Protez enfeksiyonlarında mikrobiyolojik tanı

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Laboratory Diagnosis of Prosthetic Joint Infection, Part I*

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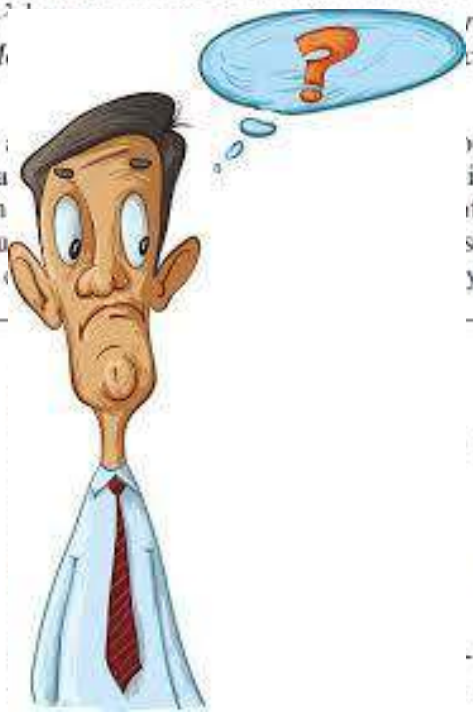
Abstract

Prosthetic joint infection (PJI), although [illegible] as the number patients undergoing arthropla[illegible] outcome. Although multiple tests have been [illegible] remains a challenge. Here, we review the cu[illegible] part article, components of the preoperative [illegible]

[illegible]n arthroplasty, is reported more frequently [illegible] is essential for adequate management and [illegible]f PJI from aseptic loosening of the prosthesis [illegible]sed for the diagnosis PJI. In Part I of this two- [illegible]y of the intraoperative evaluation is discussed.

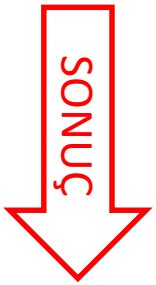


The number of total joint replacements being performed in the United States is rising and is anticipated to continue to increase for at least the next two decades. It has been projected that 576,000 primary hip arthroplasties and 3.48 million primary knee arthroplasties will be performed in the year 2030 (1). Other types of joint replacement are shoulder, which have been increasing parallel to hip and knee arthroplasty (2),

aureus and coagulase-negative *Staphylococcus* species) are the most common organisms associated with PJI, causing about 50% of cases, followed by polymicrobial infection (20%), streptococci (9%), gram-negative bacilli (8%), anaerobes (6%), and other microorganisms (6). The microbiology of prosthetic shoulder infection differs from that of hip and knee arthroplasty infection, as *Propionibacterium acnes* is a com-

Protez enfeksiyonları

- Enfeksiyon oranları
  - Diz % 0.8-1.9
  - Kalça % 0.3-1.7
  - Omuz % 0.7
  - Bilek %3
- Risk faktörleri
  - Bakteriyemi
  - Postop yara enfeksiyonu
  - Romatoid artirit
  - Malignite
  - Önceki ameliyat öyküsü

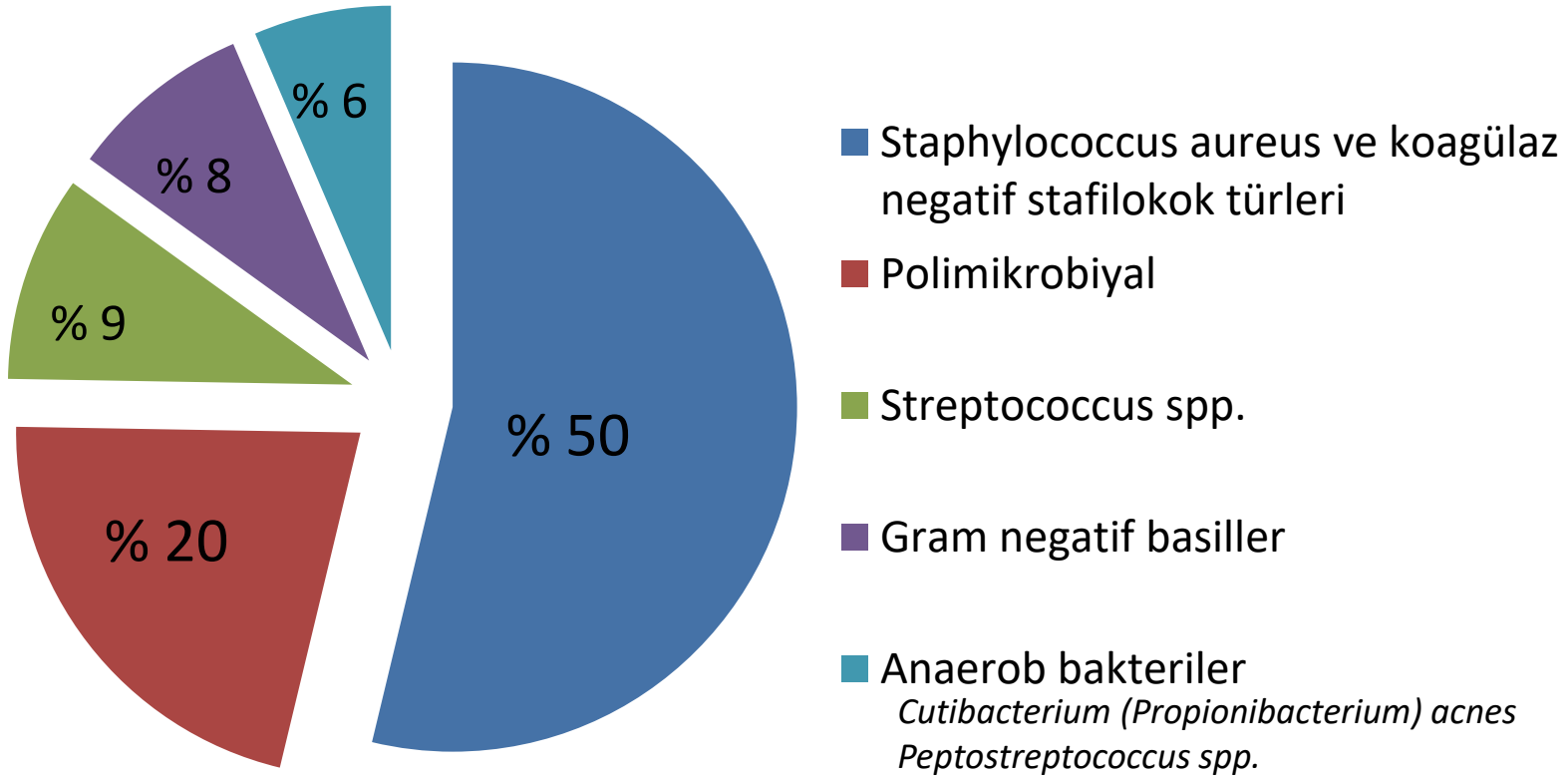


KAYIP

Fonksiyonel
Ekonomik

Protez enfeksiyonları

- Etken mikroorganizmalar



Protez enfeksiyonları

- Bulaş
  - Ameliyat sırasında protez yüzeyine
  - İmplantasyon sonrası hematojen

  - Septik?
  - Aseptik?
    - Etken virülansı yüksek bir mikrorganizma ise akut
      - *S. aureus* v.b.
    - Etken virülansı düşük bir mikrorganizma ise subakut/kronik
      - *Cutibacterium acnes* veya koagülaz negatif stafilokoklar

Definitions of the Classification Systems for Diagnosing PJI*

MSIS† (≥1 of the 2 Major Criteria OR ≥3 of 5 Minor Criteria)	IDSA† (≥1 of the Following 4 Criteria)	Proposed Criteria of the EBJIS§ (≥1 of the Following 4 Criteria)
Major criteria:	Sinus tract communicating with the prosthesis	Purulence around the prosthesis or sinus tract
2 positive periprosthetic cultures	Purulence without other etiology surrounding the prosthesis	Increased synovial fluid leukocyte count
Sinus tract communicating with the prosthesis	Acute inflammation seen on histopathological examination of the periprosthetic tissue	Positive histopathology
Minor criteria:	≥2 intraop. cultures or combination of preop. aspiration and intraop. cultures yielding an indistinguishable organism	Confirmatory microbial growth in synovial fluid, periprosthetic tissue, or sonication culture
Elevated CRP and ESR (ESR of >30 mm/hr)		
Elevated synovial fluid leukocyte count or positive leukocyte esterase strip test (++ or +++)		
Elevated synovial fluid percentage of granulocytes		
A single positive culture		
Positive histological analysis of periprosthetic tissue		

*PJI = periprosthetic joint infection, MSIS = Musculoskeletal Infection Society, IDSA = Infectious Diseases Society o Bone and Joint Infection Society, CRP = C-reactive protein, and ESR = erythrocyte sedimentation rate. †For the MSIS indicated by >10 mg/L in chronic infections or >100 mg/L in acute infections; elevated synovial fluid leukocyte count, chronic infections or >10,000 leukocytes/μL in acute infections; elevated synovial fluid percentage of granulocytes, by >90% in acute infections; and positive histological analysis of periprosthetic tissue was defined as >5 neutrophils p HPFs observed on periprosthetic tissue at ×400 magnification. ‡For IDSA, growth of a virulent microorganism (e.g., single specimen of a tissue biopsy or synovial fluid may also represent PJI. §For the proposed criteria of the EBJIS, incre count was indicated by a leukocyte count of >2,000/μL or >70% granulocytes; not interpretable within 6 weeks c disease, or after periprosthetic fracture or dislocation. Positive histopathology was defined as a mean of >23 granulo type III), according to Krenn et al.[38]. Confirmatory microbial growth in periprosthetic tissue culture was considered positive in highly virulent organisms or ≥2 specimens showed microbial growth of a low virulent pathogen, and sonication culture was considered positive if >50 colony-forming units/mL of sonication fluid grew, according to Portillo et al.[39].

Protez enfeksiyonlarında laboratuvar

Mikrobiyolojik değerlendirme

+

İnflamatuvar belirteçler

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

MSIS† (≥1 of the 2 Major Criteria OR ≥3 of 5 Minor Criteria)	IDSA† (≥1 of the Following 4 Criteria)	Proposed Criteria of the EBJIS§ (≥1 of the Following 4 Criteria)
Major criteria:	Sinus tract communicating with the prosthesis	Purulence around the prosthesis or sinus tract
2 positive periprosthetic cultures	Purulence without other etiology surrounding the prosthesis	Increased synovial fluid leukocyte count
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Elevated synovial fluid percentage of granulocytes		
A single positive culture		
Positive histological analysis of periprosthetic tissue		

*PJI = periprosthetic joint infection, MSIS = Musculoskeletal Infection Society, IDSA = Infectious Diseases Society of America, EBJIS = European Bone and Joint Infection Society, CRP = C-reactive protein, and ESR = erythrocyte sedimentation rate. †For the MSIS criteria, elevated CRP was indicated by >10 mg/L in chronic infections or >100 mg/L in acute infections; elevated synovial fluid leukocyte count, by >3,000 leukocytes/μL in chronic infections or >10,000 leukocytes/μL in acute infections; elevated synovial fluid percentage of granulocytes, by >80% in chronic infections or >90% in acute infections; and positive histological analysis of periprosthetic tissue was defined as >5 neutrophils per high-power field (HPF) in 5 HPFs observed on periprosthetic tissue at ×400 magnification. †For IDSA, growth of a virulent microorganism (e.g., *Staphylococcus aureus*) in a single specimen of a tissue biopsy or synovial fluid may also represent PJI. §For the proposed criteria of the EBJIS, increased synovial fluid leukocyte count was indicated by a leukocyte count of >2,000/μL or >70% granulocytes; not interpretable within 6 weeks of surgery, in rheumatic joint disease, or after periprosthetic fracture or dislocation. Positive histopathology was defined as a mean of >23 granulocytes per 10 HPFs (type II or type III), according to Krenn et al.[38]. Confirmatory microbial growth in periprosthetic tissue culture was considered positive if ≥1 specimen was

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

Table 1 International consensus meeting criteria for defining periprosthetic joint infection

Periprosthetic joint infection is present if one of two major criteria or three of five minor criteria exists			
Major criteria	1. A sinus tract communicating with the joint or		
	2. Two positive periprosthetic cultures (tissue or synovial fluid) with phenotypically identical microorganism		
Minor criteria		*Acute PJI (<90 days)*	*Chronic PJI (>90 days)*
	1. Elevated ESR or CRP	ESR: no threshold	ESR > 30 mm/h
		CRP > 100 mg/L	CRP > 10 mg/L
	2. Elevated SF WBC count or	10,000 cells/μL	3000 cells/μL
	Changes in the leukocyte esterase strip	+ or ++	+ or ++
	3. Elevated SF PMN%	90%	80%
	4. Positive histologic analysis of the periprosthetic tissue	>5 neutrophil per high-power field in 5 high-power fields (×400)	>5 neutrophil per high-power field in 5 high-power fields (×400)
	5. A single positive culture		

CRP C-reactive protein, *ESR* sedimentation rate, *SF WBC* synovial fluid white blood cell, *SF PMN* synovial fluid polymorphonuclear neutrophil

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

Hangi örnek?
Nasıl?

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

- Sinüs trasesi ve yüzeyel yara kültürleri
  - *S. aureus* ve gram negatif bakteriler için pozitif prediktif değer yüksek
    - Yüzeyel ve derin örnek kültür uyumu % 80
  - Diğer etkenler için yararı az

Rutin olarak tanısal değeri düşük

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

- Sinovyal sıvı incelemesi
  - Revizyon atroplasti öncesi rutin uygulama?
    - Etken izole edilirse cerrahi planı ve lokal/sistemik antibiyotik tedavisi organizasyonunda faydalı
  - Enfeksiyon şüphesi varsa fayda oranı yüksek

Diz için daha kolay
Kalça?

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

- Sinovyal sıvı incelemesi
  - Hücre sayımı
    - Diz; >1.7 x 10^9/L ve > % 65 nötrofil
    - Kalça >4.2 x 10^9/L ve > % 80 nötrofil

Duyarlılık ve özgüllük ≥ %95

  - Kültür
    - Tanıda yararlı
      - Özellikle de inflamatuvar hastalık varlığında
        - » İnflamatuvar belirteçleri ve hücre sayımlarının güvenirliğinin olumsuz etkilemesi nedeniyle

Protez enfeksiyonlarında Sinovyal sıvı kültürü

- Preoperatif ve intraoperatif örnek kültürleri arasında uyumsuzluk olabilir
- Yalancı pozitif (%3-16) ve yalancı negatif (%8-50) sonuç bildirimleri mevcut
  - Neden?
    - Anesteziklerin bakterisidal etkisi
    - Güç üreyen mikroorganizmaların varlığı
    - Düşük bakteri yükü
    - Eklem içine verilen sıvılarla mikroorganizma dilüsyonu

Protez enfeksiyonlarında Sinovyal sıvı kültürü

- Kültür duyarlığını arttırmak için ne yapabiliriz?
  - Örneklerin kan kültürü şişesine ekilmesi ile doğal ve protez eklem enfeksiyonlarında yararlanım artıyor
    - **Anerob + anerob**

Sinovyal sıvı
+
Periprostatik doku homojenatı

⇨

Duyarlılık % 87
Özgüllük % 95

Kan kültür şişesine ekimin tanısal yararı

Clin Orthop Relat Res (2010) 468:2238–2243
DOI 10.1007/s11999-010-1254-3

CLINICAL RESEARCH

Blood Culture Flasks for Culturing Synovial Fluid in Prosthetic Joint Infections

Lluís Font-Vizcarra MD, Sebastián García MD, PhD, Juan C. Martínez-Pastor MD, Josep M. Sierra MD, Alex Soriano MD, PhD

Synovial fluid samples were positive in 78 of 87 infected cases (90%), periprosthetic tissue samples were positive in 71 (82%), and swab samples were positive in 59 (68%)

All operations were performed in a standard, nonlaminar airflow operating room. Following the protocol of our hospital, the antibiotic treatment always was delayed until deep samples for culture were obtained. The protocol for sampling during surgery (open débridement or revision surgery) consisted of obtaining samples just after arthrotomy as follows: (1) synovial fluid was aspirated and immediately inoculated half into aerobic and half into anaerobic blood culture flasks (BACTEC 9240 system; BD Diagnostic Systems, BD Corporation, NJ, USA). The volume inoculated in each flask was approximately 1 to 3 mL.

Solid samples from periprosthetic tissue with visual signs of inflammation, granulation, necrosis, or purulence were obtained and placed in sterile containers without medium or saline. Finally, swab cultures were obtained by passing a sterile swab over the intracapsular area, bone, or fluid and immediately placed in transport medium (AMIES transport medium). Two samples of tissue and swabs were obtained in all patients. In the case of synovial fluid, two samples

Clin Orthop Relat Res (2010) 468:2238–2243
DOI 10.1007/s11999-010-1254-3

CLINICAL RESEARCH

Blood Culture Flasks for Culturing Synovial Fluid in Prosthetic Joint Infections

Table 4. Sensitivity, specificity, PPV and NPV of each sample according to the type of infection (acute or chronic)

Type of infection	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy
Acute					
Synovial fluid	91.39	100	100	93.6	96.19
Periprosthetic tissue	78.94	80.95	78.95	80.95	80
Swab	80.65	99.3	98.68	88.68	91.91
Chronic					
Synovial fluid	78.94	100	100	87.96	91.7
Periprosthetic tissue	56.98	80.95	67.12	73.38	71.23
Swab	39.53	99.29	97.14	73.06	76.75

Protez enfeksiyonlarında mikrobiyolojik değerlendirme

- Periprostatik doku incelemesi
  - Mikroskobi
    - Duyarlılık % 0-30
  - Kültür
    - Duyarlılık % 37-61
      - Son üç ay içinde antibiyotik tedavisi
      - Alan başına düşen mikroorganizma sayısı eşit değil
      - Etken olan mikroorganizmaların bir kısmı yavaş çoğalıyor
        - » *Cutibacterium (Propionibacterium) acnes*
          - Uzun ve anaerob inkübasyon

Periprostatik doku incelemeleri

- Kültür duyarlılığını arttırmak için ne yapabiliriz?
  - En az beş farklı alandan örnekleme
  - İnkübasyon süresini uzatma

Prolonged Bacterial Culture to Identify Late Periprosthetic Joint Infection: A Promising Strategy

Peter Schäfer,[1] Bernd Fink,[2] Dieter Sandow,[1] Andreas Margull,[1] Irina Berger,[3] and Lars Frommelt[4]

Uzun inkübasyon en çok *Propionibacterium* ve *Peptostreptococcus* türleri için yararlı

Background. The value of microbiological culture to diagnose late periprosthetic infection is limited, especially because standard methods may fail to detect biofilm-forming sessile or other fastidious bacteria. There is no agreement on the appropriate cultivation period, although this period is a crucial factor. This study was designed to assess the duration of culture that is necessary for reliable detection.

Patients and methods. Ten periprosthetic tissue specimens each were obtained during revision from 284 patients with suspected late hip or knee arthroplasty infection. Five samples were examined by microbiological culture over a 14-day period, and 5 were subjected to histologic analysis. To define infection, a pre-established algorithm was used: this included detection of indistinguishable organisms in ≥2 tissue samples or growth in 1 tissue sample and a positive result of histologic analysis (>5 neutrophils in at least 10 high-power fields). The time to detection of organisms was monitored.

Results. Infection was diagnosed in 110 patients. After 7 days (the longest incubation period most frequently reported), the detection rate via culture was merely 73.6%. Organisms indicating infection were found for up to 13 days. "Early"-detected species (mostly staphylococci) emerged predominantly during the first week, whereas "late"-detected agents (mostly *Propionibacterium* species) were detected mainly during the second week. In both populations, an unequivocal correlation between the number of culture-positive tissue samples and positive results of histologic analysis was noted, which corroborated the evidence that true infections were detected over the entire cultivation period.

Conclusions. Prolonged microbiological culture for 2 weeks is promising because it yields signs of periprosthetic infection in a significant proportion of patients that would otherwise remain unidentified.

Clinical Infectious Diseases 2008; 47:1403–9

Periprostatik doku incelemeleri

- Kültür duyarlılığını arttırmak için ne yapabiliriz?

Table 3. Association of early- and late-detected organisms with histologic findings.

Result of histologic analysis	Early-detected organisms: Total no. of samples	Early-detected organisms: No. of culture-positive tissue samples,[a] no. of samples: ≥2[c]	Early-detected organisms: No. of culture-positive tissue samples,[a] no. of samples: 1	Late-detected organisms: Total no. of samples	Late-detected organisms: No. of culture-positive tissue samples,[b] no. of samples: ≥2[c]	Late-detected organisms: No. of culture-positive tissue samples,[b] no. of samples: 1
Positive	76	65	11	21	14	7
Negative	40	9	31[d]	20	4	16[d]
All	116	74	42	41	18	23

NOTE. Early-detected species included *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterococcus* species, *Streptococcus* species, and Enterobacteriaceae. La… …a, *Propionibacterium* species, *Peptostreptococcus* species, and other s…

[a] For early-detected organisms grown in ≥2 tissue sa…

[b] For late-detected organisms grown in ≥2 tissue samples versus 1 tissue sample, $P = .007$.

[c] Growth of indistinguishable organisms.

[d] Contaminating strains.

≥2 örnek sayısı ; 3-5

Clinical Infectious Diseases 2008; 47:1403–9

Sürüntü (svab) örnekleri

- Svab ile alınan örnek kültürleri
  - Kapsüler membran
  - Kemik
  - Sinovyal sıvı
    - Doku ve sinovyal sıvı kültürüne göre düşük duyarlılık

Çıkarılan protezin sonikasyonu ile kültür

Çıkarılan protezin sonikasyonu ile kültür

Meta-Analysis of Sonication Fluid Samples from Prosthetic Components for Diagnosis of Infection after Total Joint Arthroplasty

Zanjing Zhai,[a] Haowei Li,[a] An Qin,[a] Guangwang Liu,[b] Xuqiang Liu,[a] Chuanlong Wu,[a] Huiwu Li,[a] Zhenan Zhu,[a] Xinhua Qu,[a] Kerong Dai[a]

Department of Orthopedics, Shanghai Key Laboratory of Orthopedic Implants, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China[a]; Department of Orthopaedic Surgery, the Central Hospital of Xuzhou, Xuzhou Clinical School of Xuzhou Medical College, Xuzhou Hospital (Affiliated with Medical College of Southeast University), Jiangsu, China[b]

This meta-analysis included 12 studies that evaluated sonication fluid cultures (SFC) for the diagnosis of prosthetic joint infection (PJI). The pooled sensitivity and specificity were 0.80 (95% confidence interval [CI], 0.74 to 0.84) and 0.95 (CI, 0.90 to 0.98), respectively. Subgroup analyses showed that a 14-day anaerobic culture may improve sensitivity, the use of centrifugation or vortexing may improve specificity, and the use of 400 to 500 ml of Ringer's solution for containers may improve sensitivity and specificity. The best SFC cutoff was ≥5 CFU. In conclusion, SFC has high sensitivity and very high specificity for diagnosing PJI.

Journal of Clinical Microbiology p. 1730–1736 May 2014 Volume 52 Number 5

Tanıda moleküler yöntemler ne kadar yararlı?

Archives of Orthopaedic and Trauma Surgery (2018) 138:871–878
https://doi.org/10.1007/s00402-018-2924-y

KNEE ARTHROPLASTY

Preoperative PCR analysis of synovial fluid has limited value for the diagnosis of periprosthetic joint infections of total knee arthroplasties

Bernd Fink[1,2] · Damian Oremek

Received: 29 January

gen DNA was extracted and purified for PCR analysis. Two separate PCR assays were performed with each sample using primers targeting conserved gene regions of bacterial 16S rRNA and fungal and eukaryote 18S rRNA, respectively.

Abstract

Preoperative diagnosis of periprosthetic joint infection (PJI) is important because of the therapeutic consequences. This prospective study was designed to answer the question, if preoperative PCR analysis of the synovial fluid in addition to the culture and the CRP analysis of the blood are helpful for the diagnosis of PJI in knee arthroplasties. Before revision CRP

Preoperatif değerlendirmede standart kültüre sınırlı katkı

methods. Twenty-seven prostheses were identified as infected (prevalence 23.3%). The combined analyses of the joint fluid cultivation and the CRP blood level resulted in a sensitivity of 77.8%, a specificity of 95.5%, a positive-predictive value of 84.0%, a negative-predictive value of 93.4% and an accuracy of 91.4%. The PCR analysis of the synovial fluid resulted in a sensitivity of 55.6%, a specificity of 82.0%, a positive-predictive value of 48.4%, a negative-predictive value of 85.9% and an accuracy of 75.9%. The sensitivity for culture of the aspirate and PCR analysis in combination with an elevated CRP level was 85.2%, the specificity 82.0%, the positive-predictive value 58.9%, the negative-predictive value 94.8% and the accuracy 82.7%. The preoperative PCR analysis of synovial fluid has only limited value in addition to the standard culture analysis.

Surgical Infections, VOL. 19, NO. 6 |

normal

Diagnosis of Periprosthetic Joint Infection Using Polymerase Chain Reaction: An Updated Systematic Review and Meta-Analysis

Yang Jun and Liu Jianghua

Published Online: 1 Aug 2018 | https://doi.org/10.1089/sur.2018.014

Tools Share

Abstract

Background: We aim to update a meta-analysis to evaluate the efficiency of polymerase chain reaction (PCR) for diagnosis of periprosthetic joint infection (PJI) because different types of PCR assays have yielded variable diagnostic efficiency from 2013.

Methods: We conducted our systematic review by searching for keywords in online databases from 2013 to May 2017. Studies were chosen based on inclusion and exclusion criteria and the quality of included studies was assessed. Pooled sensitivity and specificity were compared with other synovial fluid biomarkers. A total of 20 studies, comprising 2,526 participants were assessed.

Results: The pooled sensitivity, specificity, and diagnostic odds ratio (DOR) were 0.76 (95% confidence interval [CI]: 0.65–0.85), 0.94 (95% CI: 0.92–0.95), and 0.94 (95% CI: 0.92–0.96), respectively. Meta-regression analysis indicated that use of specific genes, fresh samples, and more than one sample per patient may improve sensitivity.

Conclusions: Although novel PCR assays have been developed, the sensitivity of PCR for the diagnosis of PJI had decreased compared with the previous meta-analysis (0.86, 95% CI: 0.77–0.92), whereas the high specificity is reliable for excluding PJI. Novel synovial fluid biomarker such as α-defensin, which possesses pooled sensitivity between 0.96 and 1.00, might be more efficient than PCR in PJI diagnosis.

Bone Joint J. 2018 Oct;100-B(10):1345-1351. doi: 10.1302/0301-620X.100B10.BJJ-2018-0096.R1.

Comparison of molecular diagnosis with serum markers and synovial fluid analysis in patients with prosthetic joint infection.

Kuo FC[1], Lu YD[1], Wu CT[1], You HL[2], Lee GB[3], Lee MS[1].

Author information

Abstract

AIMS: The aim of this study was to compare the results of 16S/28S rRNA sequencing with the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, and synovial fluid analysis in the diagn

PATIENTS AND METHODS: Between September 2015 and August
there were 25 patients with a PJI and 189 controls. Of the PJI patie
was 65 years (30 to 83). The ESR and CRP levels were measured,
was subjected to reverse transcription polymerase chain reaction (RT-PCR)/sequence analysis targeting the 16S/28S rRNA, and to conventional culture. Laboratory personnel who were blind to the clinical information performed all tests. The diagnosis of PJI was based on the criteria of the Mu

RESULTS: A total of
the 16S/28S rRNA g
16S/28S rRNA PCR
positive RT-PCR result. The sensitivity and specificity of the molecular diagnosis method were 100% (95% confidence interval (CI) 85.7 to 100) and 99.5% (95% CI 97.1 to 99.9), respectively, whereas the positive and negative predictive values of PCR were 96.1% (95% CI 79.6 to 99.9) and 100% (95% CI 98.1 to 100), respectively. The PCR results were significantly better than serological diagnostic methods ($p = 0.004$ and $p = 0.010$ for ESR and CRP, respectively), the synovial fluid white blood cell (WBC) count ($p = 0.036$), and percentage of polymorphonuclear cells (PMN%) ($p = 0.014$).

CONCLUSION: Stepwise RT-PCR and sequence analysis of the 16S/28S rRNA carried out under stringent laboratory conditions achieved highly sensitive and specific results for the differentiation between aseptic and septic joints undergoing arthroplasty. Sequence analysis successfully identified bacterial strains in monomicrobial infections but failed to identify molecular targets in polymicrobial infections. Further refinement of the protocols to identify the bacteria in polymicrobial infections is needed. Cite this article: Bone Joint J 2018;100-B:1345-51.

25 hasta, 189 kontrol
ESR, CRP, kültür, 16S + 23S rRNA

Monomikrobiyal enfeksiyonda mükemmel tanımlama
Polimikrobiyal enfeksiyonda etken tanımlama hataları

Tanıda inflamatuvar belirteçler

Tanıda inflamatuvar belirteçler

- Sedimantasyon hızı
- CRP
- IL-6
- TNF-alfa
- Lökosit esteraz
- Alfa-defensin

Sedimantasyon hızı ve CRP

– Belirleyici sınır ?
  - Sed > 30 mm/h
  - CRP > 10 µg/L

Table 1 International consensus meeting criteria for defining periprosthetic joint infection

Periprosthetic joint infection is present if one of two major criteria or three of five minor criteria exists			
Major criteria	1. A sinus tract communicating with the joint or		
	2. Two positive periprosthetic cultures (tissue or synovial fluid) with phenotypically identical microorganism		
Minor criteria		*Acute PJI (<90 days)*	*Chronic PJI (>90 days)*
	1. Elevated ESR or CRP	ESR: no threshold	ESR > 30 mm/h
		CRP > 100 mg/L	CRP > 10 mg/L
	2. Elevated SF WBC count or	10,000 cells/µL	3000 cells/µL
	Changes in the leukocyte esterase strip	+ or ++	+ or ++
	3. Elevated SF PMN%	90%	80%
	4. Positive histologic analysis of the periprosthetic tissue	>5 neutrophil per high-power field in 5 high-power fields (×400)	>5 neutrophil per high-power field in 5 high-power fields (×400)
	5. A single positive culture		

CRP C-reactive protein, *ESR* sedimentation rate, *SF WBC* synovial fluid white blood cell, *SF PMN* synovial fluid polymorphonuclear neutrophil

Her tip eklem enfeksiyonu için duyarlılık ve özgüllük aynı mı?
Kullanılan enfeksiyon tanımlama kriterine göre
belirleyici sınırların duyarlılık ve özgüllük?

C-Reactive Protein, Erythrocyte Sedimentation Rate and Orthopedic Implant Infection

PLoS One, 2010,5:e9358.

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Table 3. Sensitivity and specificity of CRP (>10 mg/l) and/or ESR (>30 mm/h) for the detection of infected knee, hip and shoulder arthroplasty and spinal instrumentation.

	Sensitivity	Specificity	PPV	NPV	Area Under the ROC Curve	p-value from Logistic Regression
Knee ESR >30 mm/h	71 (58/82)	89 (191/215)	71 (58/82)	89 (191/215)	0.80	<0.0001
Knee CRP >10 mg/d	83 (68/82)	79 (170/215)	60 (68/113)	92 (170/184)	0.81	<0.0001
Knee ESR >30 mm/h or CRP >10 mg/l	87 (71/82)	75 (161/215)	57 (71/125)	94 (161/172)	0.81	<0.0001
Hip ESR >30 mm/h	47 (16/34)	84 (158/187)	36 (16/45)	90 (158/176)	0.66	<0.0001
Hip CRP >10 mg/l	74 (25/34)	78 (146/187)	38 (25/66)	94 (146/155)	0.76	<0.0001
Hip ESR >30 mm/h or CRP >10 mg/l	76 (26/34)	71 (132/187)	32 (26/81)	94 (132/140)	0.74	<0.0001
Shoulder ESR >30 mm/h	16 (3/19)	98 (44/45)	75 (3/4)	73 (44/60)	0.57	0.0764
Shoulder CRP >10 mg/l	42 (8/19)	84 (38/45)	53 (8/15)	78 (38/49)	0.63	0.0269
Shoulder ESR >30 mm/h or CRP >10 mg/l	42 (8/19)	82 (37/45)	50 (8/16)	77 (37/48)	0.62	0.0455
Spine ESR >30 mm/h	64 (9/14)	83 (33/40)	56 (9/16)	87 (33/38)	0.73	0.0021
Spine CRP >10 mg/l	57 (8/14)	85 (34/40)	57 (8/14)	85 (34/40)	0.71	0.0038
Spine ESR >30 mm/h or CRP >10 mg/l	79 (11/14)	75 (30/40)	52 (11/21)	91 (30/33)	0.77	0.0013

Table 4. Sensitivity and specificity of optimized CRP and ESR for the detection of infected knee, hip and shoulder arthroplasty and spinal instrumentation.

	Sensitivity	Specificity	PPV	NPV	Area Under the ROC Curve	p-value from Logistic Regression
Knee ESR >19 mm/h	89 (73/82)	74 (159/215)	57 (73/129)	95 (159/168)	0.82	<0.0001
Knee CRP >14.5 mg/l	79 (65/82)	88 (189/215)	71 (65/91)	92 (189/206)	0.84	<0.0001
Knee ESR >19 mm/h or CRP >14.5 mg/l	94 (77/82)	69 (149/215)	54 (77/143)	97 (149/154)	0.82	<0.0001
Hip ESR >13 mm/h	82 (28/34)	60 (113/187)	27 (28/102)	95 (113/119)	0.71	<0.0001
Hip CRP >10.3 mg/l	74 (25/34)	79 (147/187)	38 (25/65)	94 (147/156)	0.76	<0.0001
Hip ESR >13 mm/h or CRP >10.3 mg/l	88 (30/34)	55 (103/187)	26 (30/114)	96 (103/107)	0.72	<0.0001
Shoulder ESR >26 mm/h	32 (6/19)	93 (42/45)	67 (6/9)	76 (42/55)	0.63	0.02
Shoulder CRP >7 mg/dl	63 (12/19)	73 (33/45)	50 (12/24)	83 (33/40)	0.68	0.01
Shoulder ESR >26 mm/h or CRP >7 mg/dl	63 (12/19)	73 (33/45)	50 (12/24)	83 (33/40)	0.68	0.01
Spine ESR >45 mm/h	57 (8/14)	90 (36/40)	67 (8/12)	86 (36/42)	0.74	0.001
Spine CRP >4.6 mg/dl	79 (11/14)	68 (27/40)	46 (11/24)	90 (27/30)	0.73	0.01
Spine ESR >45 mm/h or CRP 4.6 mg/dl	79 (11/14)	67 (27/40)	46 (11/24)	90 (27/30)	0.73	0.01

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IL-6

- Diz ve kalça için yüksek duyarlılık ve özgüllük
  - ≥ 10 pg/ml
  - Artroplasti disfonksiyonunun belirlenmesi rutin algoritmasında kullanımı ?

Prokalsitonin ve TNF-alfa

- Protez enfeksiyonlarının tanısında yararlı bir indikatör değil
    - Düşük duyarlılık, yüksek özgüllük

Lökosit esteraz

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Complications - Infection

Diagnosing Periprosthetic Joint Infection: And the Winner Is?

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ARTICLE INFO

ABSTRACT

	CRP and ESR	CRP or ESR	CRP	ESR	WBC	LE	PMN
Sensitivity	86.74 ± 1.22%	96.01 ± 0.70%	92.31 ± 0.95%	89.95 ± 1.07%	85.78 ± 1.67%	75.00 ± 4.17%	85.82 ± 1.70%
Specificity	78.81 ± 0.68%	51.47 ± 0.84%	68.13 ± 0.78%	62.05 ± 0.78%	83.00 ± 1.88%	90.93 ± 1.22%	80.84 ± 2.02%
Positive predictive value	47.13 ± 1.32%	30.12 ± 0.92%	38.48 ± 1.12%	32.80 ± 1.00%	84.62 ± 1.72%	61.83 ± 4.24%	83.26 ± 1.79%
Negative predictive value	96.47 ± 0.34%	98.34 ± 0.30%	97.62 ± 0.30%	96.77 ± 0.35%	84.26 ± 1.83%	94.89 ± 0.96%	83.70 ± 1.93%
Diagnostic odds ratio	23.33 ± 0.11	25.52 ± 0.19	25.66 ± 0.14	14.64 ± 0.12	29.45 ± 0.19	30.06 ± 0.27	25.53 ± 0.19
Positive likelihood ratio	4.09	1.98	2.90	2.37	5.05	8.27	4.48
Negative likelihood ratio	0.17	0.08	0.11	0.16	0.17	0.27	0.18

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN, polymorphonuclear; WBC, white blood cell.

Lökosit esteraz

Leukocyte Esterase as a Biomarker in the Diagnosis of Periprosthetic Joint Infection

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Table 2. Sensitivity, specificity, positive predictive value and negative predictive value of LE strips.

Items	Results	95%CI
Sensitivity (%)	91.4	75.8–97.8
Specificity (%)	96.4	79.8–99.8
Positive predictive value (%)	97.0	82.5–99.8
negative predictive value (%)	90.0	72.3–97.4

DEFENSİN; *Parlayan yıldız*

- Epitel hücreleri ve lökositlerden salınan antimikrobiyal bir peptid
  - Kemotaktik ve düzenleyici bir peptid
    - Alfa tipi nötrofil içinde yoğun
      - Eklem enfeksiyonu yanıtı olarak sinoyval sıvıya sekrete ediliyor
        - » Enfeksiyon tanısında duyarlılık (%92) ve özgüllüğü (%95) çok yüksek
        - » CRP ile kombine kullanıldığında tanısal duyarlılık (%97) ve özgüllüğü (%100)

      - Farklı etken mikroorganizma ve farklı enfeksiyon lokalizasyonlarında sonuçlar iyi
      - Sonuçlar önceki antibiyotik kullanımından ve sistemik inflamasyondan etkilenmiyor
        - » Artan inflamatuvar belirteçlere bağlı yanlış pozitif sonuç ?
      - Erken enfeksiyon tanısı için tüm geleneksel laboratuvar testlerinden üstün

Alfa-defensin

- Belirleyici sınır değer (cut-off)?
  - 5.20-7.72 ??

Alfa-defensin hasta başı test olabilir mi?

Knee Surg Sports Traumatol Arthrosc (2018) 26:1717–1722
DOI 10.1007/s00167-017-4745-x

KNEE

High performance of α-defensin lateral flow assay (Synovasure) in the diagnosis of chronic knee prosthetic infections

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Table 4 Diagnostic accuracy of the criteria proposed by the International Consensus Meeting on Chronic infection and α-defensin

Test	Sensitivity[a]	Specificity[a]	PPV[a]	NPV[a]
Two positive periprosthetic cultures with phenotypically identical organisms	75.0 (60.6–85.6)	100 (91.3–100)	100 (91.3–100)	89.7 (77.3–96.1)
A sinus tract communicating with the joint	25 (14.4–39.4)	100 (91.3–100)	100 (91.3–100)	74.5 (60–85.2)
Elevated CRP (> 10 mg/L) and ESR (> 30 mm/h)	81.3 (67.4–90.3)	82.9 (69.2–91.5)	68.4 (53.8–80.3)	90.6 (78.3–96.6)
SF WBC count > 3000/uL	75.0 (60.6–85.6)	91.4 (79.3–97.1)	80 (66–89.4)	88.9 (76.2–95.5)
SF PMN percentage > 80%	75 (60.6–85.6)	97 (86.9–99.7)	92.3 (80.4–97.5)	89.5 (76.9–95.9)
A single positive culture	18.8 (9.7–31.2)	75.6 (62.6–85.3)	21.4 (12.4–34.1)	72.3 (59.2–82.7)
Alpha-defensin (Synovasure)	87.5 (74.6–94.7)	97.1 (86.9–99.7)	93.3 (81.8–98.1)	94.4 (83.2–98.6)

PPV positive predictive value, *NPV* negative predictive value

[a]The 95% confidence intervals are shown in parenthesis

ELISA ile yüksek uyum
Tek yanlış pozitif

Alfa-defensin hasta başı test olabilir mi?

Arthroplasty

Diagnosis of prosthetic joint infection with alpha-defensin using a lateral flow device

a multicentre study

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Patients and Methods

A cohort of 121 patients comprising 85 total knee arthroplasties and 36 total hip arthroplasties was prospectively evaluated between May 2015 and June 2016 in three different orthopaedic centres. The tests were performed on patients with a chronically painful prosthesis undergoing a joint aspiration in a diagnostic pathway or during revision surgery.

Enfeksiyon tanısı/dışlanmasında mükemmel performans

Based on the MSIS criteria, 34 patients (28%) would have had a PJI, and 87 patients had no PJI. Testing with the lateral flow device had a sensitivity of 97.1% (95% confidence intervals (CI) 84.5 to 99.9) and a specificity of 96.6% (95% CI 90.3 to 99.2). The positive predictive value was 91.7% (95% CI 77.7% to 98.3), and the negative predictive value was 98.8% (95% CI 93.6 to 99.9). Receiver operator characteristics analysis demonstrated an area under the curve for the Synovasure test of 0.97 (95% CI 0.93 to 1.00).

Conclusion

Our findings suggest that the Synovasure test has an excellent diagnostic performance to confirm or reject the diagnosis of a PJI. The results are promising for the care of the painful or problematic knee and hip joint arthroplasty and the test should be considered as part of the diagnostic toolbox for PJIs.

Cite this article: *Bone Joint J* 2017;99-B:1176–82

Alfa-defensin hasta başı test olabilir mi?

Systematic review

Alpha-defensin and the Synovasure lateral flow device for the diagnosis of prosthetic joint infection

a systematic review and meta-analysis

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Laboratuvar temelli alfa-defensin tanı için ümit vaad ediyor
Lateral akım testinin performansı düşük
Daha çok çalışmaya ihtiyaç var

Materials a

Studies using alp
PJI were identifie
studies was evalu
(QUADAS) tool. M

Results

A total of 11 eligible studies were included. The median QUADAS score was 13 (interquartile range 13 to 13) out of 14. Significant conflicts of interest were identified in five studies. The pooled sensitivity for the laboratory alpha-defensin test was 0.95 (95% confidence interval (CI) 0.91 to 0.98) and the pooled specificity was 0.97 (95% CI 0.95 to 0.98) for four studies with a threshold level of 5.2 mg/l. The pooled sensitivity for the lateral flow cassette test was 0.85 (95% CI 0.74 to 0.92) and the pooled specificity was 0.90 (95% CI 0.91 to 0.98). There was a statistically significant difference in sensitivity ($p = 0.019$), but not specificity ($p = 0.47$).

Conclusion

Laboratory-based alpha-defensin testing remains a promising tool for diagnosing PJI. The lateral flow cassette has a significantly lower performance and pooled results are comparable to the leucocyte esterase test. Further studies are required before the widespread adoption of the lateral flow cassette alpha-defensin test.

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Alfa-defensin hasta başı test olabilir mi?

J Bone Joint Surg Am. 2018 May 2;100(9):742-750. doi: 10.2106/JBJS.17.01005.

Alpha Defensin Lateral Flow Test for Diagnosis of Periprosthetic Joint Infection: Not a Screening but a Confirmatory Test.

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Author information

Abstract

BACKGROUND: Determination of alpha defensin in synovial fluid has shown promising results for diagnosing periprosthetic joint infection (PJI). The purposes of our study were to assess the performance of alpha defensin lateral flow (ADLF) test for the diagnosis of acute and chronic PJI using 3 classification systems and to compare its performance with the synovial fluid leukocyte count.

METHODS: Patients in whom aspiration of a prosthetic hip or knee joint was performed before revision arthroplasty were prospectively included. In addition to standard diagnostic tests, the ADLF test was performed in synovial fluid. Patients were classified as having PJI or aseptic failure according to the definition criteria of the Musculoskeletal Infection Society (MSIS), the Infectious Diseases Society of America (IDSA), and the proposed criteria of the European Bone and Joint Infection Society (EBJIS). The performance of the ADLF test and the leukocyte count was compared using the McNemar chi-square test.

RESULTS: Of 212 included patients, 151 (71%) had a knee prosthesis and 61 (29%) had a hip prosthesis. PJI was diagnosed in 45 patients (21%) using the MSIS criteria, in 55 patients (26%) using the IDSA criteria and in 79 patients (37%) using the proposed EBJIS criteria. The sensitivity of the ADLF test was 84% (95% confidence interval [CI], 71% to 94%) with the MSIS criteria, 67% (95% CI, 53% to 79%) with the IDSA criteria, and 54% (95% CI, 43% to 66%) with the proposed EBJIS criteria. The ADLF test showed high specificity using all classification criteria (96% to 99%) and represented the most specific preoperative test for PJI, especially in the early postoperative period (91%; 95% CI, 59% to 100%). Using the proposed EBJIS definition criteria, the sensitivity of the leukocyte count was significantly higher than that of the ADLF test (86% [95% CI, 76% to 93%] compared with 54% [95% CI, 43% to 66%]; $p < 0.001$), particularly in chronic PJI (81% compared with 44%, respectively; $p < 0.001$).

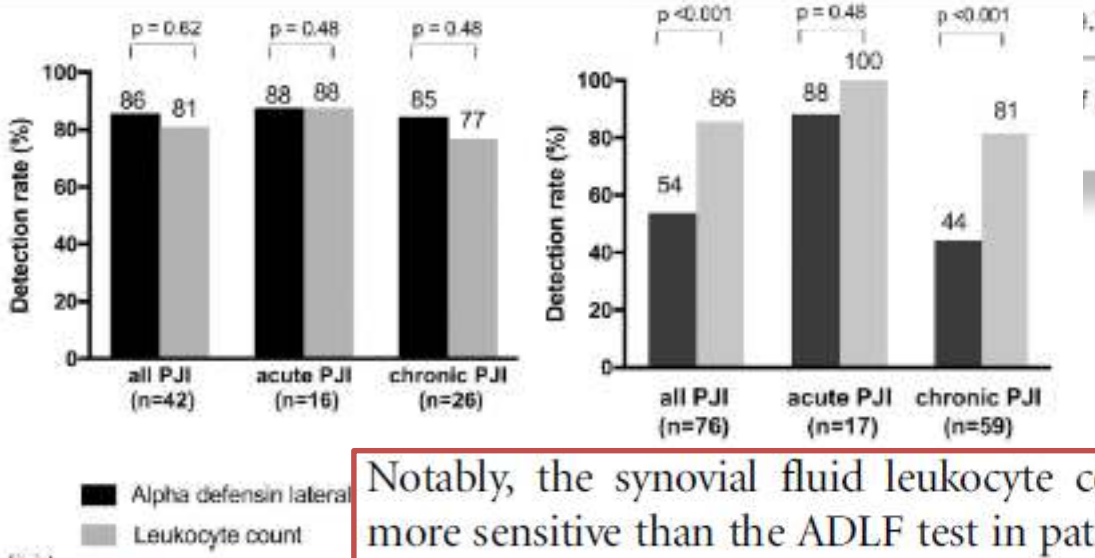
CONCLUSIONS: The ADLF test was rapid and highly specific for diagnosing PJI (>95%). However, its sensitivity was limited (54% to 84%) and it should therefore not be used for screening, but rather as a confirmatory test for PJI.

Alfa-defensin hasta başı test olabilir mi?

TABLE V Performance of ADLF Test According to the MSIS, IDSA, and Proposed EBJIS Classification Systems*

Definition Criteria	No. of Patients with Positive ADLF Test/No. of Patients with Aseptic Failure	No. of Patients with Positive ADLF Test/No. of Patients with PJI	Sensitivity (CI 95%) (%)	Specificity (CI 95%) (%)	Positive Predictive Value (CI 95%) (%)	Negative Predictive Value (CI 95%) (%)	Accuracy (%)
MSIS	6/167	38/45	84.4 (70.5-93.5)	96.4 (92.3-98.7)	86.4 (74.1-93.4)	95.8 (92.1-97.9)	93.9
IDSA	7/157	37/55	67.3 (53.3-79.3)	95.5 (91.0-98.2)	84.1 (71.5-91.8)	89.3 (85.1-92.4)	88.2
EBJIS						78.6 (74.2-82.4)	82.5

*ADLF = alpha de… Infection Society. … America, EBJIS = European Bone and Joint



Notably, the synovial fluid leukocyte count was significantly more sensitive than the ADLF test in patients with chronic PJI.

Figs. 3-A and 3-B Rates of positive results according to the synovial fluid leukocyte count and the ADLF test in patients with PJI for whom the leukocyte count was determined, with results stratified by those with acute or chronic PJI. **Fig. 3-A** Detection rate for 42 patients with PJI according to the Musculoskeletal Infection Society (MSIS) criteria. In 3 patients, no determination of leukocyte count was performed. **Fig. 3-B** Detection rates for 76 patients with PJI according to the proposed European Bone and Joint Infection Society (EBJIS) criteria.

J Bone Joint Surg Am. 2018;100:742-50

Bir olgumuz var

- 66 y, ♀, 12 yıl önce total diz protezi
- Şikayeti: 2-3 aydır bacak ağrısı
  - 1.10.2018 ; ortopedi servisine interne edilmiş
    - Sol diz protezinde septik gevşeme
  - 3.10.2018 ; diz revizyon artoplastisi+diz artoplastisi+total protez çıkarma
  - 25.10.2018; önerilerle taburcu

Bir olgumuz var

- Sinovyal Sıvı Gram Boyama: Nadir sayıda gram negatif kok görüldü.
- Sinovyal Sıvı Wright Boyama: Çok sayıda lökosit(%90 polimorfonükleer) görüldü.
- Sinovyal Sıvı Kültürü: *Salmonella* species

- <u>Antibiyogram</u>

Ampisilin	Duyarlı
Chloramphenicol	Duyarlı
Siprofloksasin	Duyarlı
Trimetoprim-Sulfametoksazol	Duyarlı

Hücre sayımı
Lökosit: 245.000/mm^3
Eritrosit: 100.000/mm^3

CRP: 431 mg/L
Sedim: 70 mm/h

Bir olgumuz var

- Doku Biyopsi
  - Kültürü: *Salmonella enterica* / Orta Miktarda (CFU/ml)
  - Gram Boyama: Herhangi bir mikroorganizma görülmedi.
  - Wright Boyama: Çok sayıda lökosit (%60 PMNL)

- Kemik
  - Kültürü: *Salmonella enterica* / Az Miktarda (CFU/ml)
  - Gram Boyama: Herhangi bir mikroorganizma görülmedi.
  - Wright Boyama: Çok sayıda lökosit (%90 PMNL)

- Abse
  - Kültürü: *Salmonella enterica* / Orta Miktarda (CFU/ml)
  - Gram Boyama: Az sayıda gram negatif basil görüldü.
  - Wright Boyama:Orta sayıda lökosit (%90 PMNL)

SONUÇ

Bu toplantıdan sonra ortak dilimiz ☺

- Sinovyal sıvı kültürü
  - Aerob ve anerob kan kültür şişelerine hasta başı ekim
    - 1 ml/ şişe
      - Ekim öncesi şişe kapağı lastiğini mutlaka silelim

İnkübasyon 14 gün

  - Ayrıca, laboratuvara gönderilen örneklerden agara ekim
    - Aerob; 7 gün inkübasyon

Bu toplantıdan sonra ortak dilimiz ☺

- Periprostatik doku kültürü
  - İntraoperatif alınan örneklerin ek olarak uygun transfer besiyerine de konularak gönderilmesi
    - Anerob izolasyon şansı

İnkübasyon 14 gün

Bu toplantıdan sonra ortak dilimiz ☺

- Hücre sayımı için
  - EDTA (mor kapaklı) tüplere 1 ml.örnek

Bu toplantıdan sonra ortak dilimiz ☺

- Çıkarılan protezler??
  - Konuşalım ☺

Teşekkür ederim