms
16S rRNA gene PCR/
sequencing, valve
PAS-D[8] histopathology stain
T. whipplei PCR, valve
Consider non-infectious
etiologies
Positive
Negative
Positive
Negative
C. burnetii PCR, valve
Bartonella PCR, valve
T. whipplei PCR, valve
Other microoganism-specific
PCR, valve[9]
16S rRNA gene PCR/
sequencing, valve
C. burnetii PCR, valve
Bartonella PCR, valve
Other microoganism-specific
PCR, valve[9]

Görüntüleme Yöntemleri

- TTE
- Trans özefagial ekokardiyografi
- Çok kesitli bilgisayarı tomografi (MDCT)
  - Trombüs, pannus, vejetasyon, paravalvüler kaçak, mikotik anevrizmalar ve apseler
  - Perianüler komplikasyonların saptanmasında faydalı olabilir
- FGD-PET
  - Vejetasyonları saptamada ek katkısı yok
  - Psödoanevrizma ve apselerin tanımlanmasında faydalı

Neth Heart J (2016) 24:96–107
Eur Radiol (2015) 25:2125–2133

- Çok kesitli bilgisayarı tomografi (MDCT)
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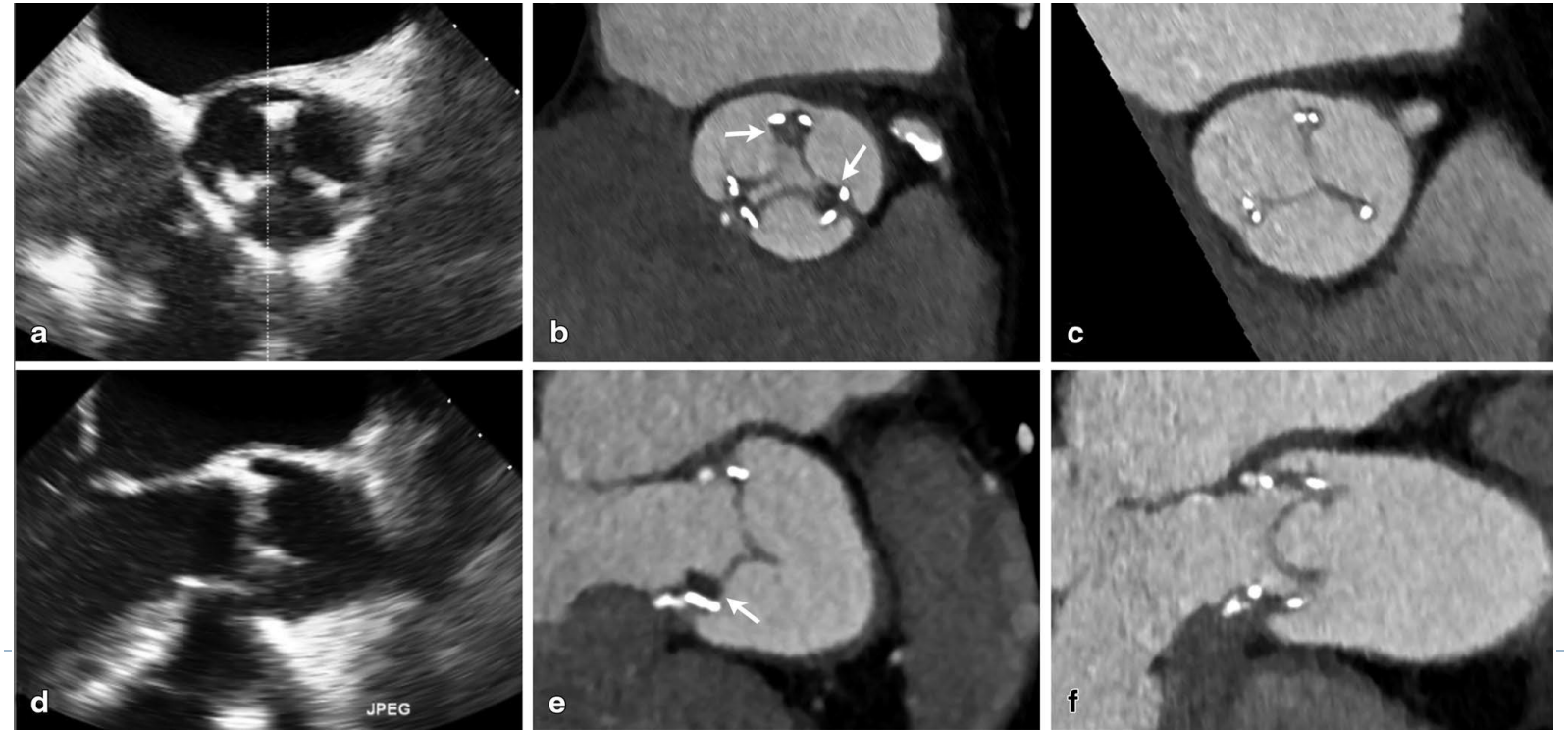
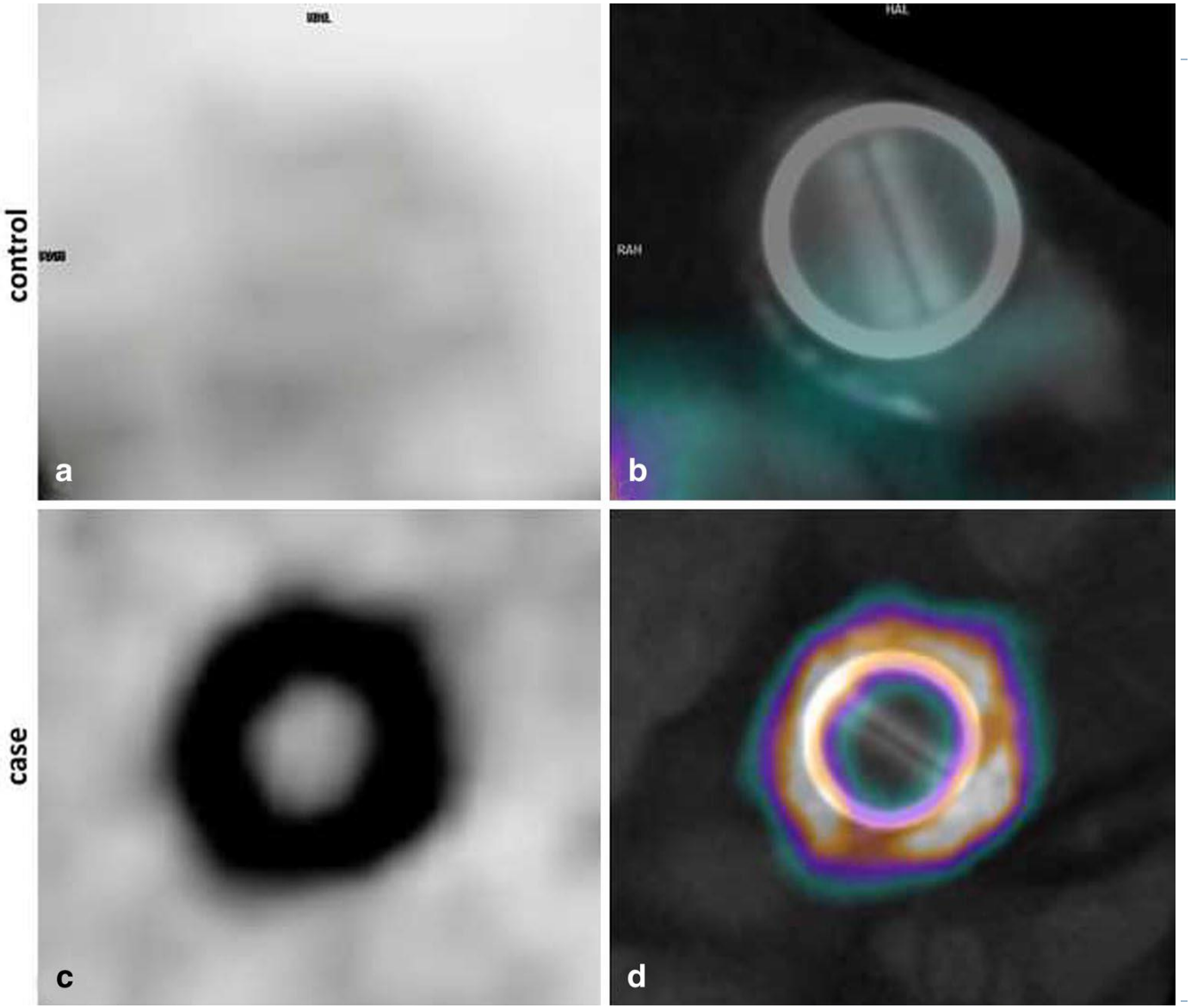
  - Perianüler komplikasyonların saptanmasında faydalı olabilir



FGD-PET

- Anatomik değil metabolik durum hakkında bilgi veriyor
- Enfekte hücrelerde FDG tutulumu daha fazla
- Vejetasyonları saptamada ek katkısı yok
  - Hareketli kapaklar ?
  - Düşük çözünürlük ?
- Psödoanevrizma ve apselerin tanımlanmasında faydalı
- Postop dönemde (<1 yıl) iyileşme ve tamir mekanizmaları yanlış pozitiflik sebebi olabilir
- Ektrakardiyak yada metastatik enfeksiyon odaklarının saptanmasında faydalı


control
case
a
b
c
d

- Kültür negatif
- EKO bulgusu olmayan
- Endokardit şüpheli hastalarda önerilen

- MDCT+ FDG-PET

Lökosit taraması (SPECT)

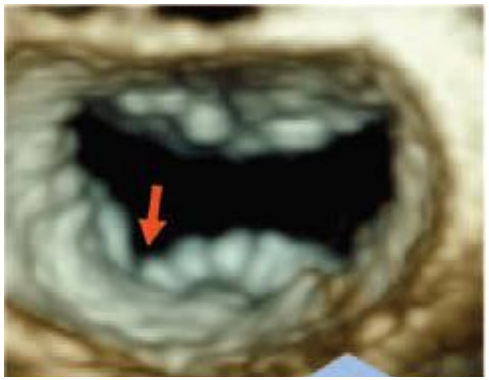
- 3D nükleer görüntüleme yöntemi
- Radyoaktif işaretli lökositler kullanılır
- Peri valvüler enfeksiyonları göstermede faydalı
- Zaman alıcı
- Postop dönemde kullanılabilir

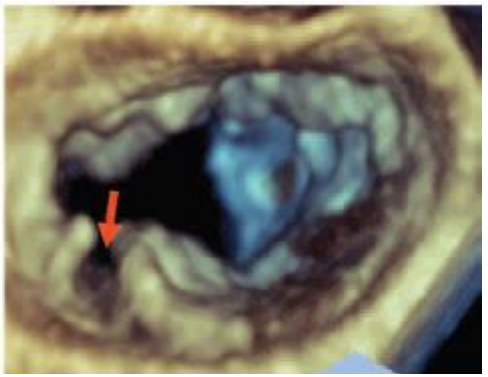
Kardiyak MRI

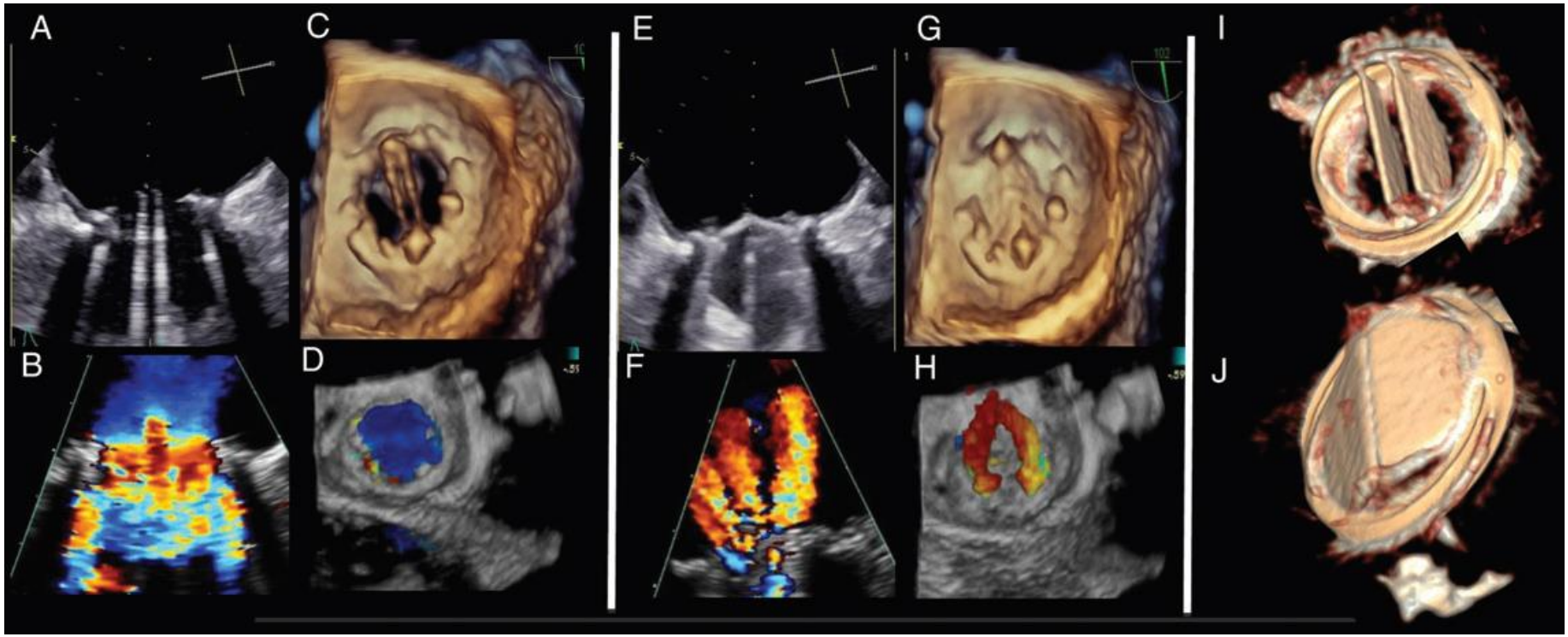
- Artefaktlar önemli bir sorun
- Aort paotlojileri de varsa daha faydalı
- Kalbin volumetrik değerlendirmesinde faydalı
- Akım paternlerinin gösterilmesinde faydalı

Üç boyutlu TEE

- Anatomi, fonksiyon ve hareketleri hakkında daha kesin bilgi ve kantitatif analize imkan sağlar
- Trombüs, pannus ve kapaklarda ayrılma
- Özellikle mitral ve aort kapaklarda faydalı
- Anteriyor kardiyak yapıları göstermede yetersiz kalabilir, aritmi?






A
C
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G
I
B
D
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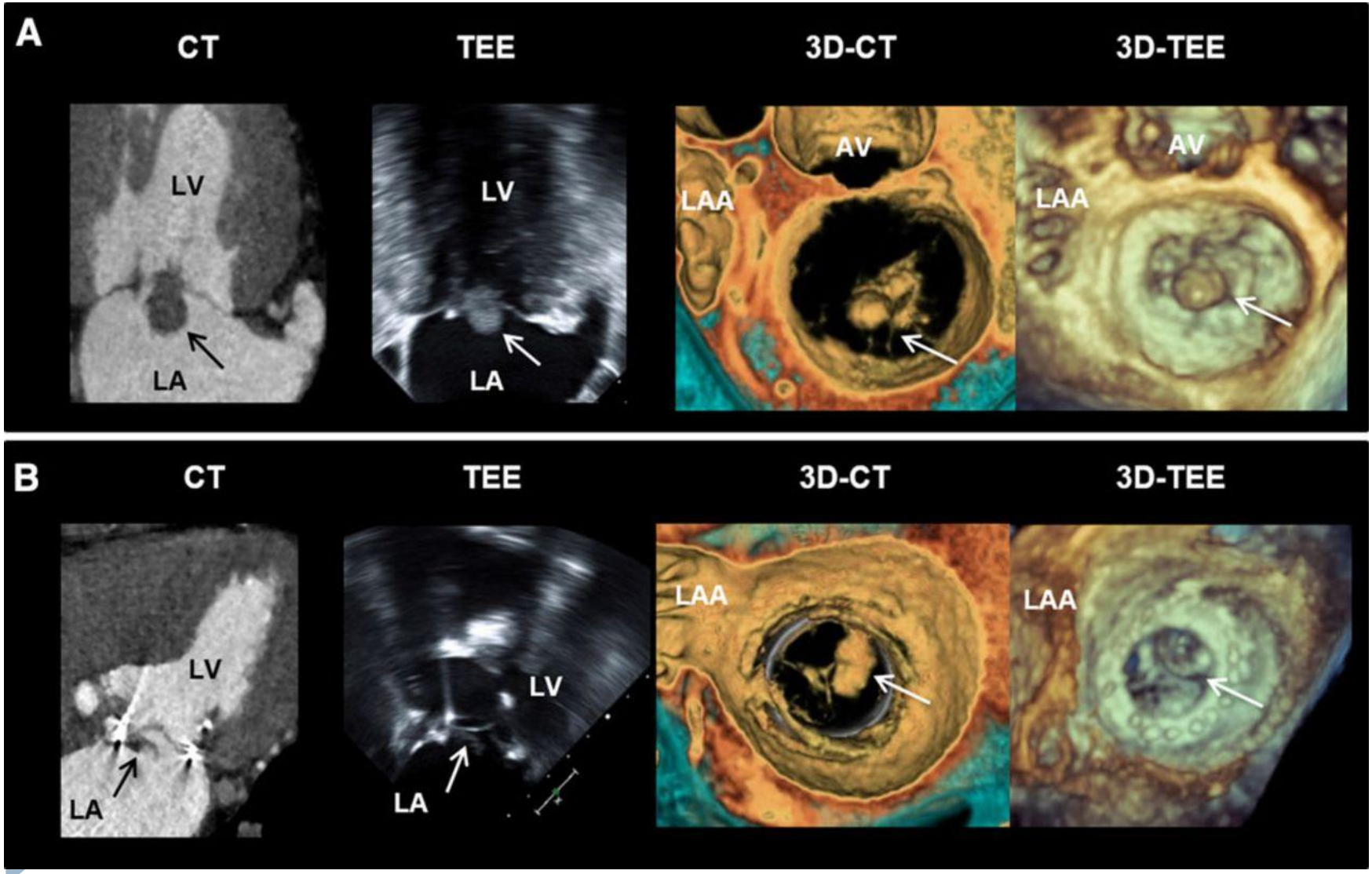
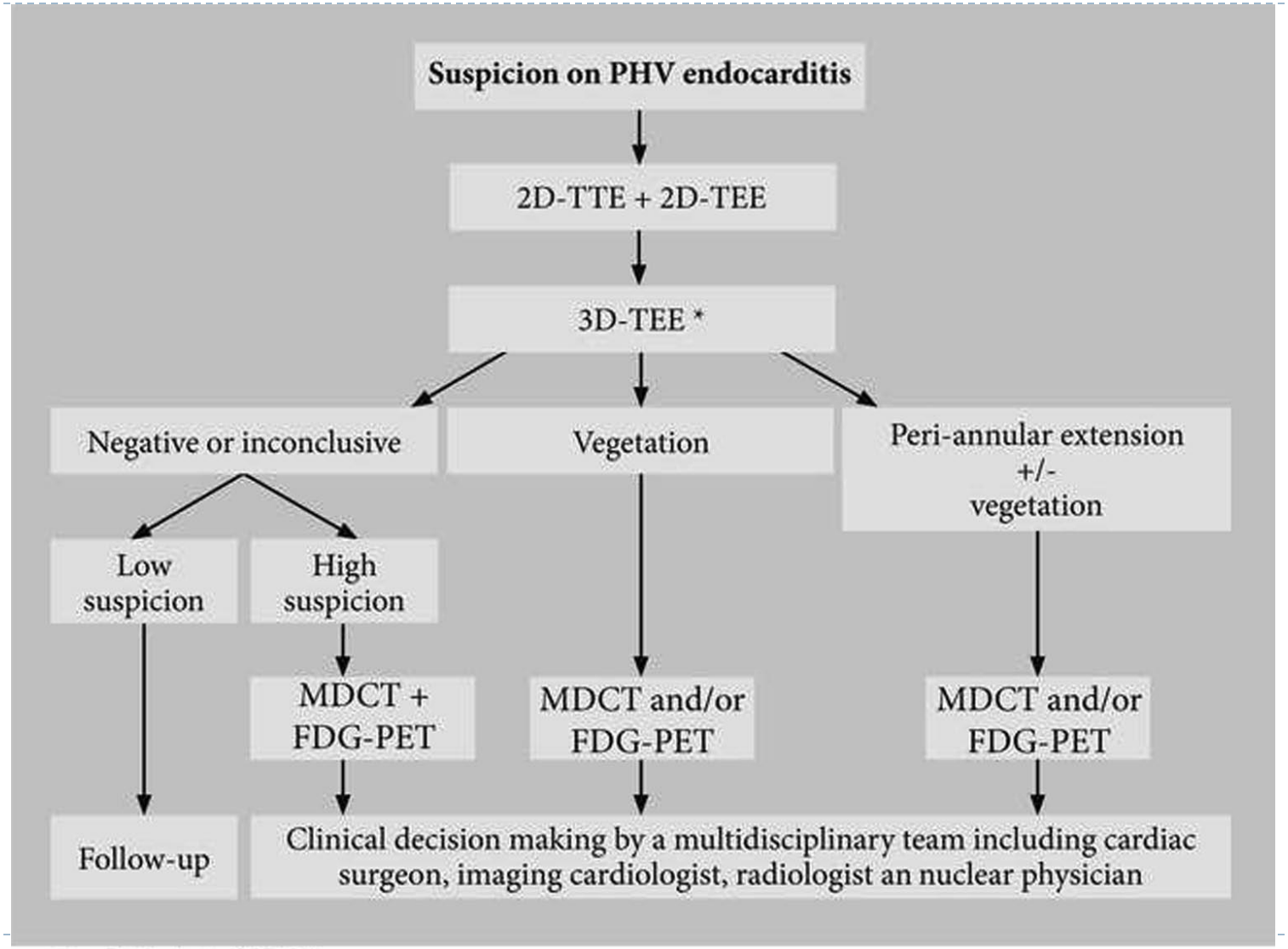
H
J


A
CT
TEE
3D-CT
3D-TEE
LV
LA
LV
LA
AV
LAA
AV
LAA
B
CT
TEE
3D-CT
3D-TEE
LV
LA
LV
LA
LAA
LAA



*If available during 2D-TEE.

Neth Heart J (2016) 24:96–107

Table 1 Observational studies of oral antibiotic therapy for infective endocarditis

Reference	Cases	Design	Case definition	Microbiology	Assessment of antibiotic susceptibility	Therapy	Cure
Colli et al, Italy [9]	12 NVIE and 2 PVIE requiring acute valve replacement(all left-sided)	Retrospective. Mean follow-up was 20.8 ± 7 months	By Duke criteria	MRSA (60%) *S. viridans* (30%) *Enterococcus sp.* (10%)	Yes	IV vancomycin for 5.3 ± 3.4 days followed by oral linezolid for 3 weeks	100%
Dworkin et al, USA [10]	13 IVDUs with NVIE (all right-sided with no systemic metastasis)	Prospective. 4-week follow-up	≥2 positive blood cultures AND any of the following: Vegetations on echocardiogram (definite – 3 cases) OR pulmonary infiltrates/ effusion or tricuspid insufficiency murmur (probable – 6 cases) OR no other identifiable source for the infection (possible – 1 case)	*S. aureus* (100%)	Yes	IV ciprofloxacin and oral rifampin for 1 week followed by oral ciprofloxacin and oral rifampin for 3 weeks	77%
Chetty et al, South Africa [11]	15 NVIE (right-sided vs. left-sided not specified, all cases were considered uncomplicated)	Prospective. 3-year follow-up	Characteristics clinical features AND any of the following: Positive blood cultures OR vegetations on echocardiogram	*Streptococcus sp.* (60%) Culture negative (40%)	Yes	High dose oral amoxycillin for 6 weeks (47% also received probenecid)	87%
Pinchas et al, Israel [12]	11 NVIE (all left-sided, considered uncomplicated)	Prospective. Follow-up varied from 3 months to 12 years	Fever AND pre-existing valvular heart disease AND multiple positive blood cultures	*S. viridans* (100%)	Yes	High dose oral ampicillin for 6 weeks with probenecid for the first 4 weeks. IM streptomycin for the first 2 weeks	90%
Phillips et al, UK [13]	13 NVIE (right-sided vs. left-sided not specified) – all children	Retrospective. Follow-up varied from 1-15 years	Pre-existing valvular disease AND characteristic clinical features AND positive blood cultures	*S, viridans* (62%) *Staphylococcus sp.* (23%) Other streptococci or *Enterococcus sp.* (15%)	Yes	IV therapy for < 2 weeks (92% ≤3 days) followed by oral penicillin V, ampicillin, cloxacillin, flucloxacillin or erythromycin for 6-8 weeks	100%
Gray et al, UK [14]	13 NVIE (right-sided vs. left-sided not specified)	Retrospective. 3-month follow-up	Not specified	*S. viridans.* (62%) *E. faecalis* (1%) Culture negative (37%)	Yes	Oral ampicillin or propicillin (with or without probenecid) for 6 weeks	92%

Oral tedavi

Table 1 Observational studies of oral antibiotic therapy for infective endocarditis *(Continued)*

Campeau et al, Canada [15]	10 NVIE (right-sided vs. left-sided not specified)	Retrospective. Follow-up varied from 6-30 months	Pre-existing valvular disease AND Characteristic clinical features AND ≥2 positive blood cultures	*S. viridans* (60%) *E. faecalis* (30%) Anaerobic bacteria (10%)	Yes	Oral phenithicillin for 4-6 weeks (IM streptomycin for the first 2 weeks in 6 cases, concomitant probenecid in 2 cases)	80%
Friedberg et al, USA [16]	11 NVIE (right-sided vs. left-sided not specified)	Retrospective. Follow-up not specified	Pre-existing rheumatic valvular disease AND Unexplained fever for ≥2½ weeks	*S. viridans* (55%) *E. faecalis* (18%) Culture negative (27%)	Yes	Oral Aureomycin for 5-8 weeks	36%
Schein et al, USA [17]	81 NVIE (right-side vs. left-sided not specified)	Retrospective. Follow-up varied from 2-8 years	Not specified	*Streptococcus sp.* (94%) *S. aureus* (1%) *Enterococcus sp.* (1%) *H. influenza* (4%)	Not specified	Oral sulfonamides (sulfanilamide, sulfapyridine, sulfathiazole or sulfadiazine) for 10 days-14 weeks	10%

NVIE denotes cases of native valve infective endocarditis. PVIE denotes cases of prosthetic valve infective endocarditis. IV denotes intravenous. IVDUs denotes intravenous drug users. MSSA denotes methicillin-sensitive *S. aureus*. MRSA denotes methicillin-resistant *S. aureus*. CoNS denotes coagulase-negative staphylococcus. GNB denotes gram-negative bacilli. Unless specified otherwise, all cohorts were primarily of adult patients. All reports reported follow-up ≥3 months.

BMC Infectious Diseases 2014, 14:140

Gender	Age	Microbial pathogen	Valve(s)/ material involved	Oral medication	Treatment duration (parental/peroral)	Surgery	Outcome
Male	43	β-Hemolytic streptococci group G	Prosthetic biological mitral valve	Fusidic acid and rifampicin	13 d/28 d	No	Success
Male	75	*Staphylococcus epidermidis*	Aortic and mitral valve	Linezolid and moxifloxacin	17 d/30 d	Yes, prosthetic biological mitral and aortic valve	Success
Male	62	*S aureus*	Mitral valve	Fusidic acid and linezolid	17 d/24 d	No	Success
Male	56	*S aureus*	Prosthetic biological mitral valve	Fusidic acid and rifampicin	29 d/15 d	No	Success
Female	74	*Streptococcus sanguinis*	Mitral valve	Linezolid and moxifloxacin	15 d/17 d	No	Success
Male	54	*S aureus*	Aortic valve	Rifampicine and linezolid	29 d/15 d	Yes, prosthetic biological aortic valve	Success
Male	78	*Enterococcus faecalis*	Prosthetic biological mitral valve	Linezolid	20 d/10 d	No	Success
Male	67	Coagulase-negative *Staphylococcus*	Pacemaker electrode	Rifampicin and linezolid	36 d/16 d	Yes, removal of infected electrode	Success
Female	65	β-Hemolytic streptococci group C	Aortic valve	Rifampicin and linezolid	24 d/6 d	Yes, prosthetic biological aortic valve	Success
Female	44	*Staphylococcus lugdunesis*	Pacemaker electrode	Penicillin and linezolid	35 d/14 d	Yes, removal of infected electrode	Success
Male	67	*Salmonella*	Aortic valve	Ciprofloxacin	42 d/21 d	Yes, prosthetic biological aortic valve	Success
Male	74	Coagulase-negative *Staphylococcus*	Aortic and mitral valve	Penicillin	40 d/5 d	Yes, prosthetic biological aortic and mitral valve	Success

Am Heart J 2013;165:116-22.)

Dalbavansin tedavisi

- Başlangıç tedavileri farklı
- Kan kültürü negatifleştikten sonra dalbavansine geçilmiş
- İlk gün 1 gr, sonra haftada bir ya da iki kez 500 mg

Table 1

Duration of DALB Therapy	Pat No.	Types of IE	Pathogen	Duration of therapy prior DALB (weeks)	Reason to change of therapy to DALB	Failure of DALB treatment	Side effects	weekly regime (once/two)
1 week (n=1)	1	Prosthetic valve	*E. faecalis*	VAN (3)	Not documented	Death	No	Once
2 weeks (n=3)	2	Native valve	*S. aureus*	FLUOX + FOSF (2) CEFAZ + DAP (4)	Poor venous access	No	No	Once
	3	Native valve	*S. aureus*	FLUOX+DAP (5)	OPAT	No	No	Two
	4	Native valve	*S. aureus*	CEFU+DAP (4)	Poor venous access	No	No	Two
4 weeks (n=5)	5	Native valve	*E. faecalis*	CEFT+AMP (2)	OPAT	No	No	Once
	6	Prosthetic valve	*Streptococcus equi*	PEN G (1)	OPAT	No	Nausea	Two
	7	CDE	*S. epidermidis*	CEFAZ+FOSF (4)	OPAT	No	No	Two
	8	CDE	*S. epidermidis*	DAP (4)	OPAT	No	No	Two
	9	Native valve	*Streptococcus mitis*	CEFT+GEN (2)	OPAT	No	No	Two
6 weeks (n=10)	10	Prosthetic valve	*S. aureus*	FLUOX+RIF (2)	OPAT*	No	No	Once
	11	Native valve	*S. hominis*	FLUOX+DAP (2)	OPAT	No	No	Once
	12	CDE	*Streptococcus* spp. *S. epidermidis*	DAP** VAN (2)	OPAT	No	No	Once
	13	Prosthetic valve	*Streptococcus equinus*	PEN G (1)	OPAT	No	No	Two
	14	Suspected prosthetic valve	*Streptococcus sanguinis*	No	OPAT	No	RCI	Two
	15	Native valve	*E. faecalis*	CEFT+AMP (1)	OPAT	No	No	Two
	16	Native valve	*Aerococcus urinae*	PEN G (2)	OPAT	No	No	Two
	17	Native valve	*S. aureus*	FLUOX+DAP(1)	Poor venous access	No	No	Two
	18	Native valve	*S. aureus*	FLUOX+FOSF (1)	OPAT	No	No	Two
	19	Native valve	*Streptococcus sanguinis* *S. hominis*	FLUOX+AMP (1)	OPAT	No	No	Two
> 6 week (n=8)	20	Native valve	*E. faecalis*	No	OPAT	No	No	Once
	21	Native valve	*Streptococcus sanguinis*	VAN (1) DAP (1)	OPAT	No	No	Once
	22	CDE	*S. epidermidis*	No	OPAT	No	No	Once
	23	CDE	*S. aureus*	FLUOX (1)	OPAT	Resistance	No	Once
	24	Native valve	*S. aureus*	CEFT (1) DAP (1)	OPAT	No	No	Two
	25	Prosthetic valve	*S. aureus*	FLUOX+RIF (1)	OPAT	No	No	Two
	26	Prosthetic valve	*Streptococcus sanguinis*	PEN G (1)	OPAT	No	No	Two
	27	Native valve IE	*S. caprae*	CEFAZ (1)	OPAT	No	No	Two

AMP (ampicillin); CEFAZ (cefazoline); CEFT (ceftriaxone); CEFU (cefuroxime); DALB (dalbavancin); DAP (daptomycin); FLUOX (flucloxacillin), FOSF (fosfomycin); GEN (gentamycin); PEN G (penicillin G), RIF (rifampicin), VAN (vancomycin), CDE (cardiac-device related endocarditis), IE (infective endocarditis), RCI (Reversible creatinine increase),*S. aureus* (*Staphylococcus aureus*), *S. epidermidis* (*Staphylococcus epidermidis*), *E.faecalis* (*Enterococcus faecalis*)

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A comparison of different antibiotic regimens for the treatment of infective endocarditis (Review)

Martí-Carvajal AJ, Dayer M, Conterno LO, Gonzalez Garay AG, Martí-Amarista CE, Simancas-Racines D

Authors' conclusions

Limited and very low quality evidence suggested that there were no conclusive differences between antibiotic regimens in terms of cure rates or other relevant clinical outcomes. However, because of the very low quality evidence, this needs confirmation. The conclusion of this Cochrane review was based on randomised controlled trials with high risk of bias. Accordingly, current evidence does not support or reject any regimen of antibiotic therapy for treatment of infective endocarditis.

- Teşekkürler