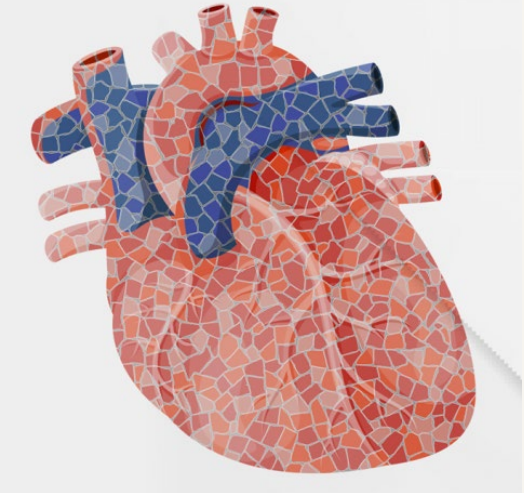
Best papers on cardiovascular infections

In memoriam Dr. Juan Galvez



Guillermo Cuervo
Infectious Diseases
Hospital Clinic de Barcelona

June 2022

16TH SYMPOSIUM ISCVID

Methods:

- **Non-systematic review**
- **Search words**: Endocarditis, Infective endocarditis, cardiac electronic devices infection, vascular graft infection
- **Restrictions**:
  - Time span : 01/06/2019 → 31/05/2022
  - Top journals
  - Topics already covered in this symposium were excluded (IDUs-IE, TAVI-IE, diagnostic Scores, etc.)
- **Selection criteria**:
  - Clinical relevance

Results:

- **Records screened**: 1336 titles
  - **Abstracts selected**: 55
    - **Full-text selected**: 10 papers
      - Infective Endocarditis (9):
        - Epidemiology (2)
        - Special populations (3)
        - Diagnosis (2)
        - Treatment (2)
      - Infections in vascular prostheses (1)

Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

THE LANCET
Global Health

- **Systematic review and meta-analysis** of studies reporting primary data for the epidemiology of IE in Africa
- **Search terms**: “endocarditis”, “Africa”, and the name of all African countries
- **Inclusion period of participants**: 1990 to 2019 (articles published between 1996 and 2020)

2141 records → **89 full-texts** → **42 articles**

42 cross-sectional studies (mostly retrospective)

Total population: 15097 patients

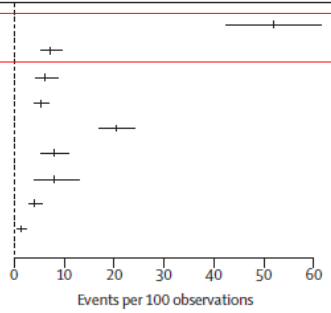
Noubiap J, et al. *Lancet Glob Health*. 2022

Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

THE LANCET
Global Health

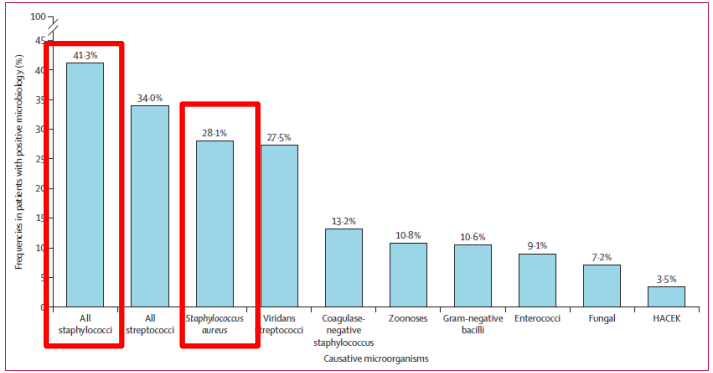
Risk factors

	Number of events	Total sample size	Number of studies	I^2	Prevalence (95% CI)
Rheumatic heart disease	1112	2351	19	0·94	52·0% (42·4–61·5)
Congenital heart disease	161	1941	15	0·57	7·2% (5·3–9·4)
Degenerative heart disease	90	1511	7	0·73	6·2% (4·1–8·6)
Previous infective endocarditis	56	1052	7	0·12	5·2% (3·9–6·7)
Prosthetic valve	438	1992	13	0·74	20·3% (16·9–24·0)
Diabetes	56	697	6	0·50	7·9% (5·3–10·8)
Intravenous drug use	75	983	5	0·86	7·9% (4·1–12·9)
Haemodialysis	31	748	3	0·00	4·1% (2·8–5·6)
Pacemaker	7	504	5	0·00	1·3% (0·5–2·4)



Pooled prevalence of risk factors for infective endocarditis

Microbiology



Pooled prevalence of microorganisms in positive blood cultures in infective endocarditis

Noubiap J, et al. *Lancet Glob Health*. 2022

Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

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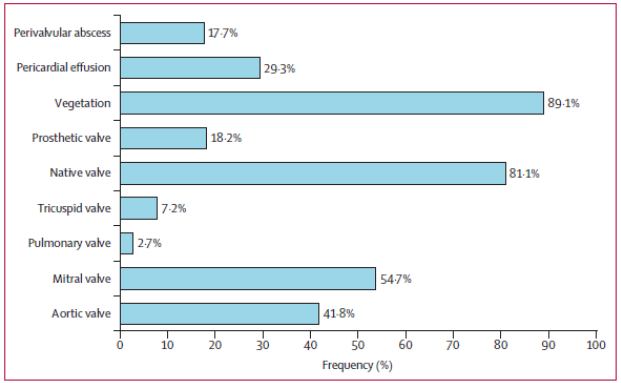
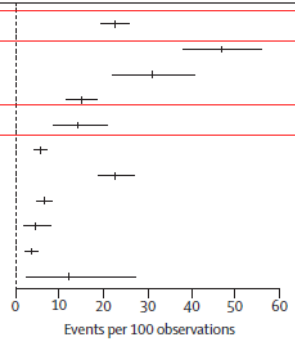
Echocardiogram



Pooled distribution of echocardiographic features of infective endocarditis

Complications

	Number of events	Total sample size	Number of studies	Incidence (95% CI)	I^2
Death	441	1869	13	22·6% (19·5–25·9)	0·60
Heart failure	727	1674	10	47·0% (38·2–56·0)	0·87
Embolic events	378	1064	7	31·1% (22·2–40·8)	0·92
All stroke	222	1372	8	15·1% (11·8–18·8)	0·64
Ischaemic stroke	182	1120	7	14·2% (8·7–20·9)	0·91
Intracranial haemorrhage	52	890	6	5·8% (4·3–7·4)	0·00
Acute kidney injury	237	1022	5	22·8% (18·8–27·0)	0·66
Mycotic aneurysm	59	888	4	6·6% (5·0–8·3)	0·00
Splenic infarction	86	1364	8	4·6% (2·0–8·0)	0·90
Cerebral abscess	25	650	4	3·7% (2·4–5·3)	0·21
Conduction abnormalities	38	299	3	12·2% (2·6–27·5)	0·93



Pooled incidence proportions of complications from infective endocarditis

Pooled rate of surgical treatment → 49.1%

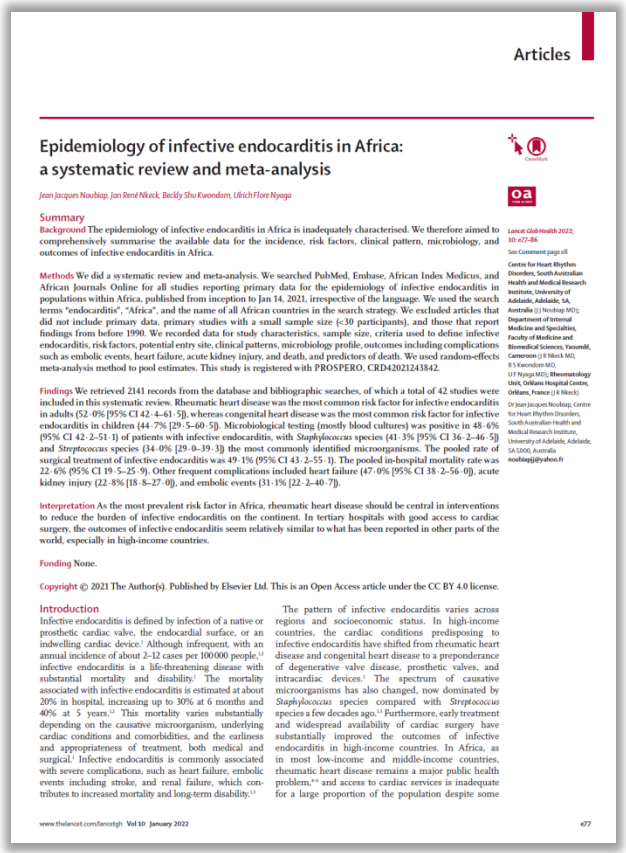
Noubiap J, et al. *Lancet Glob Health*. 2022

Why this paper?

- First comprehensive summary of the epidemiology of IE endocarditis in Africa

Take-home messages:

- Rheumatic heart disease is the most common RF for IE in adults (CHD in children)
- *Staphylococci* are the most common causative microorganisms
- The proportion of patients receiving surgical treatment for IE, the frequency of complications and fatality rates are similar to those reported in high-income countries (referral bias)



Articles

Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

Jean Jacques Noubiap, Jan René Nkeck, Beckly Shu Kwondom, Ulrich Flore Nyaga

Summary

Background The epidemiology of infective endocarditis in Africa is inadequately characterised. We therefore aimed to comprehensively summarise the available data for the incidence, risk factors, clinical pattern, microbiology, and outcomes of infective endocarditis in Africa.

Methods We did a systematic review and meta-analysis. We searched PubMed, Embase, African Index Medicus, and African Journals Online for all studies reporting primary data for the epidemiology of infective endocarditis in populations within Africa, published from inception to Jan 14, 2021, irrespective of the language. We used the search terms "endocarditis", "Africa", and the name of all African countries in the search strategy. We excluded articles that did not include primary data, primary studies with a small sample size (<30 participants), and those that report findings from before 1990. We recorded data for study characteristics, sample size, criteria used to define infective endocarditis, risk factors, potential entry site, clinical patterns, microbiology profile, outcomes including complications such as embolic events, heart failure, acute kidney injury, and death, and predictors of death. We used random-effects meta-analysis method to pool estimates. This study is registered with PROSPERO, CRD42021243842.

Findings We retrieved 2141 records from the database and bibliographic searches, of which a total of 42 studies were included in this systematic review. Rheumatic heart disease was the most common risk factor for infective endocarditis in adults (52·0% [95% CI 42·4–61·5]), whereas congenital heart disease was the most common risk factor for infective endocarditis in children (44·7% [29·5–60·5]). Microbiological testing (mostly blood cultures) was positive in 48·6% (95% CI 42·2–51·1) of patients with infective endocarditis, with *Staphylococcus* species (41·3% [95% CI 36·2–46·5]) and *Streptococcus* species (34·0% [29·0–39·3]) the most commonly identified microorganisms. The pooled rate of surgical treatment of infective endocarditis was 49·1% (95% CI 43·2–55·1). The pooled in-hospital mortality rate was 22·6% (95% CI 19·5–25·9). Other frequent complications included heart failure (47·0% [95% CI 38·2–56·0]), acute kidney injury (22·8% [18·8–27·0]), and embolic events (31·1% [22·2–40·7]).

Interpretation As the most prevalent risk factor in Africa, rheumatic heart disease should be central in interventions to reduce the burden of infective endocarditis on the continent. In tertiary hospitals with good access to cardiac surgery, the outcomes of infective endocarditis seem relatively similar to what has been reported in other parts of the world, especially in high-income countries.

Funding None.

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Introduction

Infective endocarditis is defined by infection of a native or prosthetic cardiac valve, the endocardial surface, or an indwelling cardiac device.[1] Although infrequent, with an annual incidence of about 2–12 cases per 100 000 people,[1,2] infective endocarditis is a life-threatening disease with substantial mortality and disability.[1] The mortality associated with infective endocarditis is estimated at about 20% in hospital, increasing up to 30% at 6 months and 40% at 5 years.[3,4] This mortality varies substantially depending on the causative microorganism, underlying cardiac conditions and comorbidities, and the earliness and appropriateness of treatment, both medical and surgical.[1] Infective endocarditis is commonly associated with severe complications, such as heart failure, embolic events including stroke, and renal failure, which contributes to increased mortality and long-term disability.[3,4]

The pattern of infective endocarditis varies across regions and socioeconomic status. In high-income countries, the cardiac conditions predisposing to infective endocarditis have shifted from rheumatic heart disease and congenital heart disease to a preponderance of degenerative valve disease, prosthetic valves, and intracardiac devices.[1] The spectrum of causative microorganisms has also changed, now dominated by *Staphylococcus* species compared with *Streptococcus* species a few decades ago.[3,4] Furthermore, early treatment and widespread availability of cardiac surgery have substantially improved the outcomes of infective endocarditis in high-income countries. In Africa, as in most low-income and middle-income countries, rheumatic heart disease remains a major public health problem,[5,6] and access to cardiac services is inadequate for a large proportion of the population despite some

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Lancet Glob Health 2022; 10: e77–86

See Comment page e8

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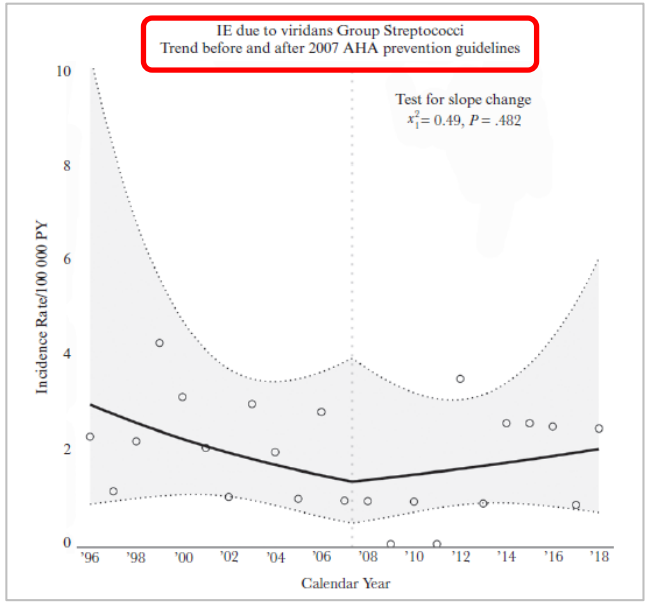
Noubiap J, et al. *Lancet Glob Health*. 2022

Temporal Trends of Infective Endocarditis in Olmsted County, Minnesota, Between 1970 and 2018: A Population-Based Analysis

Open Forum Infectious Diseases
MAJOR ARTICLE

- 269 cases of IE (possible or definite) over 49 years (1970-2018)
- Average age: 67 years. 34% females.
- Global incidence of 7.9/100,000 person-years
- Significant increase in incidence of endocarditis (p: .021)
  - Increase in *Enterococcus* spp. (p: .018)
  - Seasonal increase of *S. aureus* (winter months)



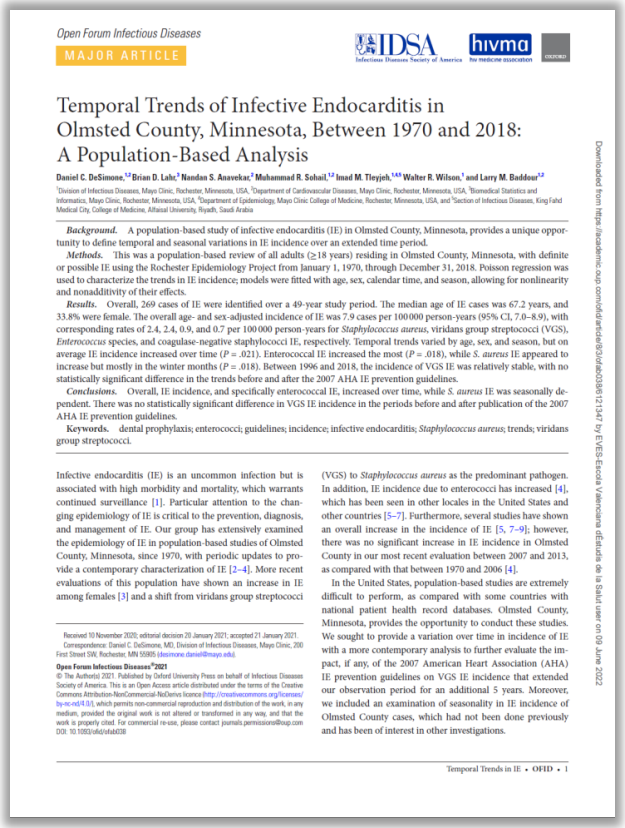
DeSimone D, et al. *Open Forum Infect Dis*. 2021

Why this paper ?

- Detailed population-based cohort study over a nearly 5-decade period

Take-home messages:

- Significant increase in overall incidence of IE from 1970 to 2018
- There was no statistically significant increase in VGS IE incidence in a pre vs. post-2007 AHA IE prevention guideline comparison



Open Forum Infectious Diseases

MAJOR ARTICLE

Temporal Trends of Infective Endocarditis in Olmsted County, Minnesota, Between 1970 and 2018: A Population-Based Analysis

Daniel C. DeSimone,[1,2] Brian D. Lahr,[3] Nandan S. Anavekar,[2] Muhammad R. Sohail,[1,2] Imad M. Tleyjeh,[1,4,5] Walter R. Wilson,[1] and Larry M. Baddour[1,2]

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Background. A population-based study of infective endocarditis (IE) in Olmsted County, Minnesota, provides a unique opportunity to define temporal and seasonal variations in IE incidence over an extended time period.

Methods. This was a population-based review of all adults (≥18 years) residing in Olmsted County, Minnesota, with definite or possible IE using the Rochester Epidemiology Project from January 1, 1970, through December 31, 2018. Poisson regression was used to characterize the trends in IE incidence; models were fitted with age, sex, calendar time, and season, allowing for nonlinearity and nonadditivity of their effects.

Results. Overall, 269 cases of IE were identified over a 49-year study period. The median age of IE cases was 67.2 years, and 33.8% were female. The overall age- and sex-adjusted incidence of IE was 7.9 cases per 100 000 person-years (95% CI, 7.0–8.9), with corresponding rates of 2.4, 2.4, 0.9, and 0.7 per 100 000 person-years for *Staphylococcus aureus*, viridans group streptococci (VGS), *Enterococcus* species, and coagulase-negative staphylococci IE, respectively. Temporal trends varied by age, sex, and season, but on average IE incidence increased over time ($P = .021$). Enterococcal IE increased the most ($P = .018$), while *S. aureus* IE appeared to increase but mostly in the winter months ($P = .018$). Between 1996 and 2018, the incidence of VGS IE was relatively stable, with no statistically significant difference in the trends before and after the 2007 AHA IE prevention guidelines.

Conclusions. Overall, IE incidence, and specifically enterococcal IE, increased over time, while *S. aureus* IE was seasonally dependent. There was no statistically significant difference in VGS IE incidence in the periods before and after publication of the 2007 AHA IE prevention guidelines.

Keywords. dental prophylaxis; enterococci; guidelines; incidence; infective endocarditis; *Staphylococcus aureus*; trends; viridans group streptococci.

Infective endocarditis (IE) is an uncommon infection but is associated with high morbidity and mortality, which warrants continued surveillance [1]. Particular attention to the changing epidemiology of IE is critical to the prevention, diagnosis, and management of IE. Our group has extensively examined the epidemiology of IE in population-based studies of Olmsted County, Minnesota, since 1970, with periodic updates to provide a contemporary characterization of IE [2–4]. More recent evaluations of this population have shown an increase in IE among females [3] and a shift from viridans group streptococci (VGS) to *Staphylococcus aureus* as the predominant pathogen. In addition, IE incidence due to enterococci has increased [4], which has been seen in other locales in the United States and other countries [5–7]. Furthermore, several studies have shown an overall increase in the incidence of IE [5, 7–9]; however, there was no significant increase in IE incidence in Olmsted County in our most recent evaluation between 2007 and 2013, as compared with that between 1970 and 2006 [4].

In the United States, population-based studies are extremely difficult to perform, as compared with some countries with national patient health record databases. Olmsted County, Minnesota, provides the opportunity to conduct these studies. We sought to provide a variation over time in incidence of IE with a more contemporary analysis to further evaluate the impact, if any, of the 2007 American Heart Association (AHA) IE prevention guidelines on VGS IE incidence that extended our observation period for an additional 5 years. Moreover, we included an examination of seasonality in IE incidence of Olmsted County cases, which had not been done previously and has been of interest in other investigations.

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Open Forum Infectious Diseases®2021

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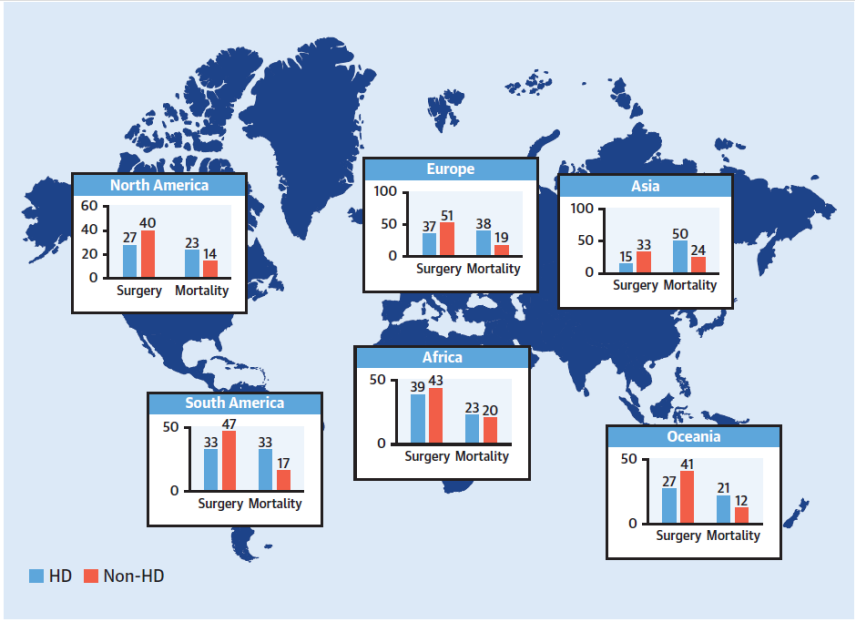
DeSimone D, et al. *Open Forum Infect Dis*. 2021

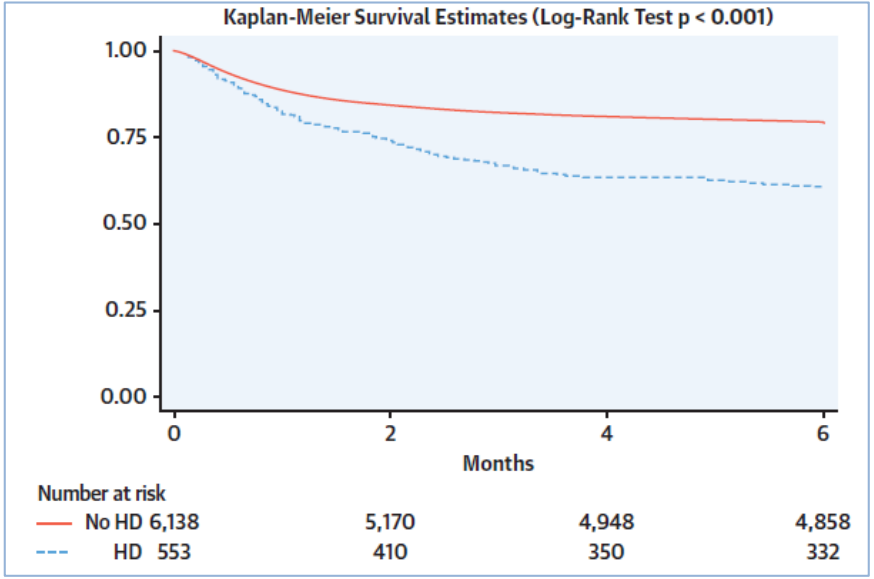
Infective Endocarditis in Patients on Chronic Hemodialysis

- ICE-PCS + ICE-plus cohorts: 6,691 p (553 HD – 6,138 non-HD)
- **HD patients**:
  - Nosocomial acquisition (HD catheter main predisposing factor)
  - *S. aureus* 47.8% / enterococci 15.4%
  - Native valve involvement (77%), Mitral + freq (32%)
  - Lower frequency of surgery
  - More relapses
  - Higher mortality (In-hospital and at 6 months)



Pericàs JM, et al. *J Am Coll Cardiol*. 2021

Infective Endocarditis in Patients on Chronic Hemodialysis



Independent risk factors for mortality (at 6 months):

- Charlson score (HR: 1,26)
- **Stroke (HR: 3,11)**
- Other embolisms (HR: 1,73)
- Persistent bacteraemia (HR: 1,79)
- **Acute Heat Failure (HR: 2,37)**

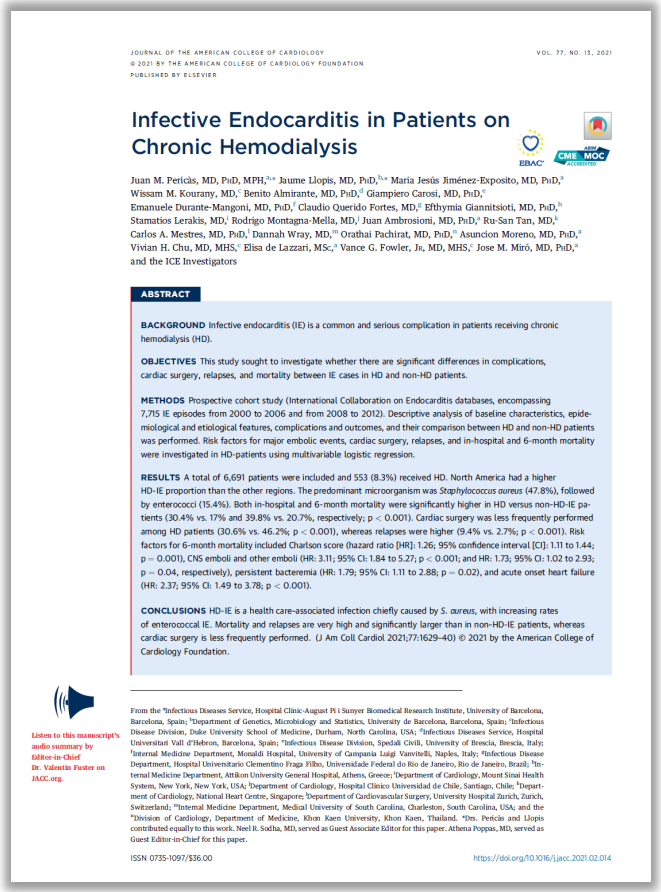
Pericàs JM, et al. *J Am Coll Cardiol*. 2021

Why this paper?

- The largest cohort to date of IE patients on chronic HD

Take-home messages:

- Higher rate of HD-associated IE than in prior series
- The leading causative microorganism is *S. aureus*, with increasing rates of enterococcal IE
- Cardiac surgery rates are lower than in non–HD-IE patients
- Mortality and relapses are very high and significantly greater than in non–HD-IE



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Infective Endocarditis in Patients on Chronic Hemodialysis

Juan M. Pericàs, MD, PhD, MPH,[a,*] Jaume Llopis, MD, PhD,[b,*] Maria Jesús Jiménez-Exposito, MD, PhD,[a] Wissam M. Kourany, MD,[c] Benito Almirante, MD, PhD,[d] Giampiero Carosi, MD, PhD,[e] Emanuele Durante-Mangoni, MD, PhD,[f] Claudio Querido Fortes, MD,[g] Efthymia Giannitsioti, MD, PhD,[h] Stamatios Lerakis, MD,[i] Rodrigo Montagna-Mella, MD,[j] Juan Ambrosioni, MD, PhD,[a] Ru-San Tan, MD,[k] Carlos A. Mestres, MD, PhD,[l] Dannah Wray, MD,[m] Orathai Pachirat, MD, PhD,[n] Asuncion Moreno, MD, PhD,[a] Vivian H. Chu, MD, MHS,[c] Elisa de Lazzari, MSc,[a] Vance G. Fowler, Jr, MD, MHS,[c] Jose M. Miró, MD, PhD,[a] and the ICE Investigators

ABSTRACT

BACKGROUND Infective endocarditis (IE) is a common and serious complication in patients receiving chronic hemodialysis (HD).

OBJECTIVES This study sought to investigate whether there are significant differences in complications, cardiac surgery, relapses, and mortality between IE cases in HD and non-HD patients.

METHODS Prospective cohort study (International Collaboration on Endocarditis databases, encompassing 7,715 IE episodes from 2000 to 2006 and from 2008 to 2012). Descriptive analysis of baseline characteristics, epidemiological and etiological features, complications and outcomes, and their comparison between HD and non-HD patients was performed. Risk factors for major embolic events, cardiac surgery, relapses, and in-hospital and 6-month mortality were investigated in HD-patients using multivariable logistic regression.

RESULTS A total of 6,691 patients were included and 553 (8.3%) received HD. North America had a higher HD-IE proportion than the other regions. The predominant microorganism was *Staphylococcus aureus* (47.8%), followed by enterococci (15.4%). Both in-hospital and 6-month mortality were significantly higher in HD versus non-HD-IE patients (30.4% vs. 17% and 39.8% vs. 20.7%, respectively; $p < 0.001$). Cardiac surgery was less frequently performed among HD patients (30.6% vs. 46.2%; $p < 0.001$), whereas relapses were higher (9.4% vs. 2.7%; $p < 0.001$). Risk factors for 6-month mortality included Charlson score (hazard ratio [HR]: 1.26; 95% confidence interval [CI]: 1.11 to 1.44; $p = 0.001$), CNS emboli and other emboli (HR: 3.11; 95% CI: 1.84 to 5.27; $p < 0.001$; and HR: 1.73; 95% CI: 1.02 to 2.93; $p = 0.04$, respectively), persistent bacteremia (HR: 1.79; 95% CI: 1.11 to 2.88; $p = 0.02$), and acute onset heart failure (HR: 2.37; 95% CI: 1.49 to 3.78; $p < 0.001$).

CONCLUSIONS HD-IE is a health care-associated infection chiefly caused by *S. aureus*, with increasing rates of enterococcal IE. Mortality and relapses are very high and significantly larger than in non-HD-IE patients, whereas cardiac surgery is less frequently performed. (J Am Coll Cardiol 2021;77:1629–40) © 2021 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

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Pericàs JM, et al. *J Am Coll Cardiol*. 2021

Infective endocarditis and solid organ transplantation: Only worse outcomes during initial transplantation hospitalization

AHJ
American Heart Journal
www.ahjonline.com

Nationwide Readmissions Database
N= 99,281,858

Period covered: 2013-2018

Analysis 1

- Less surgery in patients with SOT-IE
- Same mortality as patients with non-SOT-IE

Analysis 2

- More frequent in TCO (45%)
- **Higher mortality in SOT-IE** than in SOT recipients without endocarditis

Eichenberger E, et al. *Am Heart J*. 2021

Why this paper?

- To date, largest study of SOT-IE from a large sample (over one-half of all US hospitalizations)

Take-home messages:

- SOT recipients with IE do not experience worse outcomes than non-SOT recipients with IE
- IE-SOT during index transplant hospitalization leads to greater complications and substantially higher mortality than SOT recipients without IE

Clinical Investigations

Infective endocarditis and solid organ transplantation: Only worse outcomes during initial transplantation hospitalization

Emily M. Eichenberger, MD[a], Michael Dagher, MD[a], Matthew R. Sinclair, MD[b], Stacey A. Maskarinec, MD, PhD[a], Vance G. Fowler Jr., MD, MHS[a], and Jerome J. Federspiel, MD, PhD[c,d] *Durham, North Carolina; Baltimore, MD*

Background The epidemiology, and outcome of infective endocarditis (IE) among solid organ transplant (SOT) recipients is unknown.

Methods We used data from the 2013-2018 Nationwide Readmissions Database (NRD). IE- and SOT-associated hospitalizations were identified using diagnosis and procedure codes. Outcomes included inpatient mortality, length of stay, and inpatient costs. Adjusted analyses were performed using weighted regression models.

Results A total of 99,052 IE-associated hospitalizations, corresponding to a weighted national estimate of 193,164, were included for analysis. Of these, 794 (weighted n = 1,574) were associated with transplant history (SOT-IE). Mortality was not significantly different between SOT-IE and non-SOT-IE (17.2% vs. 15.8%, adjusted relative risk [aRR]: 0.86, 95% confidence interval [CI] [0.71, 1.03]), and fewer SOT-IE patients underwent valve repair or replacement than non-SOT-IE (12.5% vs. 16.2%, aRR 0.82, 95% CI [0.71, 0.95]). We then compared outcomes of patients diagnosed with IE during their index transplant hospitalization (index-SOT-IE) to patients without IE during their transplant hospitalization (index-SOT). Index-SOT-IE occurred most frequently among heart transplant recipients (45.1%), and was associated with greater mortality (27.1% vs. 2.3%, aRR 6.07, 95% CI [3.32, 11.11]).

Conclusion Dual diagnosis of SOT and IE was associated with worse outcomes among SOT recipients during index hospitalization, but not overall among patients with IE. (Am Heart J 2021;240:63–72.)

Infective endocarditis (IE) is a rare but devastating disease. Despite advances in the diagnosis and treatment of IE, mortality remains high. In addition, rates of IE are increasing.[1,2] The rise in IE in the past decade may be due in part to the opioid epidemic[3], as well as the emergence of new risk factors, including increased healthcare contact and immunosuppression.[2]

With over 30,000 solid organ transplants (SOT) performed annually in the United States alone, there is a growing population of immunocompromised patients at increased risk for infection. The prevalence and impact of IE in the SOT population (SOT-IE), however, is unknown. The existing literature is limited to small case series and single center retrospective studies.[4,5,6] The present study uses a large national administrative database to further address these issues. We present the largest study to date investigating the prevalence of IE in SOT recipients. We compare the risk factors, inpatient cost, and mortality of SOT-IE as compared to non-SOT-IE patients in the US. We also investigate the impact of IE on the outcome of SOT recipients during index transplant hospitalization.

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Submitted March 15, 2021; accepted June 16, 2021

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0002-8703

https://doi.org/10.1016/j.ahj.2021.06.007

Methods

Study design, data source and study population

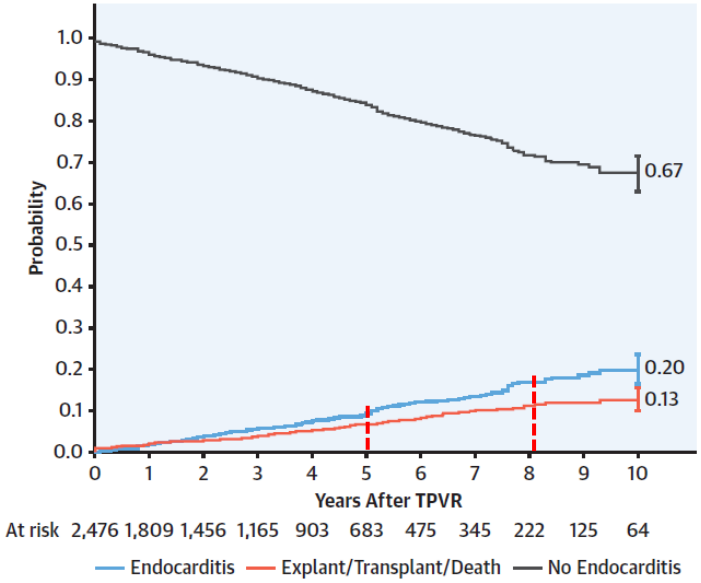
This retrospective cohort study used data from the 2013-2018 Nationwide Readmissions Database (NRD), Healthcare Cost and Utilization Project, United States Agency for Healthcare Research and Quality. The NRD is an all-payer administrative dataset containing most acute care and short stay hospitalizations from participating

Eichenberger E, et al. *Am Heart J*. 2021

Multicenter Study of Endocarditis After Transcatheter Pulmonary Valve Replacement

JACC

- International multicenter study (15 centers)
- From 2005 to 2020. Median follow-up: 2.8 years (IQR: 0.8-5.4)
- 2,476 patients underwent TPVR
  - 2,038: Melody/Medtronic valve
  - 438: Sapien/Edwards valve
- **182 definite or possible IE (7.4%)** → 2.2 IE/100,000 patient-years
- **TPVR-IE risk factors**:
  - Younger age (HR: 0.98)
  - Previous endocarditis (HR: 2.19)
  - High residual gradient (HR: 1.3)
  - **NOT the type of valve**

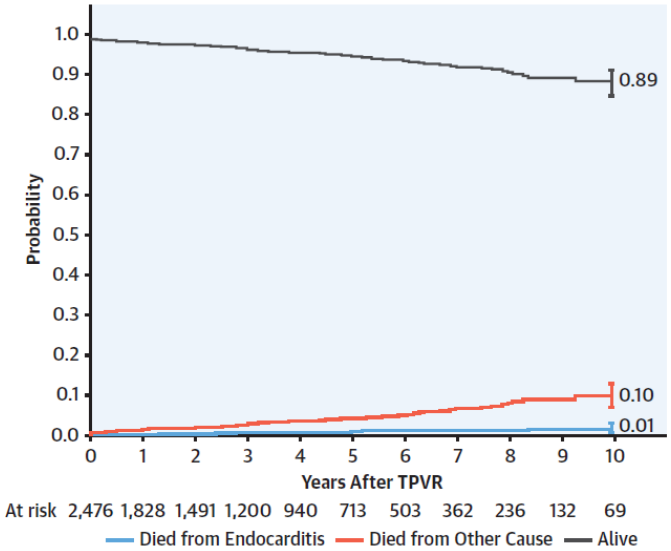


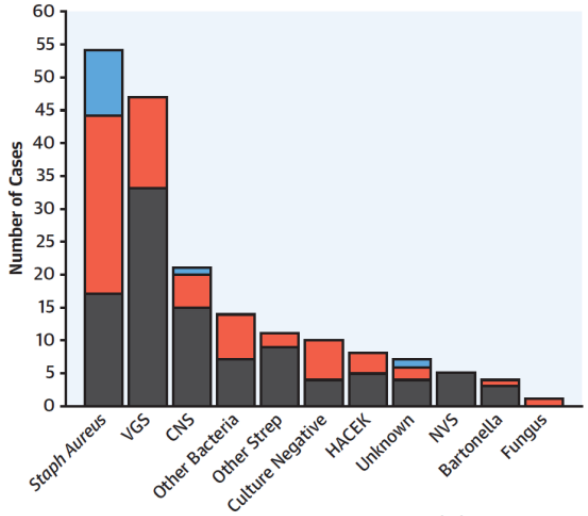
McElhinney D, et al. *J Am Coll Cardiol*. 2021

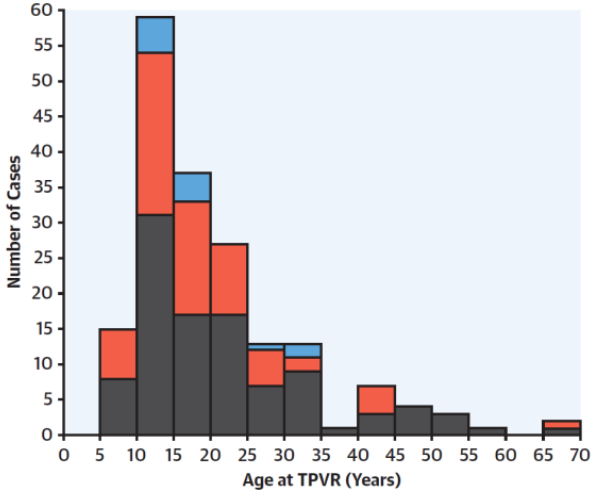
Multicenter Study of Endocarditis After Transcatheter Pulmonary Valve Replacement

JACC

IE-related Mortality: 6.6% (12 pt)







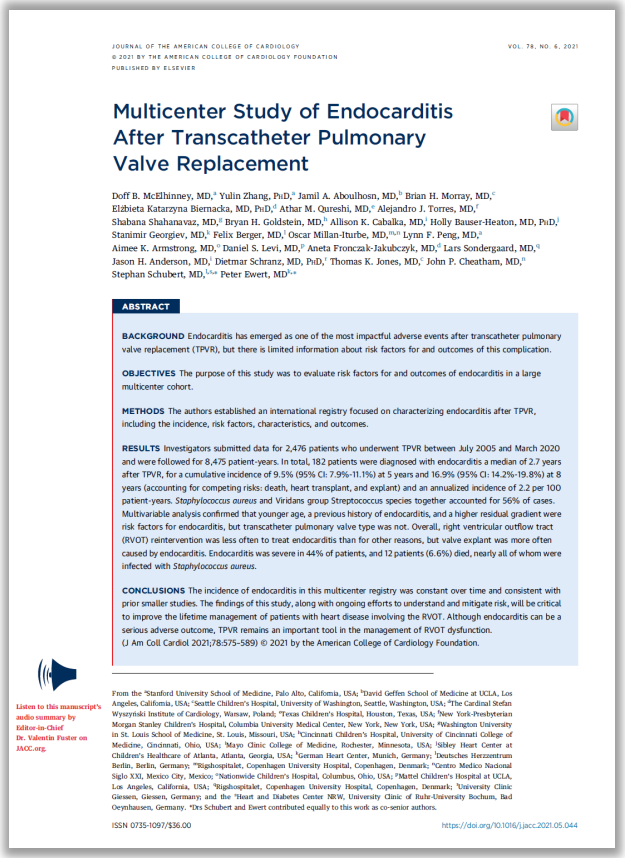
McElhinney D, et al. *J Am Coll Cardiol*. 2021

Why this paper?

- Largest series of TVPR-IE from a multicentre prospective cohort

Take-home messages:

- Incidence: 2.2/100,000 p-y. Risk constant over time
- Some modifiable risk factors
  - Previous IE → relative contraindication?
  - Residual gradient
  - VGS as a second most frequent microorganisms
- High mortality in *S. aureus* infections



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Multicenter Study of Endocarditis After Transcatheter Pulmonary Valve Replacement

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ABSTRACT

BACKGROUND Endocarditis has emerged as one of the most impactful adverse events after transcatheter pulmonary valve replacement (TPVR), but there is limited information about risk factors for and outcomes of this complication.

OBJECTIVES The purpose of this study was to evaluate risk factors for and outcomes of endocarditis in a large multicenter cohort.

METHODS The authors established an international registry focused on characterizing endocarditis after TPVR, including the incidence, risk factors, characteristics, and outcomes.

RESULTS Investigators submitted data for 2,476 patients who underwent TPVR between July 2005 and March 2020 and were followed for 8,475 patient-years. In total, 182 patients were diagnosed with endocarditis a median of 2.7 years after TPVR, for a cumulative incidence of 9.5% (95% CI: 7.9%-11.1%) at 5 years and 16.9% (95% CI: 14.2%-19.8%) at 8 years (accounting for competing risks: death, heart transplant, and explant) and an annualized incidence of 2.2 per 100 patient-years. *Staphylococcus aureus* and Viridans group Streptococcus species together accounted for 56% of cases. Multivariable analysis confirmed that younger age, a previous history of endocarditis, and a higher residual gradient were risk factors for endocarditis, but transcatheter pulmonary valve type was not. Overall, right ventricular outflow tract (RVOT) reintervention was less often to treat endocarditis than for other reasons, but valve explant was more often caused by endocarditis. Endocarditis was severe in 44% of patients, and 12 patients (6.6%) died, nearly all of whom were infected with *Staphylococcus aureus*.

CONCLUSIONS The incidence of endocarditis in this multicenter registry was constant over time and consistent with prior smaller studies. The findings of this study, along with ongoing efforts to understand and mitigate risk, will be critical to improve the lifetime management of patients with heart disease involving the RVOT. Although endocarditis can be a serious adverse outcome, TPVR remains an important tool in the management of RVOT dysfunction.
(J Am Coll Cardiol 2021;78:575–589) © 2021 by the American College of Cardiology Foundation.

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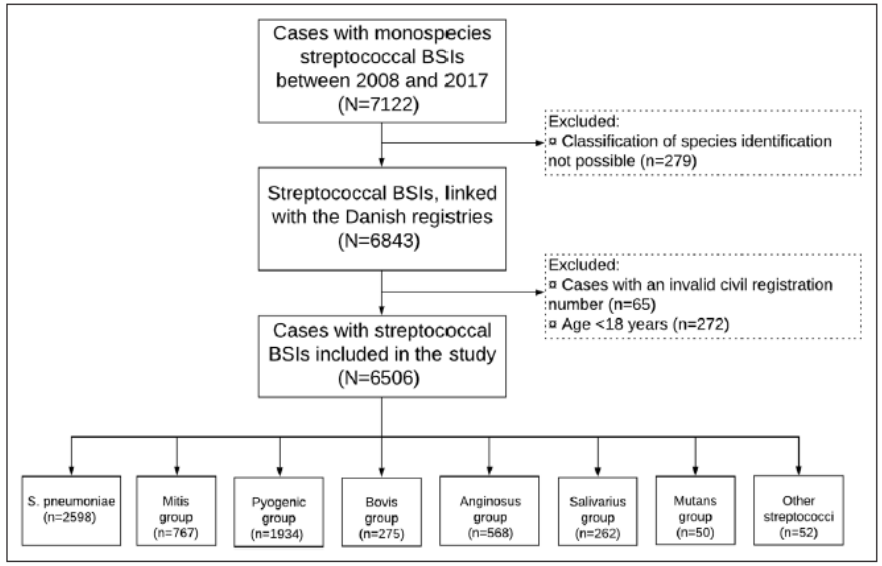
McElhinney D, et al. *J Am Coll Cardiol*. 2021

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

Circulation

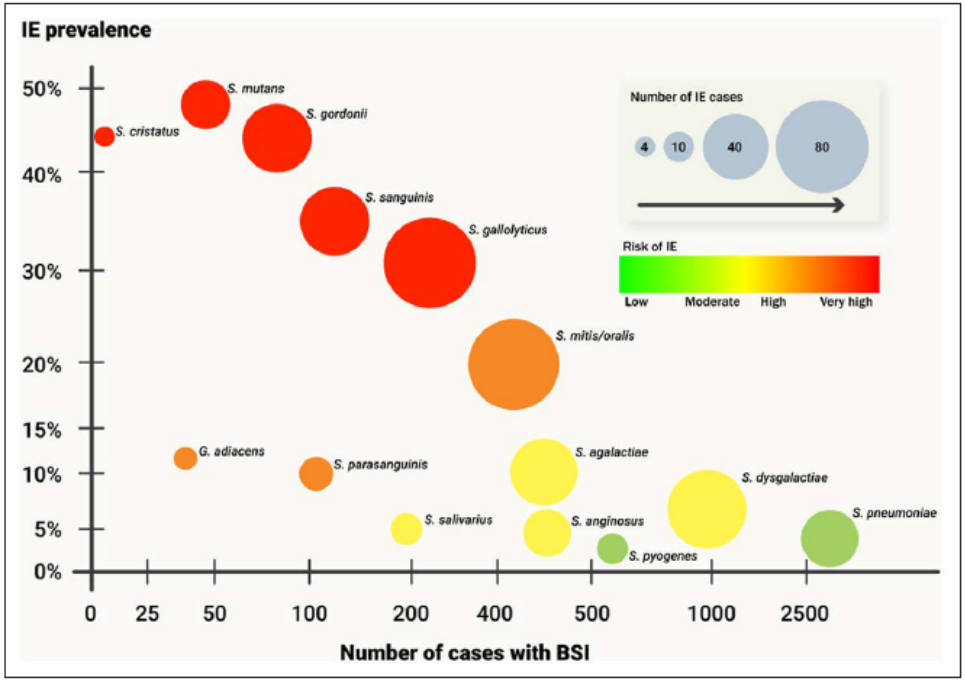
- Data from the Danish National Patient Registry
- Adult patients admitted with monospecies streptococcal BSI in the Capital Region of Denmark between 2008 to 2017
- Identification at species level (Maldi-TOF since 2010)
- Data were crosslinked with Danish nationwide registries for identification of concomitant hospitalization with IE
- The risk of IE according to streptococcal species was evaluated by a multivariable logistic regression analysis

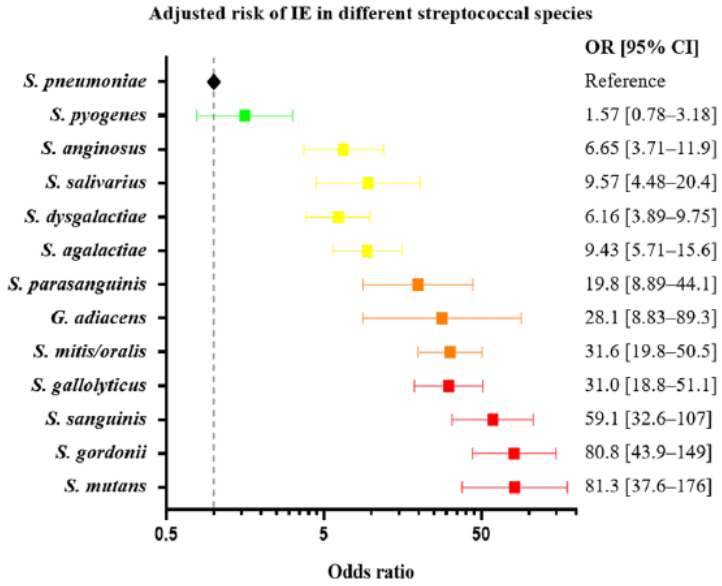


Chamat-Hedemand S, et al. *Circulation*. 2020

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

Circulation





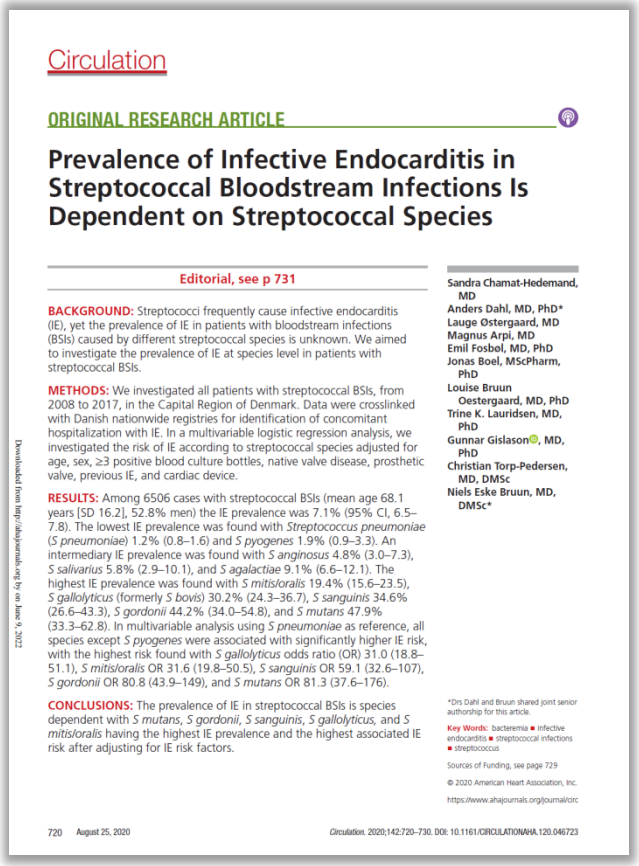
Chamat-Hedemand S, et al. *Circulation*. 2020

Why this paper?

- Extensive and deep analysis of IE risk according to Streptococcal species, adjusted for confounders

Take-home messages:

- The most common streptococcal BSIs had a relatively low prevalence of IE
- Substantial variation in IE prevalence within streptococcal groups
  - The risk of IE should be evaluated **on species level**



Circulation

ORIGINAL RESEARCH ARTICLE

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

Editorial, see p 731

Sandra Chamat-Hedemand, MD
Anders Dahl, MD, PhD*
Lauge Østergaard, MD
Magnus Arpi, MD
Emil Fosbøl, MD, PhD
Jonas Boel, MScPharm, PhD
Louise Bruun Oestergaard, MD, PhD
Trine K. Lauridsen, MD, PhD
Gunnar Gislason, MD, PhD
Christian Torp-Pedersen, MD, DMSc
Niels Eske Bruun, MD, DMSc*

BACKGROUND: Streptococci frequently cause infective endocarditis (IE), yet the prevalence of IE in patients with bloodstream infections (BSIs) caused by different streptococcal species is unknown. We aimed to investigate the prevalence of IE at species level in patients with streptococcal BSIs.

METHODS: We investigated all patients with streptococcal BSIs, from 2008 to 2017, in the Capital Region of Denmark. Data were crosslinked with Danish nationwide registries for identification of concomitant hospitalization with IE. In a multivariable logistic regression analysis, we investigated the risk of IE according to streptococcal species adjusted for age, sex, ≥3 positive blood culture bottles, native valve disease, prosthetic valve, previous IE, and cardiac device.

RESULTS: Among 6506 cases with streptococcal BSIs (mean age 68.1 years [SD 16.2], 52.8% men) the IE prevalence was 7.1% (95% CI, 6.5–7.8). The lowest IE prevalence was found with *Streptococcus pneumoniae* (*S pneumoniae*) 1.2% (0.8–1.6) and *S pyogenes* 1.9% (0.9–3.3). An intermediary IE prevalence was found with *S anginosus* 4.8% (3.0–7.3), *S salivarius* 5.8% (2.9–10.1), and *S agalactiae* 9.1% (6.6–12.1). The highest IE prevalence was found with *S mitis/oralis* 19.4% (15.6–23.5), *S gallolyticus* (formerly *S bovis*) 30.2% (24.3–36.7), *S sanguinis* 34.6% (26.6–43.3), *S gordonii* 44.2% (34.0–54.8), and *S mutans* 47.9% (33.3–62.8). In multivariable analysis using *S pneumoniae* as reference, all species except *S pyogenes* were associated with significantly higher IE risk, with the highest risk found with *S gallolyticus* odds ratio (OR) 31.0 (18.8–51.1), *S mitis/oralis* OR 31.6 (19.8–50.5), *S sanguinis* OR 59.1 (32.6–107), *S gordonii* OR 80.8 (43.9–149), and *S mutans* OR 81.3 (37.6–176).

CONCLUSIONS: The prevalence of IE in streptococcal BSIs is species dependent with *S mutans*, *S gordonii*, *S sanguinis*, *S gallolyticus*, and *S mitis/oralis* having the highest IE prevalence and the highest associated IE risk after adjusting for IE risk factors.

*Drs Dahl and Bruun shared joint senior authorship for this article.

Key Words: bacteremia ■ infective endocarditis ■ streptococcal infections ■ streptococcus

Sources of Funding, see page 729

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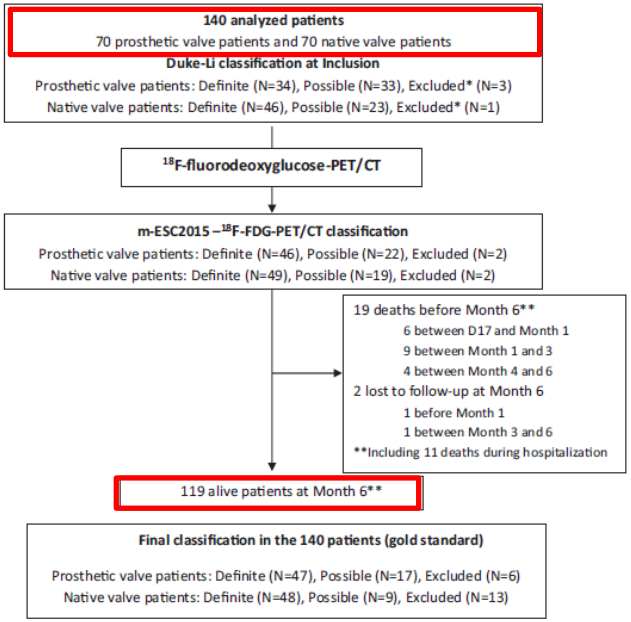
Chamat-Hedemand S, et al. *Circulation*. 2020

Impact of Systematic Whole-body ^{18}F-Fluorodeoxyglucose PET/CT on the Management of Patients Suspected of Infective Endocarditis: The Prospective Multicenter TEPvENDO Study

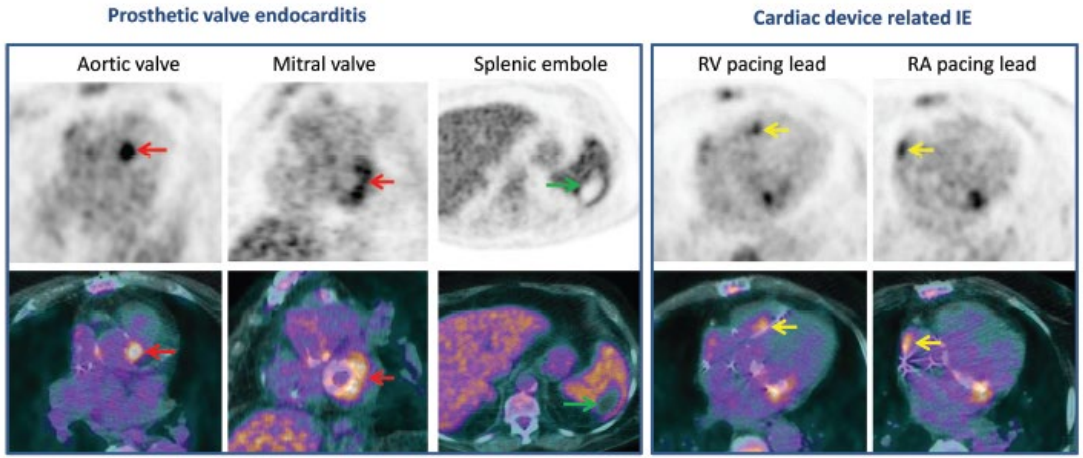
Clinical Infectious Diseases

MAJOR ARTICLE

Multicenter study (8 French hospitals)



Change in Dx classification → 24.3% (PVE) and 5.7% (NVE)



Duval X, et al. *Clin Infect Dis*. 2021

Impact of Systematic Whole-body ^{18}F-Fluorodeoxyglucose PET/CT on the Management of Patients Suspected of Infective Endocarditis: The Prospective Multicenter TEPvENDO Study

Clinical Infectious Diseases

MAJOR ARTICLE

Modifications in management:

- 21.4% (PVE)
- **31.4% (NVE)**

	PVE	NVE
ATB Treatment	7	**11**
Cardiac surgery	3	3
Both treatments	3	5
Anticoagulation	1	1
Other	1	2
Total	**15**	**22**

	Patients Who Did Not Benefit From ^{18}F-FDG-PET/CT	Patients Who Benefit From ^{18}F-FDG-PET/CT	*P*-value
	n=84	n=56	
Age, median (IQR)	67 (56.75–76.25)	66.5 (56.75–78.25)	.79
Male, n (%)	61 (72.6)	43 (76.8)	.69
Diabetes, n (%)	14 (16.7)	15 (26.8)	.20
Nature of the cardiac valve			.63
Native valve, **n (%)**	43 (51.8)	27 (50.0)	
Bioprosthesis valve, **n (%)**	24 (28.9)	13 (24.1)	
Mechanical valve, **n (%)**	16 (19.3)	14 (25.9)	
Causative microorganisms			.51
Staphylococcus aureus	16 (19.1)	10 (17.9)	
Coagulase-negative staphylococci	10 (11.9)	7 (12.5)	
Oral streptococci	12 (14.3)	13 (23.2)	
Streptococcus bovis	5 (5.9)	6 (10.7)	
Enterococcus	8 (9.5)	4 (7.1)	
HACEK	3 (3.6)	2 (3.6)	
Other	13 (15.5)	10 (17.9)	
Negative blood cultures	17 (20.2)	4 (7.1)	
Echocardiography			
Noncontributing echocardiography[a]	22 (26.2)	34 (60.7)	**<.001**
Duke-Li classification at inclusion[c]			
Definite	55 (65.5)	25 (44.6)	
Possible	27 (32.1)	29 (51.8)	**.04** [b]
Excluded[c]	2 (2.4)	2 (3.6)	

Duval X, et al. *Clin Infect Dis*. 2021

Why this paper?

- Prospective multicentre study evaluating the usefulness of systematic PET-CT in IE patients

Take-home messages:

- The overall impact of PET-CT was independent of the nature of the valve (native or prosthetic)

Clinical Infectious Diseases
MAJOR ARTICLE

Impact of Systematic Whole-body ^{18}F-Fluorodeoxyglucose PET/CT on the Management of Patients Suspected of Infective Endocarditis: The Prospective Multicenter TEPvENDO Study

Xavier Duval,[1,2,3,4] Vincent Le Moing,[5] Sarah Tubiana,[1,2,3] Marina Esposito-Farèse,[1,2,6] Emila Ilic-Habensus,[1,2] Florence Leclercq,[7] Aurélie Bourdon,[8] François Goehringer,[9] Christine Selton-Suty,[10] Elodie Chevalier,[11] David Boutoille,[12] Nicolas Péricé,[13,14] Thierry Le Tourneau,[15] Catherine Chirouze,[16] Marie-France Seronde,[16] Olivier Morel,[17] Lionel Piroth,[18] Jean-Christophe Eicher,[19] Olivier Humbert,[20] Matthieu Revest,[21,22] Elise Thébault,[23] Anne Devillers,[24] François Delahaye,[25] André Boibieux,[26] Bastien Grégoire,[26] Bruno Hoen,[3] Cédric Leouenan,[1,2,3,4,a] Bernard Iung,[1,2,3,4,a] and François Rouzet[1,2,3,4,27,a], for the AEPEI-TEPvENDO study group

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(See the Editorial Commentary by Rojas-Moreno on pages 404–5.)

Background. Diagnostic and patients' management modifications induced by whole-body ^{18}F-FDG-PET/CT had not been evaluated so far in prosthetic valve (PV) or native valve (NV) infective endocarditis (IE)-suspected patients.

Methods. In sum, 140 consecutive patients in 8 tertiary care hospitals underwent ^{18}F-FDG-PET/CT. ESC-2015-modified Duke criteria and patients' management plan were established jointly by 2 experts before ^{18}F-FDG-PET/CT. The same experts reestablished Duke classification and patients' management plan immediately after qualitative interpretation of ^{18}F-FDG-PET/CT. A 6-month final Duke classification was established.

Results. Among the 70 PV and 70 NV patients, 34 and 46 were classified as definite IE before ^{18}F-FDG-PET/CT. Abnormal perivalvular ^{18}F-FDG uptake was recorded in 67.2% PV and 24.3% NV patients respectively ($P < .001$) and extracardiac uptake in 44.3% PV and 51.4% NV patients. IE classification was modified in 24.3% and 5.7% patients ($P = .005$) (net reclassification index 20% and 4.3%). Patients' managements were modified in 21.4% PV and 31.4% NV patients ($P = .25$). It was mainly due to perivalvular uptake in PV patients and to extra-cardiac uptake in NV patients and consisted in surgery plan modifications in 7 patients, antibiotic plan modifications in 22 patients and both in 5 patients. Altogether, ^{18}F-FDG-PET/CT modified classification and/or care in 40% of the patients (95% confidence interval: 32–48), which was most likely to occur in those with a noncontributing echocardiography ($P < .001$) or IE classified as possible at baseline ($P = .04$), while there was no difference between NV and PV.

Conclusions. Systematic ^{18}F-FDG-PET/CT did significantly and appropriately impact diagnostic classification and/or IE management in PV and NV-IE suspected patients.

Clinical Trials Registration. NCT02287792.

Keywords. ^{18}F-FDG-PET/CT; infective endocarditis; diagnostic impact; patient management.

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[a]C. L., B. I., and F. R. contributed equally.

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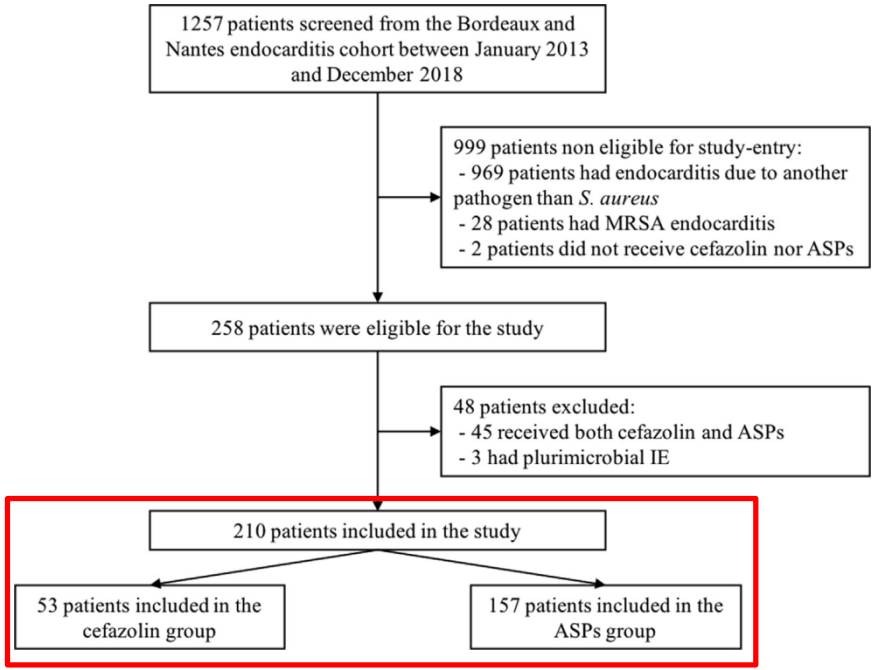
Infective endocarditis (IE) diagnosis is often challenging, particularly when the causative microorganism is difficult to identify and/or when echocardiography is noncontributing [1, 2]. In such situations, guidelines recommend resorting to other imaging techniques to confirm or exclude valve involvement and/or search for clinically silent IE extracardiac manifestations [3, 4]. These investigations may help practitioners establish or rule out the IE diagnosis and adapt also patients' management,

Duval X, et al. *Clin Infect Dis*. 2021

Comparative outcomes of cefazolin versus antistaphylococcal penicillins in methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a *post hoc* analysis of a prospective multicentre French cohort study

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

- French multicentre study (2013-2018)
- Retrospective analysis of prospectively obtained data
- Patients with MSSA definite IE treated either with cefazolin or ASPs
- **Primary end-point**: 90-day mortality (any cause)
- **Statistical analysis**: uni and MV analysis (binary logistic regression)



Lecomte R, et al. *Clin Microbiol Infect*. 2021

Characteristic	Overall ($n = 210$)	Cefazolin ($n = 53$)	ASP ($n = 157$)	p
Aminoglycoside	164 (78.1)	33 (62.3)	131 (83.4)	0.002
Modified ICU admission[e]	71 (33.8)	11 (20.8)	60 (38.2)	0.031
Sepsis	49 (23.3)	7 (13.2)	42 (26.8)	0.068

90-day all-cause mortality: 27.6%

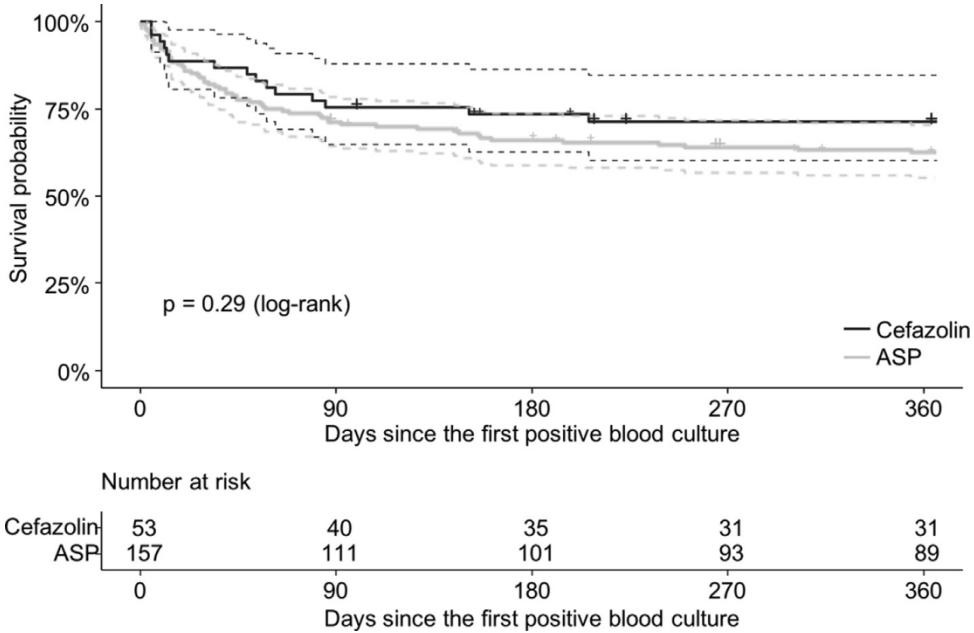
Association with ATB treatment (cefazolin vs. ASP):

Univariate analysis:

24.5% (13/53) vs. 28.7% (45/157); *p*=0.561

Multivariate analysis :

ORa 1.2 (95% IC: 0.49-2.91); *p*=0.681



Lecomte R, et al. *Clin Microbiol Infect*. 2021

Comparative outcomes of cefazolin versus antistaphylococcal penicillins in methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a *post hoc* analysis of a prospective multicentre French cohort study

CMI CLINICAL MICROBIOLOGY AND INFECTION
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Outcome	Overall ($n = 210$)	Cefazolin ($n = 53$)	Oxacillin or cloxacillin ($n = 157$)	p
Secondary outcomes				
Length of stay (days), median (IQR)[a]	36 (18–53)	33.5 (16–52)	38 (18–54)	0.240
90-day unplanned valvular surgery[b]	77 (36.7)	19 (35.8)	58 (36.9)	0.886
Receiving treatment for embolism	22 (10.5)	2 (3.8)	20 (12.7)	0.073
Duration of bacteraemia (days), median (IQR)	3 (1–5)	3 (0–5)	3 (1–5)	0.557
Persistently positive blood cultures >72 hours while receiving treatment[c]	57/201 (28.4)	13/51 (25.5)	44/150 (29.3)	0.729
Discontinuation[d]	13 (6.2)	0 (0.0)	13 (8.3)	0.042
Relapse	4/194 (2.6)	0/44 (0.0)	4/148 (2.7)	0.574
One-year all-cause mortality	73/194 (37.6)	15/44 (34.1)	58/147 (39.5)	0.421

Lecomte R, et al. *Clin Microbiol Infect*. 2021

Why this paper?

- First prospective comparison between ASPs and cefazolin, specifically in patients with IE (relatively large cohort)

Take-home messages:

- Cefazolin is apparently as effective yet less toxic than ASPs

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Original article

Comparative outcomes of cefazolin versus antistaphylococcal penicillins in methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a *post hoc* analysis of a prospective multicentre French cohort study

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Inoculum effect
Staphylococcus aureus

ABSTRACT

Objectives: Current guidelines recommend cefazolin as an alternative to antistaphylococcal penicillins (ASPs) in methicillin-susceptible Staphylococcus aureus (MSSA) infective endocarditis despite the lack of comparative study. The objective of this study was to evaluate the comparative outcomes of cefazolin vs. ASPs in MSSA infective endocarditis.
Methods: This was a retrospective analysis of an observational multicentre cohort study using prospectively collected data from patients with MSSA endocarditis confirmed by endocarditis team and treated either with cefazolin or ASPs between July 2013 and December 2018. Patients were excluded if they received both treatments. The primary outcome was 90-day all-cause mortality.
Results: Of 210 patients included, 53 patients (25.2%) received cefazolin and 157 (74.8%) received ASPs. The overall 90-day mortality rate was 27.6% (58/210 patients), 24.5% (13/53) in the cefazolin group vs. 28.7% (45/157) in the ASP group (p 0.561). Premature antimicrobial discontinuation due to adverse events occurred less frequently with cefazolin than with ASPs (0/53 vs. 13/157 patients; p 0.042). In multivariate analysis, there was no difference in 90-day mortality between cefazolin and ASPs (adjusted odds ratio (aOR), 1.2; 95% confidence interval (CI), 0.49–2.91; p 0.681), while age (aOR, 1.06; 95% CI, 1.03–1.09; p < 0.001), Charlson comorbidity index (aOR, 1.18; 95% CI, 1.02–1.36 p 0.023), cerebral embolism (aOR, 2.83; 95% CI, 1.33–6.14; p 0.007) and intensive care unit admission (aOR, 4.16; 95% CI, 1.89–9.59; p 0.001) were factors significantly associated with higher mortality.
Conclusions: Cefazolin seems to be a possible alternative to ASPs in MSSA endocarditis. More studies are needed to confirm these results and determine which treatment should be recommended as first-line therapy. **Raphaël Lecomte, Clin Microbiol Infect 2021;27:1015**

Introduction

Staphylococcus aureus is the leading cause of infective endocarditis (IE), whether on native or prosthetic valves, and is associated with higher mortality and embolic events rates than other microorganism [1–4]. Cefazolin, an intravenous first-generation cephalosporin, is used in the management of methicillin-

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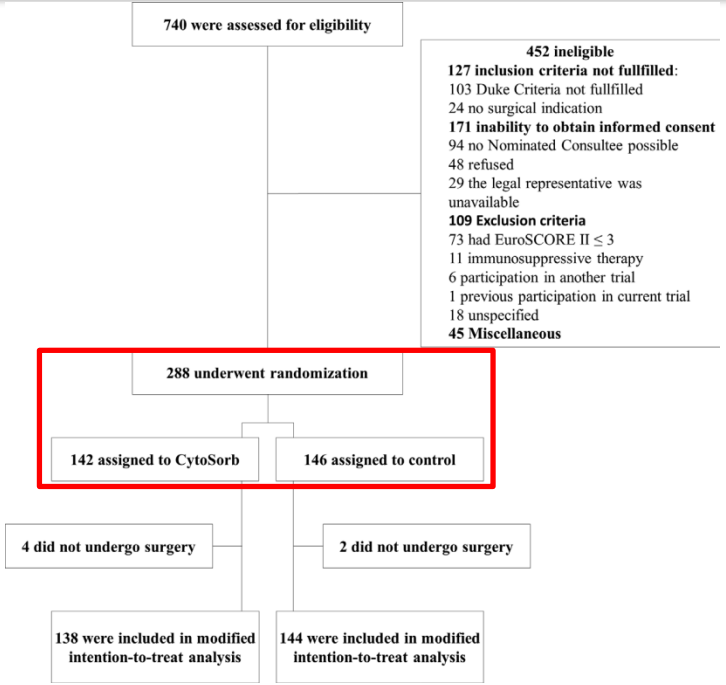
Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial

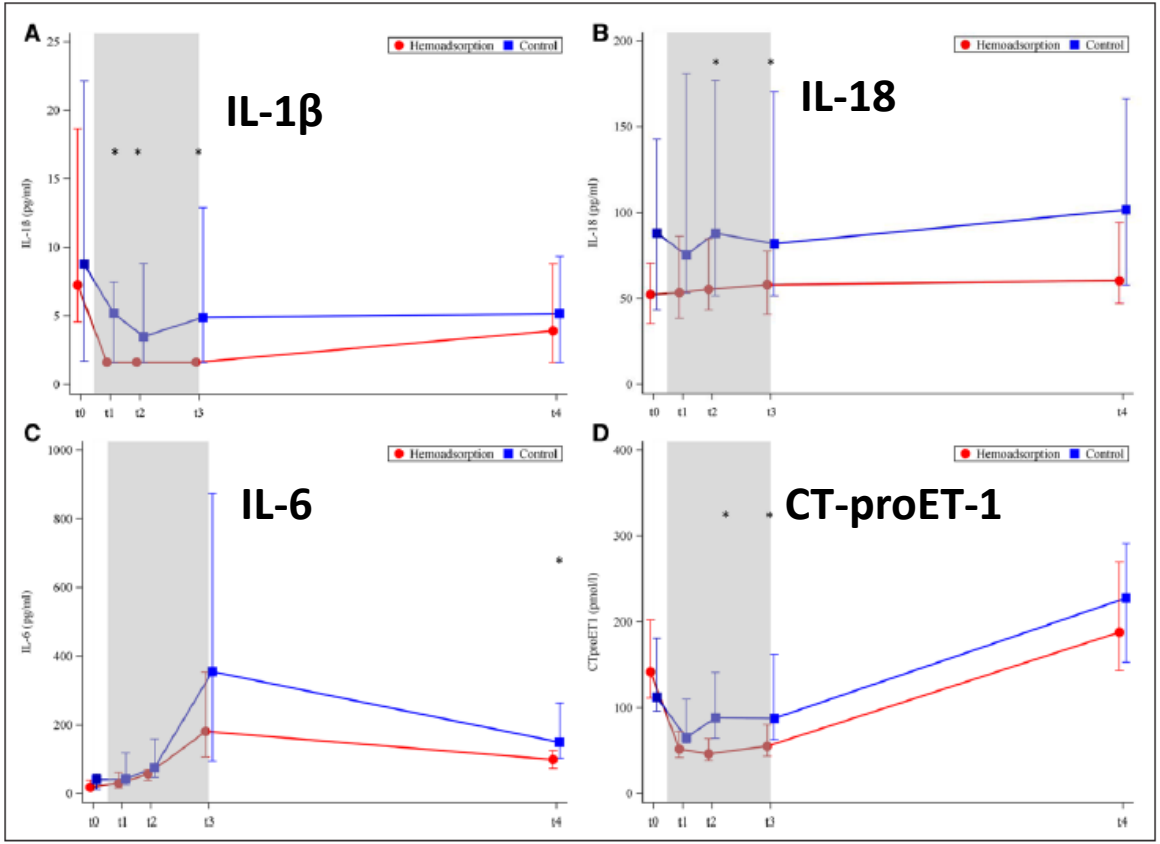
Circulation

- **REMOVE trial** (Revealing Mechanisms and Investigating Efficacy of Hemoadsorption for Prevention of Vasodilatory Shock in Cardiac Surgery Patients With Infective Endocarditis)
- Multicenter (14 cardiac surgery centers in Germany) randomized, non-blinded, controlled trial with 2 groups designed for assessing superiority
- Patients undergoing cardiac surgery for IE were randomly assigned to receive hemoadsorption during cardiopulmonary bypass using CytoSorb or to the control group.
- **Primary outcome:** change in sequential organ failure assessment score [ΔSOFA]

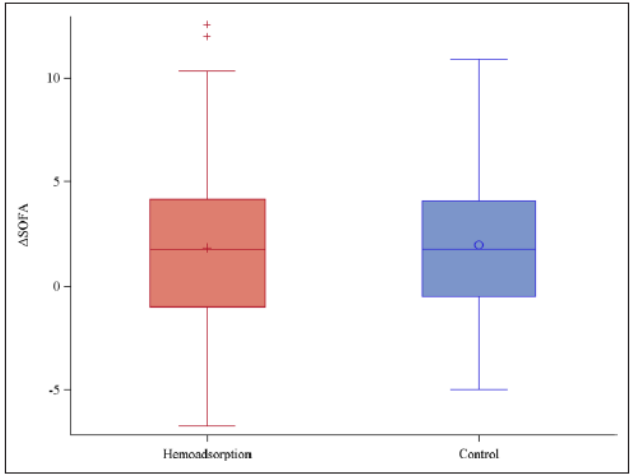


Diab M, et al. *Circulation*. 2022

Intraoperative and postoperative plasma levels of citokynes



Primary Outcome: Δ SOFA



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Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial

Circulation

Table 2. Secondary Outcomes

Outcomes	Hemoadsorption group (n=138)	Control group (n=144)	*P* value	Difference (95% CI)*
30-day mortality	29 (21.0)	32 (22.4)	0.782	0.94 (0.60–1.47)
Postoperative stroke	5 (3.6)	3 (2.1)	0.442	1.73 (0.42–7.09)
Hospital stay, d	20 (13–30)	19 (12–29)	0.392	1 (0–2)
ICU stay, d	7 (3–12)	6 (3–10)	0.241	1 (0–2)
Duration of postoperative hemodialysis, d	0 (0–1)	0 (0–2)	0.791	0 (0–0)
Duration of postoperative ventilation, d	1 (0–7)	1 (0–3)	0.165	0.5 (0–1)
Duration of postoperative vasopressors therapy, d	3 (1–8)	3 (1–7)	0.896	0 (−1–1)
Δ SOFA: CVS subscore	1.57±1.52	1.67±1.49	0.841	−0.04 (−0.39 to 0.32)
Δ SOFA: CNS subscore	0.16±0.54	0.19±0.40	0.560	−0.04 (−0.16 to 0.09)
Δ SOFA: coagulation subscore	0.52±0.88	0.50±0.83	0.487	−0.08 (−0.31 to 0.15)
Δ SOFA: hepatic subscore	0.42±0.84	0.46±0.82	0.840	−0.02 (−0.27 to 0.22)
Δ SOFA: renal subscore	−1.86±1.94	−1.93±1.73	0.392	−0.16 (−0.54 to 0.22)
Δ SOFA: respiratory subscore	0.94±1.29	0.85±1.22	0.662	−0.05 (−0.27 to 0.17)

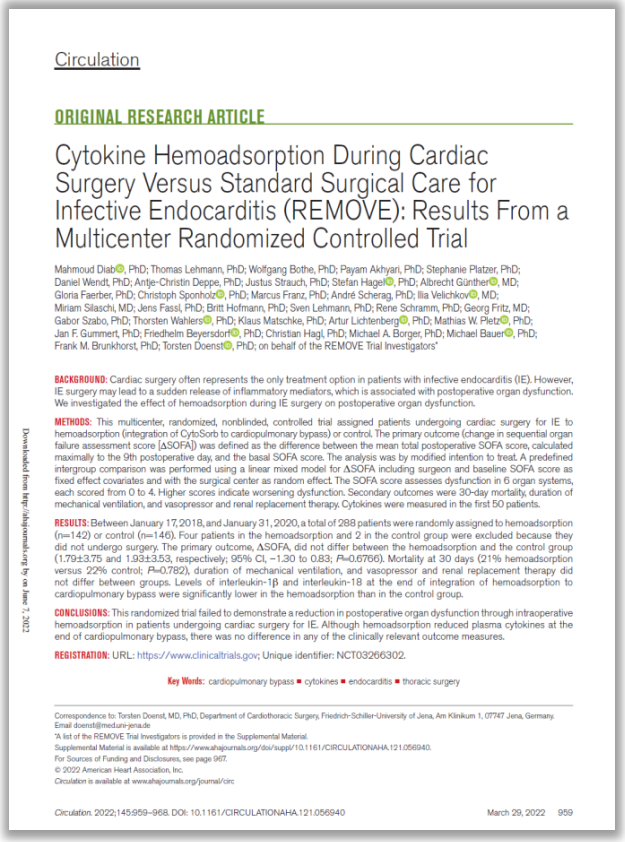
Diab M, et al. *Circulation*. 2022

Why this paper?

- Clinical trial that randomised almost 290 patients with IE and surgical indication

Take-home messages:

- Hemoadsorption reduced plasma cytokines at the end of cardiopulmonary bypass
- There was no difference in any of the clinically relevant outcome measures



Circulation

ORIGINAL RESEARCH ARTICLE

Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial

Mahmoud Diab, PhD; Thomas Lehmann, PhD; Wolfgang Bothe, PhD; Payam Akhyari, PhD; Stephanie Platzer, PhD; Daniel Wendt, PhD; Antje-Christin Deppe, PhD; Justus Strauch, PhD; Stefan Hagel, PhD; Albrecht Günther, MD; Gloria Faerber, PhD; Christoph Sponholz, PhD; Marcus Franz, PhD; André Scherag, PhD; Ilia Velichkov, MD; Miriam Silaschi, MD; Jens Fassl, PhD; Britt Hofmann, PhD; Sven Lehmann, PhD; Rene Schramm, PhD; Georg Fritz, MD; Gabor Szabo, PhD; Thorsten Wahlers, PhD; Klaus Matschke, PhD; Artur Lichtenberg, PhD; Mathias W. Pletz, PhD; Jan F. Gummert, PhD; Friedhelm Beyersdorf, PhD; Christian Hagl, PhD; Michael A. Borger, PhD; Michael Bauer, PhD; Frank M. Brunkhorst, PhD; Torsten Doenst, PhD; on behalf of the REMOVE Trial Investigators*

BACKGROUND: Cardiac surgery often represents the only treatment option in patients with infective endocarditis (IE). However, IE surgery may lead to a sudden release of inflammatory mediators, which is associated with postoperative organ dysfunction. We investigated the effect of hemoadsorption during IE surgery on postoperative organ dysfunction.

METHODS: This multicenter, randomized, nonblinded, controlled trial assigned patients undergoing cardiac surgery for IE to hemoadsorption (integration of CytoSorb to cardiopulmonary bypass) or control. The primary outcome (change in sequential organ failure assessment score [ΔSOFA]) was defined as the difference between the mean total postoperative SOFA score, calculated maximally to the 9th postoperative day, and the basal SOFA score. The analysis was by modified intention to treat. A predefined intergroup comparison was performed using a linear mixed model for ΔSOFA including surgeon and baseline SOFA score as fixed effect covariates and with the surgical center as random effect. The SOFA score assesses dysfunction in 6 organ systems, each scored from 0 to 4. Higher scores indicate worsening dysfunction. Secondary outcomes were 30-day mortality, duration of mechanical ventilation, and vasopressor and renal replacement therapy. Cytokines were measured in the first 50 patients.

RESULTS: Between January 17, 2018, and January 31, 2020, a total of 288 patients were randomly assigned to hemoadsorption (n=142) or control (n=146). Four patients in the hemoadsorption and 2 in the control group were excluded because they did not undergo surgery. The primary outcome, ΔSOFA, did not differ between the hemoadsorption and the control group (1.79±3.75 and 1.93±3.53, respectively; 95% CI, −1.30 to 0.83; P=0.6766). Mortality at 30 days (21% hemoadsorption versus 22% control; P=0.782), duration of mechanical ventilation, and vasopressor and renal replacement therapy did not differ between groups. Levels of interleukin-1β and interleukin-18 at the end of integration of hemoadsorption to cardiopulmonary bypass were significantly lower in the hemoadsorption than in the control group.

CONCLUSIONS: This randomized trial failed to demonstrate a reduction in postoperative organ dysfunction through intraoperative hemoadsorption in patients undergoing cardiac surgery for IE. Although hemoadsorption reduced plasma cytokines at the end of cardiopulmonary bypass, there was no difference in any of the clinically relevant outcome measures.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03266302.

Key Words: cardiopulmonary bypass ▪ cytokines ▪ endocarditis ▪ thoracic surgery

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*A list of the REMOVE Trial Investigators is provided in the Supplemental Material.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.121.056940.
For Sources of Funding and Disclosures, see page 967.

Circulation is available at www.ahajournals.org/journal/circ

Diab M, et al. *Circulation*. 2022

Editor's Choice – Validation of the Management of Aortic Graft Infection Collaboration (MAGIC) Criteria for the Diagnosis of Vascular Graft/Endograft Infection: Results from the Prospective Vascular Graft Cohort Study

MAGIC criteria

Lyon O, et al. *Eur J Vasc Endovasc Surg*. 2016

	CLINICAL / SURGICAL	RADIOLOGY	LABORATORY
MAJOR CRITERIA	• Pus (confirmed by microscopy) around graft or in aneurysm sac at surgery • Open wound with exposed graft or communicating sinus • Fistula development e.g. aorto-enteric or aorto-bronchial • Graft insertion in an infected site e.g. fistula, mycotic aneurysm or infected pseudoaneurysm	• Peri-graft fluid on CT scan ≥ 3 months after insertion • Peri-graft gas on CT scan ≥ 7 weeks after insertion • Increase in peri-graft gas volume demonstrated on serial imaging	• Organisms recovered from an explanted graft • Organisms recovered from an intra-operative specimen • Organisms recovered from a percutaneous, radiologically-guided aspirate of peri-graft fluid
MINOR CRITERIA	• Localized clinical features of AGI e.g. erythema, warmth, swelling, purulent discharge, pain • Fever ≥38°C with AGI as most likely cause	• Other e.g. suspicious peri-graft gas/fluid/soft tissue inflammation; aneurysm expansion; pseudoaneurysm formation; focal bowel wall thickening; discitis/ osteomyelitis; suspicious metabolic activity on FDG PET/ CT; radiolabelled leukocyte uptake	• Blood culture(s) positive and no apparent source except AGI • Abnormally elevated inflammatory markers with AGI as most likely cause e.g. ESR, CRP, white cell count

- **VASGRA** is an open, prospective, observational cohort study of adults receiving vascular graft implantations at the University Hospital Zurich, Switzerland
- Patients included between 2013 and 2019 in the VASGRA cohort were analyzed:
  - 257 patients (137/53% with infected prostheses)

This cohort was used to validate the MAGIC criteria

Anagnostopoulos A, et al. *Eur J Vasc Endovasc Surg*. 2021

Table 3. Comparison of infection status according to the Vascular Graft Infection Cohort Study (VASGRA) and Management of Aortic Graft Infection Collaboration (MAGIC) adjudication in 137 patients with and 120 patients without vascular graft/endograft infection (VGEI)

MAGIC adjudication	VASGRA adjudication				Total
	Confirmed VGEI	Suspected VGEI	Rejected VGEI	Control patients	
Confirmed VGEI	126 (93.3)	1 (50)	5 (14)	3 (3)	135 (52.5)
Suspected VGEI	8 (5.9)	1 (50)	25 (71)	14 (16)	48 (18.7)
Excluded VGEI	1 (0.7)	0 (0)	5 (14)	0 (0)	6 (2.3)
Control patients	0 (0)	0 (0)	0 (0)	68 (80)	68 (26.4)
Total	135 (100)	2 (100)	35 (100)	85 (100)	257 (100)

Overestimation of suspected VGEI

Table 4. Accuracy of Management of Aortic Graft Infection Collaboration (MAGIC) criteria by graft location depending on the composition of "diseased" and "not diseased" groups in 257 patients with or without vascular graft/endograft infection (VGEI)

	Sensitivity (95% CI) — %	Specificity (95% CI) — %
"Diseased" = definite and suspected VGEI; "not diseased" = rejected VGEI and controls		
Overall	99 (96–100)	61 (52–70)
Intracavitary abdominal VGEI	100 (93–100)	62 (51–72)
Thoracic aorta VGEI	98 (88–100)	42 (15–72)
Peripheral arteries VGEI	NA	N/A
"Diseased" = definite VGEI; "not diseased" = suspected VGEI, rejected VGEI, and controls		
Overall	93 (88–97)	93 (87–97)
Intracavitary abdominal VGEI	94 (84–99)	92 (85–96)
Thoracic aorta VGEI	86 (73–95)	100 (74–100)
Peripheral arteries VGEI	100 (91–100)	67 (9.0–99)

Anagnostopoulos A, et al. *Eur J Vasc Endovasc Surg*. 2021

Why this paper?

- VASGRA is an homogeneous cohort: patients are followed up prospectively and undergo an exhaustive and methodical diagnostic workup

Take-home messages:

- In patients with definite infection, the MAGIC criteria offered a good sensitivity but a reduced specificity
- Using the MAGIC criteria led to an overestimation of suspected VGEI

Vascular Infection

Eur J Vasc Endovasc Surg (2021) 62, 251–257

EJVES Open Access

Editor's Choice – Validation of the Management of Aortic Graft Infection Collaboration (MAGIC) Criteria for the Diagnosis of Vascular Graft/Endograft Infection: Results from the Prospective Vascular Graft Cohort Study

Alexia Anagnostopoulos [a,**,†], Fabienne Mayer [a,†], Bruno Ledergerber [a], Judith Bergadà-Pijuan [a], Lars Husmann [b], Carlos A. Mestres [c], Zoran Rancic [d], Barbara Hasse [a,*], the VASGRA Cohort Study

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WHAT THIS PAPER ADDS

The Management of Aortic Graft Infection Collaboration (MAGIC) criteria have been proposed as a novel diagnostic test for vascular graft/endograft infection (VGEI). The criteria were validated retrospectively in a prospective cohort of patients with definite and suspected vascular graft infections. For a definite VGEI diagnosis, the criteria had a good sensitivity but reduced specificity, owing to suspected VGEI. To improve the accuracy, further modifications of the criteria should be evaluated.

Objective: The timely management of vascular graft/endograft infection (VGEI) is crucial to a favourable outcome, yet can be challenging as there is no validated gold standard diagnostic test. Recently, a new case definition has been proposed by the Management of Aortic Graft Infection Collaboration (MAGIC) to close the diagnostic gap. The aim of this study was to validate the MAGIC criteria as a suggested diagnostic standard for the diagnosis of suspected VGEI in the prospective Vascular Graft Cohort study (VASGRA).
Methods: VASGRA is an open, prospective, observational cohort study. Prospective participants in VASGRA between 2013 and 2019 were included (257 patients; 137 with VGEI). The accuracy of the MAGIC criteria for a diagnosis of VGEI was evaluated retrospectively by calculating the sensitivity and specificity *vs.* the consensually adjudicated VASGRA infection status.
Results: The VASGRA cohort categorised 137 (53.3%) patients as "diseased" and 120 patients as "not diseased"; using the MAGIC criteria, 183/257 (71.2%) patients were considered to be "diseased". Thus, for the MAGIC criteria, a sensitivity of 99% (95% confidence interval [CI] 96–100) and a specificity of 61% (95% CI 52–70) were calculated. Considering suspected VGEI according to the MAGIC criteria as "not diseased" achieved congruent assessments of the VASGRA team and the MAGIC criteria, with a sensitivity of 93% and a specificity of 93%. The accuracy of the MAGIC criteria for the different graft locations were also compared. If the suspected VGEIs were assigned to the "not diseased" group, VGEIs of the thoracic aorta seemed to have a poorer sensitivity (86%; 95% CI 73–95) than the other graft locations.
Conclusion: The current MAGIC criteria offer good sensitivity and specificity in the context of true infections but a reduced specificity for a possible VGEI.

Keywords: Diagnostic accuracy, MAGIC criteria, Sensitivity, Specificity, Validation, Vascular graft/endograft infection (VGEI)
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1078-5884/
https://doi.org/10.1016/j.ejvs.2021.05.010

INTRODUCTION

Vascular infections involving prosthetic graft material cause substantial morbidity, lethality, and high healthcare costs.[1,2] The timely and accurate assessment and diagnosis of vascular graft/endograft infection (VGEI) seems to be crucial for a favourable outcome. A VGEI may be obvious in patients with bacteraemia and abscess formation around a vascular graft. However, a definite VGEI diagnosis is challenging, and usually involves multiple findings rather than one gold standard diagnostic test. Physicians often rely on a diversity

Anagnostopoulos A, et al. *Eur J Vasc Endovasc Surg*. 2021

UNIVERSITAT DE BARCELONA

Many Thanks!

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