Prevalence and Risk Factors for Infective Endocarditis in Patients with *Staphylococcus aureus* bacteremia

Palraj B, Baddour LM, Steckelberg JM, Wilson WR, Sohail MR

Division of Infectious Diseases, Division of Cardiovascular Diseases, Department of Medicine, Mayo Clinic College of Medicine, Rochester, Minnesota, USA.

Background

Infective endocarditis (IE) is a serious complication in patients with *Staphylococcus aureus* bacteremia (SAB). *Staphylococcus aureus* is a highly virulent pathogen with propensity to cause valvular destruction and perivalvular abscess formation.

Study Aim

The aim of the present investigation was to determine the prevalence and the risk factors for infective endocarditis in patients with SAB.

Methods

All adult (age>18) patients hospitalized in a tertiary care referral center (Mayo Clinic, Minnesota) with *S. aureus bacteremia* (SAB) during 5-year period (July 2006 till June 2011) were included in the study. Retrospective chart review was done to collect data regarding baseline demographics; microbiology, echocardiography and clinical signs and symptoms of IE during hospitalization and a 3-month follow up period. Modified Dukes Criteria was used to define infective endocarditis. Patients, who did not undergo TEE and for whom follow up data at 3 months were unavailable, were excluded from the analysis.

A total of 703 SAB cases (24% community-onset, 57% healthcare-associated and 19 % hospital-aquired) were included in the analysis.

Results

The mean patient age was 65 years, 65% were men, and 14% were hemodialysis-dependent. Six percent of patients had a prosthetic valve, 7% of patients had a permanent pacemaker (PPM) and 5% of patients had implantable cardiovertor defibrillator (ICD). Definite IE was present in 86 patients (12.2%). The prevalence of IE was 21.1% (35/166) in community acquired SAB, 10.5% (42/401) in community-onset healthcare associated and 6.6% (9/136) in nosocomial SAB. The prevalence of IE was 14.7% (14/95) in patients with hemodialysis, 31.8 % (14/44) in patients with prosthetic valve and 42.9 % (21/49) in patients with PPM and 27.8 % (21/36) in patients with ICD.

In multivariable analysis, community onset of SAB, PPM or ICD therapy, presence of prosthetic heart valve, and prolonged bacteremia (>3days) were independently associated with IE in patients with SAB. (Table 1)

Conclusions

The prevalence of IE is high in patients with community-onset SAB and those with intra-cardiac prosthetic devices. In addition, prolonged *S. aureus* bacteremia (SAB >3 days) is an independent risk factor associated with infective endocarditis. .

Disclosures:

Sohail MR: CONSULTING FEES/HONORARIA: TYRX Inc. (Monmouth Junction, NJ)

Others: Nothing to Disclose

Table 1

Risk Factors	HR (95% CI) [p-value]
ICD	3.77 (1.58, 9.00) [0.003]
PPM	7.12 (3.46, 14.63) [<.001]
Prosthetic valve	2.98 (1.31, 6.81) [0.010]
Prolonged Bacteremia (> 3 days)	5.03 (2.77, 9.12) [<.001]
Community-Onset SAB	4.28 (1.83, 10.03) [<.001]
Healthcare-associated SAB	1.85 (0.82, 4.15) [0.138]

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Characteristics of infective endocarditis in French West Indies : a 13-year observational study

E. Fernandes,[1] C. Olive,[2] J. Inamo,[3] R. Théodose,[2] F. Roques,[4] D. Courcier,[5] A. Cabié,[6] B. Hoen,[1] P. Hochedez,[6]

[1] Dept of Infectious Diseases, Dermatology, and Internal Medicine, University Medical Center of Guadeloupe, [2] Laboratory of bacteriology, University Hospital of Martinique, [3] Dept of Cardiology, University Hospital of Martinique, [4] Dept of Thoracic and Cardiovascular Surgery, University Hospital of Martinique, [5] Dept of Public Health, University Hospital of Martinique, [6] Dept of Infectious Diseases, University Hospital of Martinique

Introduction

Infective endocarditis (IE) is a rare but severe disease. In the recent years, the epidemiology of IE has significantly changed in western countries. There are no data about characteristics of IE in the French West Indies (FWI). These knowledge are essential to optimize the management of patients affected by this disease. We conducted a 13-year observational study to describe the characteristics of IE in FWI and to identify variables associated with in-hospital mortality.

Materials and Methods

The records of all the patients admitted for the diagnosis and treatment of IE to the University Hospital of Martinique between January 1st, 2000 and December 31st, 2012 were abstracted in an electronic CRF. Only Duke-Li definite cases were considered for this analysis, which included the following variables: patient's history (cardiac and extracardiac), procedures and situations at risk of IE, clinical characteristics, location of IE, causative microorganism, echocardiographic profile, complications, medical and surgical treatment, and in-hospital mortality. Variables associated with in-hospital mortality were tested using multivariate logistic regression analysis.

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Results

Variable	% (N=201)
Age, years, mean [IQR]	58 [45-71]
Age ≥ 70 years	28.4
Male sex	67
1st symptoms-diagnostic ≤ 4 weeks	67
Cardiac history	
- No previously known heart disease	45.8
- Prosthetic valve	21.4
- Previously known native valve disease	32.8
- Previous IE	7
Location of IE	
- Mitral	42.3
- Aortic	34.8
- Aortic and mitral	8
- Right-sided IE	7
- Bilateral	2
- Cardiac device IE	5
- Unknown	2
Mode of acquisition	
- Community	59.7
- Healthcare-related	38.3
- Intravenous drug use	1.5

Variable	% (N=201)
Microorganisms in blood cultures	79.1
- Streptococci	30.3
Oral streptococci	15.4
Group D streptococci	5.9
Other streptococci	9
- Enterococci	5
- Staphylococcus aureus	22.9
- Coagulase-negative staphylococci	6
- Other microorganism	10.9
- ≥ 2 microorganism	4
- No microorganism in blood culture	20.9
No microorganism identified	16.4

Variable	% (N=42)
Blood culture-negative EI	
- Antibiotics prior to blood cultures	38
- Serological identification	4.8
- Heart valve culture	16.6

Variable	% (N=201)
Cardiac Surgery	53
In-hospital death	19

Variable	Multivariate logistic regression OR(95%CI)	P
Age > 50 years	3.84(1.42-10. 38)	<0.01
S.aureus IE	3.45(1.63-7.29)	<0.01
Healthcare-related IE	4.71(2.21-10.08)	<0.01

Conclusions

The epidemiological and microbiological profile of IE in FWI is in-between those observed in developed countries and developing countries: patients were younger, blood cultures were more frequently negative, and IE due to group D streptococci and enterococci were less common than in industrialized countries.

Length of Treatment and Outcome of Enterococcal Endocarditis treated with Ampicillin plus Ceftriaxone. A comparison with Standard Ampicillin plus Gentamicin Regimen.

Juan M. Pericás, Carlos Cervera, Asunción Moreno, Cristina Garcia de la Mària, Manel Almela, Carlos Falces, Yolanda Armero, Jose M. Gatell, Carlos A. Mestres, Jose M. Miró; and the Hospital Clinic Endocarditis Study Group†

Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer. Universitat de Barcelona, Spain.

Introduction

Enterococci are the third most common causal agent of infective endocarditis (IE) worldwide[1] and it is increasingly prevalent.[2]

The combination of betalactams and aminoglycosides (A+G) has been the treatment of choice from the 1950s and it is still the first recommendation in European[3] and American[4] guidelines. The classical indications of long course (6 weeks) or short course (A+G) are based on the duration of symptoms, the type of IE (native vs. prosthetic) and the presence of complications.[5] However, long courses of aminoglycosides imply a high likehood of renal toxicity, especially among the elderly, such are the current paradigmatic enterococcal IE patients.

One alternative to reduce the risk of nephrotoxicity is to shorten the aminoglycoside course to 2 weeks. In a recent study conducted in Denmark, Dahl et al demonstrated that this option did not lead to lower efficacy, while renal impairment was significantly less frequent in the aminoglycoside short course group.[6]

Nevertheless, another difficulty, besides aminoglycosides nephrotoxicity, raised during the last decade in the treatment of enterococcal IE: increasing rates of high-level aminoglycosides resistance have been detected worldwide.[7]

Since the efficacy of double beta-lactam therapy was firstly described in the mid-1990s *in vitro*,[8] and thereafter has been proved in animal models[9] and in a small non-randomized clinical trial performed in Spain,[10] this option have spread as a good alternative, specially in France and Spain. Although ampicillin + ceftriaxone (A+C) is only recommended as a second line rescue option in international guidelines, and always using an 8-weeks course, a recent multicenter study[11] showed that 6 weeks of A+C was equivalent to 6 weeks of A+G in terms of efficacy, and significantly higher rates of nephrotoxicity leading to treatment discontinuation were found with the latter combination.

Our aim was to analyze differences on efficacy between 4 weeks (4w) and 6 weeks (6w) of antibiotic treatment with A+G and A+C.

Materials and Methods

Retrospective analysis of a prospectively collected cohort from 1997 to 2013. All patients were initially treated either with A+G or A+C and completed 4w or 6w of treatment (4w: native, non-complicated; 6w: prosthetic, complicated or >3-month of symptoms) and ≥6-month follow-up. Analysis was performed by an intention-to-treat basis. Demographic features, microbiological and clinical outcomes and toxicity were analysed.

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Results

78 patients were included. Baseline characteristics are displayed in **Table 1**, while main outcomes can be seen in **Table 2**.

Fifty-eight percent of A+G patients presented renal failure (4 in 4w and 14 in 6w arms) and 10 had to discontinue treatment due to this reason (at day 18 on median; IQR 15-25). One patient in each A+G group presented ototoxicity and one in 6w presented vestibular toxicity. One patient in 4w A+C developed haematological toxicity and in 6w A+C 2 patients presented *Clostridium difficile*-associated diarrhoea and 2 developed infections due to betalactam-resistant agents. Discontinuation of treatment was higher in the A+G group (p<0.001), reaching 44% when the treatment was prolonged to 6 weeks. A trend towards higher incidence of relapses (19%) was found in the A+C group treated for 4 weeks, while no relapse was found in the A+C group for 6 weeks.

There were no differences in mortality between groups.

Table 1. Epidemiological and basal clinical features of patients

	A+G (N=31)		A+C (N=47)		*P*
	4w (N=9)	6w (N=22)	4w (N=16)	6w (N=31)	
Median age in years (IQR)	75 (66-76)	74 (68-78)	72 (63-82)	67 (62-73)	0.223
Male gender (%)	6 (67%)	17 (77%)	9 (56%)	15 (48%)	0.191
Year of diagnosis					<0.001
• 1997-2006	8 (89%)	18 (82%)	4 (25%)	26 (84%)	
• 2007-2013	1 (11%)	4 (12%)	12 (75%)	5 (16%)	
Transferred from other centres	1 (8%)	12 (55%)	2 (13%)	5 (17%)	0.004
Median Charlson Score (IQR)	2.0 (0-3)	3.0 (1-4)	3.0 (2-4)	2. 0 (1-3)	0.529
Comorbidities					
• Diabetes mellitus	2 (22%)	9 (41%)	4 (25%)	12 (39%)	0.598
• Chronic renal failure	4 (44%)	4 (18%)	2 (13%)	9 (29%)	0.260
• Hemodyalisis	3 (33%)	1 (5%)	0	1 (3%)	0.006
• Cancer	1 (11%)	6 (27%)	6 (38%)	4 (13%)	0.192
• Chronic lung disease	1 (11%)	6 (27%)	3 (19%)	8 (26%)	0.743
• Liver cirrhosis	0	1 (5%)	4 (25%)	4 (13%)	0.163
• Previous IE	1 (11%)	1 (5%)	2 (13%)	7 (23%)	0.308
Type of acquisition					0.297
• Community	2 (22%)	6 (27%)	6 (38%)	10 (32%)	
• Nosocomial	5 (56%)	14 (64%)	4 (25%)	13 (42%)	
• Non-nosocomial healthcare-associated	2 (22%)	2 (9%)	6(38%)	8 (26%)	
HLAR					0.115
• Only to streptomycin	2 (22%)	6 (27%)	1 (6%)	4 (13%)	
• Only to gentamicin	0	0	2 (13%)	6 (19%)	
• To both	0	0	4 (25%)	4 (13%)	
Follow-up in days, median (IQR)	205 (170-398)	290 (93-365)	345 (155-365)	293 (86-365)	0.188

A+G: ampicillin plus gentamicin; A+C: ampicillin plus ceftriaxone; 4w: four weeks of treatment; 6w: 6 weeks of treatment; IE: Infectious Endocarditis; HLAR: High-level aminoglycoside resistance

Table 2. Clinical profile and outcomes.

	A+G (N=31)		A+C (N=47)		*P*
	4w (N=9)	6w (N=22)	4w (N=16)	6w (N=31)	
Type of endocarditis					-
• Native valve	8 (89%)	13 (59%)	14 (88%)	11 (36%)	
• Prosthetic valve	0	9 (41%)	0	19 (61%)	
• Pacemaker lead	1 (11%)	0	2 (13%)	1 (3%)	
Duration of symptoms in days, median (IQR)	5 (2-18)	30 (8-60)	7 (2-15)	10 (2-30)	0.023
Echocardiographic features					
• Presence of vegetations	7 (78%)	19 (86%)	9 (56%)	23 (74%)	0.215
• Vegetations size in mm, median (IQR)	10 (5-13)	10 (5-14)	9 (5-17)	10 (6-13)	0.970
• Periannular complications	0	5 (23%)	0	5 (16%)	0.116
Clinical complications					
• Heart failure (Killip ≥3)	0	9 (41%)	1 (6%)	15 (48%)	0.023
• Renal failure	4 (44%)	14 (64%)	2 (12%)	12 (39%)	0.049
• Major emboli	0	5 (23%)	1 (6%)	8 (26%)	0.105
Persistent bacteremia	1 (11%)	1 (5%)	3 (19%)	1 (3%)	0.253
Antibiotic treatment adverse events					
• Mielotoxicity	0	0	1 (6%)	0	0.270
• Skin rash	0	1 (5%)	1 (6%)	1 (3%)	0.880
• *C. difficile* diarhoea	0	0	0	2 (6%)	0.112
• Superinfections due to betalactams resistant agents	0	0	0	2 (6%)	0.112
• Ototoxicity/Vestibular toxicity	1 (11%)	2 (10%)	-	-	0.239
Discontinuation of antibiotic therapy	1 (11%)	9 (41%)	1 (6%)	0	<0.001
Surgical treatment					
• In-hospital	1 (11%)	9 (41%)	0	12 (39%)	0.014
• At 6-months	3 (33%)	13 (59%)	4 (25%)	15 (48%)	0.172
Mortality					
• In-hospital mortality	3 (33%)	5 (23%)	3 (19%)	7 (23%)	0.871
• One-year mortality	3 (33%)	6 (27%)	4 (25%)	7 (23%)	0.930
Relapses*	1 (11%)	1 (5%)	3 (19%)	0	0.077

* One of the patients who relapsed in the A+C 4w group had a pacemaker that was not removed due to high surgical risk.

Conclusions

- Our data suggest that four weeks A+C treatment for enterococcal endocarditis may be associated with high incidence of relapses and consequently A+C must be prolonged for at least 6 weeks in all groups of enterococcal endocarditis.
- Together with results of Fernández-Hidalgo,[11] our study suggest that 6w of A+C is enough and it is not necessary to systematically use 8 weeks as recommended in ESC and AHA guidelines.
- As this is a retrospective, single-center and non-randomized study, further studies are warranted to confirm these results.

Value of PET/CT for the diagnosis and management of infective endocarditis

N. Fernández-Hidalgo[1], G. Oristrell[2], M.N. Pizzi[2], A. Roque[3], M.T. Gonzàlez-Alujas[2], M. Galiñanes[4], S. Aguadé[5], P. Tornos[2], B. Almirante[1]
[1]Infectious Diseases, [2]Cardiology, [3]Radiology, [4]Cardiac Surgery, and [5]Nuclear Medicine Departments. Hospital Universitari Vall d'Hebron, Barcelona, Spain

INTRODUCTION

-Transesophageal echocardiogram (TEE) is a cornerstone in the diagnosis and management of infective endocarditis (IE) but there are some circumstances, such as prosthetic valve IE, in which paravalvular images can be very difficult to interpret.
-The aim of this study was to evaluate the value of PET/CT for the diagnosis of IE.

PATIENTS AND METHODS

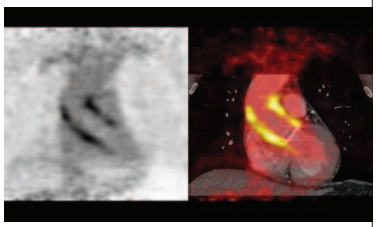
-A prospective study was conducted in a teaching hospital, referral centre for cardiac surgery.
-Period of study: November 2012 - February 2014.
-All consecutive adult patients with suspected prosthetic or intracardiac device-associated IE were included.
-A PET/CT was performed and compared with TEE findings.

RESULTS

-34 men and 11 women entered the study (med age 65 y, IRQ 60-78).
-Prosthetic valves 17, intracardiac devices 11, aortic tubes 6, prosthetic valves plus devices 6, and congenital cardiac corrections 5.

RESULTS (continuation)

-PET/CT and TEE findings were concordant in 25 episodes: 15 +, 10 -.
-In 14/45 (31%) episodes, PET/CT increased the sensitivity of TEE allowing the diagnosis of definite IE: 4/17 prosthetic valves, 2/11 devices, 3/6 aortic tubes, 2/6 prosthetic valves plus devices, and 3/5 congenital cardiac corrections.
-In 4 patients with equivocal findings on TEE, PET/CT completely ruled out the diagnosis of EI.
-In 2 episodes PET/CT provided an alternative diagnosis: pneumonia and spondylodiscitis.
-In 1 episode, TEE and PET/CT were negative for IE, but PET/CT showed the presence of a pulmonary septic embolism leading to a definite diagnosis of IE.
-PET/CT clearly identified the site of infection in patients with concomitant presence of prosthetic valves and devices, avoiding unnecessary removal of uninfected valves.
-No patient in whom EI was ruled out by PET/CT showed signs of infection after removing antimicrobials.
-PET/CT led to the diagnosis in 5 neoplasm (colon 3, lung 2), 4 of them in early stage and therefore potentially curable.



CONCLUSIONS

1. PET/CT seems a useful tool in the early management of IE of cardiac prostheses and for the precise identification of the location of the infection when more than one device is in place.
2. PET/CT allows the early diagnosis of tumors in elderly population.
3. Future studies are warranted in order to define the precise role of PET/CT in the diagnosis of IE.

Mortality determinants in 4340 infective endocarditis cases in France

S. Sunder[1,2], L. Grammatico-Guillon[2,3,4], C. Gaborit[2], L. Pericart[2], E. Rusch[2,3,4], L. Fauchier[2,4], S. Baron[2,3], L. Bernard[2,4]

[1]CH de Blois, [2]CHRU de Tours, [3] EE1 EES, [4]Université F. Rabelais de Tours, France

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eP128

Introduction

The mortality of infective endocarditis (IE) has been well studied in the past, but not at a population level.
In this study, we assessed the determinants of hospital mortality in IE in France, using the national hospital discharge database (HDD) in 2011.

Materials and Methods

• In France, all stays in public or private hospitals are coded using diagnosis codes (ICD-10) and acts codes.

•IE stays were extracted from the national HDD, with a definition based on IE-related diagnosis codes.

• Definition for a stay for IE: Hospital stay longer than 24 hours of a patient resident in France with a principal (PD) or associated (AD) diagnosis code of IE, which can be associated to other diagnosis codes related to IE (bacteraemia codes, complication codes …). Patients with a stay for IE in 2010 were excluded.

• The case definition has been previously assessed by checking a sample of medical charts of EI in one French region in 2011 (198 patients, Se 90%, PPV 87.4%).[1] The frequency of definite IE according to Duke criteria linked to the HD summary was 74.4%, 95% CI 67.9%-80.9%. [1]

• Risk Factors of inhospital mortality were estimated using logistic regression model.

• Correlation between regional frequency of surgery and regional mortality was analyzed

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Results

The analysis included 4,340 patients.
A valvular surgery was performed in 23% of cases. The hospital mortality was 20.9%. There was disparity in frequency of surgery and mortality according to the region of domiciliation of patients, without correlation between theses variables (r=0.088, figure)

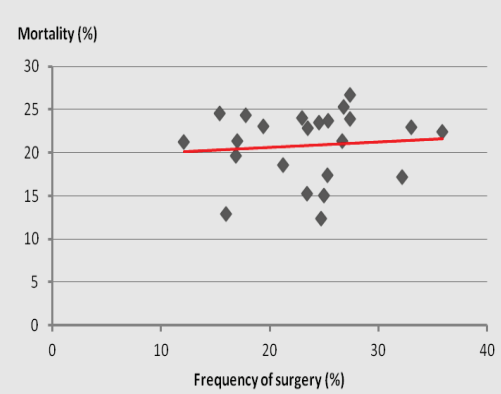

Figure: Frequency of surgery and mortality by regions

Variable	Multivariate analysis OR (95% CI)
Age < 70 years	-
Age ≥ 70 years	1.77 (1,49 – 2.10)
Predisposing diseases	
Chronic respiratory insufficiency	1.35 (1.07 – 1.72)
Cancer	1.64 (1.32 – 2.05)
IDU	0.37 (0.16 – 0.90)
Valvular status	
Native valve	-
Prosthetic valve	0.81 (0.67 – 0.99)
Microorganism (monomicrobial)	
Staphylococcus aureus	2.17 (1.78 – 2.63)
Pseudomonas aeruginosa	2.03 (1.10 – 3.73)
Escherichia coli	0.60 (0.38 – 0.96)
Complications	
Ischemic stroke	1.71 (1.34 – 2.18)
Hemorrhagic stroke	3.04 (2.15 – 4.31)
Acute limb ischemia	1.64 (1.05 – 2.59)
Vertebral osteomyelitis	0.42 (0.26 – 0.66)
Cardiogenic shock	6.05 (4,77 – 7.69)
Valvular surgery	0.47 (0.37 – 0.60)

Conclusions

• Risk factors of inhospital mortality in IE were age > 70 years, chronic respiratory insufficiency, cancer, *Staphylococcus aureus* and *Pseudomonas aeruginosa* infection, neurological complication and cardiogenic shock.
• Protective factors for mortality were IE in IDU (right heart IE), vertebral osteomyelitis and valvular surgery.
• Valvular surgery was considerably less frequent in this study than in the previous published data interesting a French population (near 50%) whereas mortality was similar.[2] Differences in population (only definite IE in this study) could partially but not fully explain the lower frequency of surgery.
• There were significant regional differences in frequency of surgery but it did not impact mortality.
• A validation of our case definition in others regions, especially in those were the frequency of surgery is low, would validate our results.
• Valvular surgery is beneficial in well definite indications (large vegetations, cardiac insufficiency, uncontrolled infection), but in others situations its contribution to reduce mortality remain uncertain.

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Preoperative assessment of factors associated with mortality after cardiac surgery for infective endocarditis

P0502

S Patrat-Delon [1]; A Rouxel [2]; A Gacouin [1]; M. Revest [1];E Flecher [3]; O Fouquet [4]; Y Le Tulzo [1]; N Lerolle [2]; P Tattevin [1]; JM Tadié [1]

[1]Infectious Diseases and ICU, Rennes University Hospital, France

[2] ICU and hyperbaric medecine unit, Angers University Hospital, France , [3] Cardiothoracic surgery unit, Rennes University Hospital, France, [4]Cardiothoracic surgery unit, Angers University Hospital, France

BACKGROUND

Cardiac surgery in infective endocarditis (IE) is performed for half of patients with left-sided IE during index hospitalization, with considerable risk of death and morbidity; current American and European guidelines recommend early surgery in case of heart failure, uncontrolled infection, high risk of embolism or intracardiac damages [Habib 2009, Baddour 2007].

Recent studies advocate earlier surgical treatment to improve the outcome of patients with left-sided IE [Kang 2012, Lalani 2010, Aksoy 2006].

However, surgery is still challenging and postponed or cancelled in a significant proportion of patients when the risk of operation is considered too high. Risk prediction models in cardiac surgery, as EuroSCORE and EuroSCORE II, were developed to provide information on risk to both clinicians and patients, and to guide decision making; but no study has evaluated the accuracy of EuroSCORE II in cardiac surgery for IE to predict mortality.

Others factors associated with mortality after cardiac surgery in IE have not been clearly identified.

OBJECTIVES

The aim of this study was to identify pre-operative markers that are associated with poor outcome after cardiac surgery for IE and to evaluate the accuracy of EuroSCORE II to predict mortality in this setting.

METHODS

Retrospective, observational study in the ICU of two university hospitals

Cases were identified through our computerized database and data were collected from medical files and nurses reports through standardized questionnaire.

Inclusion criteria:

- all adult patients > 18 years old
- with definite infective IE (modified Duke criteria)
- managed in ICU after cardiac surgery for IE
- between 01/01/2003 and 12/31/2013

RESULTS

Patients characteristics:

During years 2003-2013, 169 patients were included. Median age was 64 years old [IQR 52-73], and sex ratio ♂/♀ was 3,65.

Of these, 112/149 (75%) presented at least one chronic comorbidity with 14.6% of patients suffering from obesity; 114/149 patients (77%) had native valve endocarditis.

Microbiological datas:

S. *aureus* and streptococci were each involved in 52 cases (35%). Resistance to methicillin of S. *aureus* was observed in 9.6% (5/149). Enterococci and coagulase-negative staphylococci accounted both for 7% of patients. Ten patients (7%) had no microorganism identified (all of them were already receiving antibiotics prior blood cultures).

Main complications before cardiac surgery:

- left ventricular dysfunction in 51% (76/149) / right in 11% (17/149)
- central nervous system symptomatic events in 34% (47/149)
- septic shock (24%) (36/149)

Most patients (142/149, 95%) presented valve regurgitation, and 73/149 (49%) had large perivalvular abscess.

Cardiac surgery:

- was performed with a median delay of 12 days after IE diagnosis [IQR 5-24], and within the day after the decision for 50 patients (34%).
- Indication was hemodynamic for 116 patients (78%), uncontrolled infection for 60 (40%), and embolic for 52 (35%).
- Median EuroSCORE II was 9,8% [IQR, 3,9-23,2]
- Median duration of extracorporeal circulation was 118 minutes [IQR, 89,5-158,5]

In-hospital mortality was 21%:

After univariate analysis, we found that factors associated with mortality reflect surgical difficulties and severity of infection (table1). Multivariate analysis is shown in table 2.

	Dead patients	Alive patients	P value
Obesity (15%)	10 (31%)	12 (10%)	0.003
Mechanical valve IE (23%)	7 (22%)	9 (8%)	0.02
Multivalvular IE (26%)	13 (41%)	26 (22%)	0.04
S. aureus IE (35%)	16 (50%)	36 (31%)	0.04
Septic shock (24%)	14 (44%)	22 (19%)	0.003
Perivalvular abscess (49%)	22 (69%)	50 (43%)	0.001
EuroSCORE II median (IQR)	25.2 (14.3-46.3)	6.55 (3.2-18.8)	<0.0001

Obesity	OR = 3.67, IC 95% 1.10-12.19	P = 0.03
Vegetation > 15 mm	OR = 6.72 IC 95% 1.46-30.98	P = 0.01
Septic shock	OR = 4.87, IC 95% 1.67-14.28	P = 0.004
Mechanical valve IE	OR = 4.99 IC 95% 1.72-28.57	P = 0.007

Post-operative complications in ICU 82/149 = 55% :

- ARDS, n=35
- Acute renal failure requiring dialysis, n=43
- Nosocomial infection, n=38
- Unexpected additional cardiac surgery, n=45

Correlated with severity of patients and EuroSCORE II (table 3).

	With post-operative complications (n=82)	Without post-operative complications (n=67)	P value
EuroSCORE II median (IQR)	18.17 (7.02-32.43)	5.28 (2.79-14.01)	<0.0001
Multivalvular IE	27 (33%)	12 (18%)	0.04
Septic shock	22 (27%)	14 (20%)	0.003
SOFA	8 (6-11)	5 (4-7)	<0.0001
IGS II	46 (36-57)	33 (24-42)	<0.0001
Mechanical ventilation duration	5 (1-10)	1 (0-3)	<0.0001
catecholamine infusion duration	6 (2-17)	1 (1-4)	<0.0001

EuroSCORE II:

EuroSCORE II is associated with mortality and complications (table 4) but under-estimates mortality (table 5).

EuroSCORE II median (IQR) Overall population = 9.8 (3.9-23.2)		
Dead patient **25.2 (14.3-46.4)**	Alive patient **6.5 (3.2-18.8)**	p < 0.0001
With post-operative complications **18.2 (7-32.4)**	Without post-operative complications **5.3 (2.8-14)**	p <0.0001
S. aureus IE **18.4 (5.8-32.8)**	No *S. aureus* IE **7.4 (3.8-19)**	p = 0.02

Predicted mortality EuroSCORE II	Observed mortality % of death	nb (%) of patients
0 - 10 %	5%	75 (50%)
10 - 20 %	26%	30 (20%)
20 - 30 %	41%	17 (11%)
30 - 40 %	45%	11 (7.3%)
> 40 %	50%	16 (10.6%)

***Staphylococcus aureus* IE versus non-*S. aureus* IE:**

•More septic and embolic pre-operative complications:

-Neurological embolism 42% vs 26% (p=0.04)

-Septic shock 33% vs 20% (p=0.07)

-Perivalvular abscess 62% vs 41% (p=0.02)

-Less left ventricular dysfunction 19% vs 45% (p=0.02)

•Operative risk higher:

-EuroSCORE II median (IQR) = 18.4 (5.8-32.8) vs 7.4 (3.8-19) (p=0.02)

-Longer median duration of extracorporeal circulation = 127 minutes (100-179) vs 108 (86-152) (p=0.03)

•Post-operative period more difficult:

-Longer duration of mechanical ventilation = 6 days (1-18) vs 2 days (1-6) (p=0.001)

-More post-operative complications : nosocomial infections = 38% vs 19% (p=0.008) , dialysis = 44% vs 21% (p=0.002)

DISCUSSION

In this study, infective endocarditis remains a serious disease that carries a considerable risk of death of 21%, with a complications rate after surgery very high, of 55%.

Factors independently predictive of mortality after cardiac surgery for IE are obesity, septic shock, large vegetation, and mechanical prosthetic valve IE. Many observational studies [Lalani 2010, Bannay 2009, Kiefer 2011, Vikram 2003] also attempt to identify prognostic factors that may assist in therapeutic decision; interpretation is always difficult. However, such studies, as ours, may help to defined these criteria and to evaluate effectiveness of surgery during active IE in clinical practice.

We found that the EuroSCORE II is insufficient to adequately predict mortality in infective endocarditis surgery. In fact, in our study, EuroSCORE II was associated with mortality and postoperative complications, but underestimated mortality in patients with predicted mortality over 10%. It is known that IE is a high-risk surgery, and some previous studies have demonstrated that the calibration of EuroSCORE models for emergency surgery was poor [Morris 2005]. We suppose that EuroSCORE II doesn't take into account surgical difficulties due to extent of locally infected tissue, importance of systemic sepsis, or microbiological specificities.

CONCLUSION

- Cardiac surgery during the acute phase of infective endocarditis is associated with high risk of operative mortality and frequent post-operative complications.
- Obesity, mechanical valve endocarditis, large vegetation and septic shock are the main risk factor for mortality. Some of these factors reflect surgical difficulties and severity of infection.
- Commonly used EuroSCORE II under-estimates mortality and should be used with caution to guide surgical decision in this setting.
- However, given that most of these patients would die without cardiac surgery, even characteristics associated with very high-risk of surgical complications and death should not be considered as definite contra-indications for cardiac surgery
- Additional studies are needed to better characterize the benefit-ratio risk of cardiac surgery during the acute phase of IE, and to further evaluate long term outcome of cardiac surgery in these patients.

For additional information please contact : Dr Solène Patrat-Delon, Infectious Diseases and ICU at Rennes University Hospital, solene.patrat-delon@chu-rennes.fr

P0484

Unique blood culture for diagnosis of bloodstream infections - A prospective multicentre study

Sylvie Dargere[1*], Jean-Jacques Parienti[2], Pierre-Emmanuel Gancel[3], Nadia Smaiti[4], Caroline Loiez[5], Luc-Marie Joly[6], Ludovic Lemée[7], Renaud Verdon[1], Roland Leclercq[8], Vincent Cattoir[8] and the UBC study group.

[1]Service de Maladies Infectieuses, CHU de Caen, France; [2]Unité de Recherche Clinique et Biostatistiques, CHU de Caen, France; [3]Département des Urgences, CHU de Caen, France; [4]Pôle de l'Urgence, CHU de Lille, France; [5]Pôle de Microbiologie, CHU de Lille, France; [6]Département d'Anesthésie et de Réanimation, CHU de Rouen, France; [7]Département de Microbiologie, CHU de Rouen, France; [8]Service de Microbiologie, CHU de Caen, France.

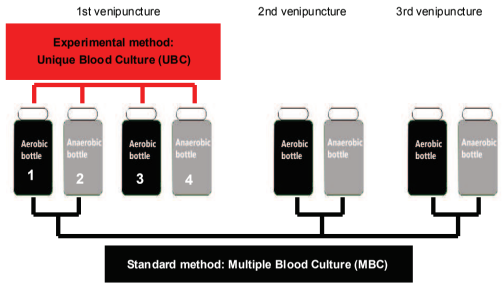
***Contact:** dargere-s@chu-caen.fr*

Background

Detection of microorganisms by blood cultures (BCs) is essential in managing patients with bloodstream infection (BSI). Increasing the number of BC increases the likelihood of isolation of microorganisms but also the rate of contaminations. Since the volume of blood drawn is considered paramount in efficient detection of pathogens rather than the number of punctures and to minimize the risk of contamination, we have evaluated the performance of a unique phlebotomy drawing a large volume of blood *versus* the standard multisampling method.

Methods

A one-year prospective multicentre study in 3 adult emergency departments was performed, comparing a unique 40-ml blood culture (UBC) to the standard method of multiple blood culture (MBC). Each patient was his own control (see figure). For MBC analysis, the first bottle pair was mimicked by taking into account the culture results of the first two bottles of the UBC set.

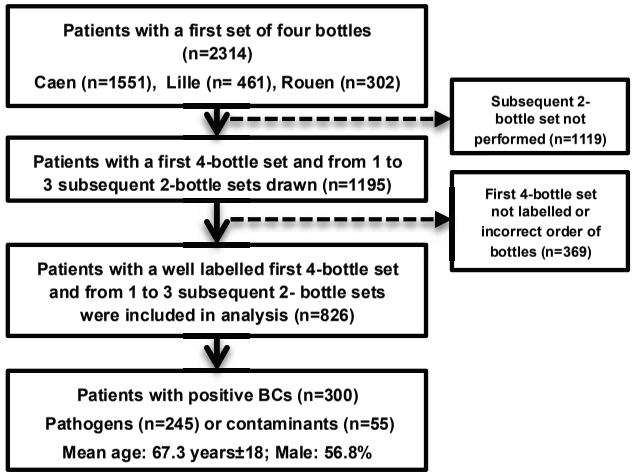


BCs were collected from patients admitted with one of the following signs: fever ≥38.5°C, hypothermia ≤36°C, chills or shock.

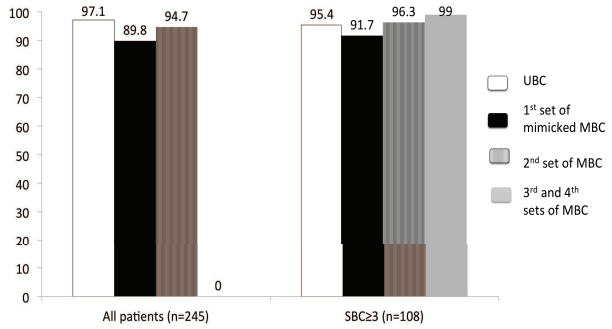
The exclusion criteria were: patients <18 years, patients for whom direct venipuncture was impossible, patients who had an invasive procedure during the first 24 hours, patients for whom the first 4-bottle set was not correctly labelled and patients for whom subsequent 2-bottle sets were not performed.

Results

Patients included



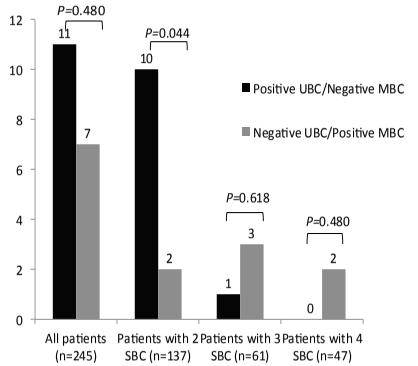
Percentage of bacteremic patients



Overall, UBC allowed detecting pathogens in the blood of 97.1% of patients *versus* 95.5% for MBC (89.8% with the first mimicked set of MBC and 94.7% with the two BCs). The difference between UBC and MBC was due to the lower performance of MBC in the two-BC sub-group.

The proportion of positive BCs was greater (99%) in the subgroup of 108 patients with ≥3 BCs.

Discrepancies in the detection of pathogens between UBC and MBC



In the sub-group of 137 patients with only two BCs, UBC was superior to MBC (*P*=0.044).

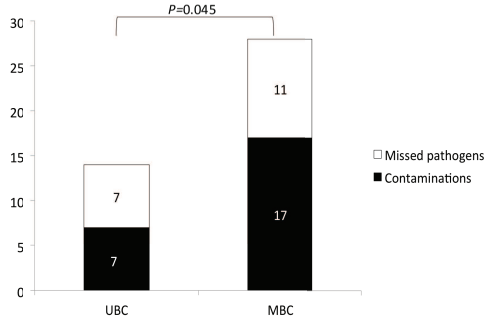
Contaminants from BCs

Bacterial species	Number of isolates
UBC and MBC positive	
Coagulase-negative staphylococci	27
Streptococcus viridans	1
Coryneform bacteria	2
Micrococcus sp.	2
Bacillus sp.	1
UBC positive and MBC negative	
Coagulase-negative staphylococci	6
Streptococcus viridans	1
UBC negative and MBC positive	
Coagulase-negative staphylococci	14
Streptococcus viridans	3
Total	57*

*In two patients, one in each group, two contaminants were detected.

Confirmed contaminants were detected in 55 patients (2.4%) while 31 patients had contaminated BCs by both UBC and MBC strategies. Most contaminants (n=25) were detected in the first aerobic bottle that account for both the UBC and MBC groups. Seven patients had contaminated UBC only and 17 had contaminated MBC only (*P*=0.062).

Sums of pathogens missed and contaminants



The goal of the study was to compare UBC and MBC strategies both for efficient isolation of pathogens and for minimization of BC contaminants. Accounting for both parameters, difference between performances of UBC and MBC was statistically significant.

Cost savings

Comparing UBC to the standard MBC with 2, 3 and 4 sets of BCs, the cost savings related to less material and labour time, amounted to €193,275 annually (for Caen University Hospital only).

Conclusion

Considering the complete picture of cost savings, efficient detection of pathogens and decrease in BC contamination, UBC offers an alternative to MBC.

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Microbiological diagnosis in Cardiac Device Infections: the role of sonication

Oliva A., Nguyen B.L., Mascellino M.T., Riitano G., Cipolla A., D'Abramo A., Iannetta M., Mastroianni C.M., Vullo V.

P-0497

alessandra.oliva81@gmail.com

Department of Public Health and Infectious Diseases
'Sapienza' University of Rome

Background

Cardiac implantable electronic device (CIED) infections are life-threatening conditions associated with significant morbidity, mortality and rising global healthcare cost. A clear diagnosis of Cardiac Device Infections (CDIs) infection is of crucial importance in order to start an appropriate antimicrobial therapy. Traditional pocket swabs and tissue specimens exhibit low sensitivity and specificity for diagnosing CIED infections whereas blood cultures are generally positive only in case of systemic dissemination. Sonication of cardiac devices has been recognized as an useful tool showing high sensitivity in the diagnosis of Cardiac Device Infections (CDIs). However, there are no data regarding its specificity in clinical practice.

Objective

Aim of the study was to assess the role of sonication in the microbiological diagnosis of Cardiac Device Infections.

Methods

Patients who underwent explantation of permanent pacemaker (PPM) or implantable cardioverter defibrillator (ICD) because of infection at the Electrophysiology Service at Sapienza University of Rome between January 2013 and November 2013 were enrolled in the study. Diagnosis of CDI was made according to the international definitions of pocket infection and device-related endocarditis.

A complete device removal including generators, atrial and/or ventricular leads was performed. As controls, 37 subjects who removed generators in the absence of infection were included. Lead extraction was performed manually with or without the assistance of traction devices including stylets, locking stylets (Lead Locking Device 1, 2, and EZ LLDTM, Spectranetics®, Colorado Springs, CO, USA), snares, laser or radiofrequency.

A total of 75 collected devices (45 generators and 30 electrodes) was submitted to culture after sonication. After collection devices were covered with sterile NaCl 0.9% or Ringer solution then vortexed for 30 s, sonicated for 5 min at a frequency >20 kHz, vortexed again for 30 s and centrifuged at 3200 rpm for 15 min. The BactoSonic (BANDELIN electronic GmbH & Co. KG) was used for sonication. Anaerobic and aerobic sheep blood agar plates were incubated at 37° C for up to 10 days and the microorganisms were identified using conventional methods. The VITEK-2 (Bio-Merieux) system was used to perform the antimicrobial susceptility testing. For daptomycin, gradient test diffusion (E-test) was used to perform antimicrobial susceptibility. Of *Staphylococcus spp.*

Statistical analysis were performed using STATA 9 software (STATA corp., College Station, USA). Categorical variables were compared by using the X2 or Fisher's exact test, as appropriate. Continuous data were analyzed with Student's t-test or the non-parametric Mann-Whitney in case of values not normally distributed. A p value <0.05 was considered statistically significant.

Results

Figure1: Diagnostic flowchart. A total of 75 device components (45 generators and 30 leads) collected from 51 subjects (14 with CDI, 37 without CDI) were included in the study. Intra-operatory pocket swabs were performed in 12 subjects. Leads included atrial and/or ventricular electrodes, wires.

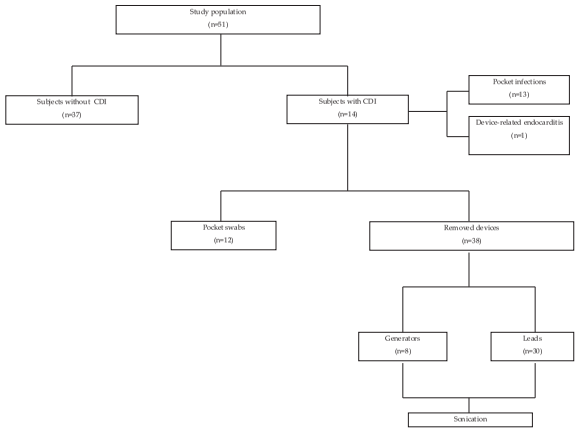


Table1: General characteristics of study population.

Characteristics	Subjects with CDI (n=14)	Subjects without CDI (n= 37)
Mean age, yr	67	80
Males, no. (%)	12 (85%)	26 (70%)
Females, no. (%)	2 (15%)	11 (30%)
Type of implanted device n (%)		
PPM	13 (93%)	37 (100%)
ICD	1 (7%)	0 (0%)
Reason for Device implantation, no. (%)		
Sick sinus syndrome	1 (7%)	0
Atrioventricular block type III	3 (21%)	7 (18%)
Chronic atrial fibrillation	4 (29%)	25 (69%)
Secundary prevention	2 (14%)	2 (5%)
Other	4 (29%)	3 (8%)
Previous pocket revision, no. (%)	12 (92%)	3 (8%) (p=0.0001)
Symptoms:		n.a.
Fever	11 (37.9%)	
Fistula	10 (41.6%)	
Pocket tenderness	21 (72.4%)	
Decubitus	19 (65.5%)	
Outcome		n.a.
Survival	13 (93%)	
Complication	1 (7%)	
Death	0 (0%)	

Table 2: Performance of sonication in the diagnosis of CDIs

Sensitivity	12/14 (86%)
Specificity	33/37 (89%)
Negative Predictive Value (NPV)	**33/35 (94%)**
Positive Predictive Value (PPV)	12/16 (75%)

Table 3: Causative microorganisms of CDIs

Subjects with infection	Microorganisms
Subject 1	*S. epidermidis*
Subject 2	*S. warneri*
Subject 3	*S. lentus*
Subject 4	*S. epidermidis*
Subject 5	*S. haemolyticus*
Subject 6	*S. schleferi e S. auricularis*
Subject 7	*S. lugdunensis*
Subject 8	*S. hominis hominis*
Subject 9	*S. epidermidis*
Subject 10	*S. haemolyticus*
Subject 11	*Sphyngomonas paucimobilis, S. epidermidis*
Subject 12	*S. aureus, S. epidermidis, S. hominis hominis*

Coagulase-Negative Staphylococci (CoNS): 88%

S. aureus: 6%

Gram-negative bacilli: 6%

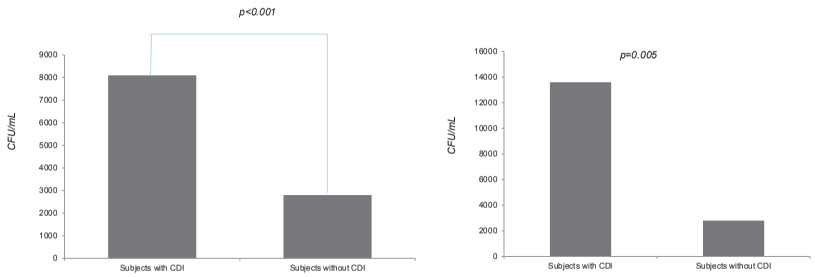
Monomicrobial infections: 75%

Polimicrobial infections: 25%

	Oxacillin	Daptomicin
% of senstivity (*Staphylococcus spp*)	33	100

Determination of Daptomicin MIC (E-test): MIC50/MIC90 0.25mcg/mL

Figure 2: Quantification of microorganisms detected by sonication.



Conclusions

Sonication before culture showed high sensitivity, specificity and negative predictive value in the setting of CDIs. This is mainly due to the fact that bacteria, which are adherent to the device and embedded in the biofilm, can be efficiently dislodged from foreign body throughout this technique.

The usefulness of sonication relies not only on the microbiological diagnosis but also on understanding the pathogenesis of CDI. In this setting, it is important to collect and analyze both generators and electrodes in order to establish how and when electrodes are colonized or infected by bacteria. In fact, knowing which type of patient is at major risk of developing endocarditis compared to those who only develop pocket infection might have important clinical and therapeutic implications.

Coagulase-negative Staphylococci were the most represented pathogens, thus confirming their causative role in implant-associated infections. This result, together with the fact that only 33% of Staphylococcal strains were oxacillin-resistant, supports the concept that wound contamination at the time of implantation or during the device procedure is crucial in the development of infection. Moreover, a previous pocket revision was more frequent in subjects with CDIs than in subjects without CDIs.

Subjects with CDIs had significantly higher bacterial load in the sonication fluid than subjects without CDIs.

In conclusion, sonication should always be performed in the microbiology laboratory in order to provide physicians information regarding the pathogenesis, the causative agents and the best therapeutic approach of CDIs.