openheart

Infective endocarditis in the Pacific: clinical characteristics, treatment and long-term outcomes

Mariana Mirabel,[1,2,3] Romain André,[1] Paul Barsoum Mikhaïl,[1,4] Hester Colboc,[5] Flore Lacassin,[5] Baptiste Noël,[4] Jacques Robert,[4] Marie Nadra,[4] Corinne Braunstein,[4] Shirley Gervolino,[6] Eloi Marijon,[1,2,3] Bernard Iung,[7] Xavier Jouven[1,2,3]

ABSTRACT

Introduction: Data on clinical characteristics and outcomes of infective endocarditis (IE) in the Pacific are scarce.

Methods: Retrospective hospital-based study in New Caledonia, a high-income country, on patients aged over 18 years with definite IE according to the modified Duke criteria (2005–2010).

Results: 51 patients were included: 31 (60.8%) men; median age of 52.4 years (IQR 33.0–70.0). Left-sided IE accounted for 47 (92.2%) patients: native valve IE in 34 (66.7%) and prosthetic valve IE in 13 (25.5%). The main underlying heart disease included: rheumatic valve disease in 19 (37.3%), degenerative heart valve disease in 12 (23.5%) and congenital heart disease in 6 (11.8%). Significant comorbidities (Charlson's score >3) were observed in 20 (38.7%) patients. Infection was community acquired in 43 (84.3%) patients. Leading pathogens included *Staphylococcus aureus* in 16 (31.4%) and *Streptococcus* spp in 15 (29.4%) patients. Complications were noted in 33 patients (64.7%) and 24 (47.1%) were admitted to the intensive care unit. Cardiac surgery was eventually performed in 22 of 40 (55.0%) patients with a theoretical indication. None underwent emergent cardiac surgery (ie, first 24 h); 2 (3.9%) were operated within 7 days; and 20 (39.2%) beyond 7 days. 11 (21.6%) patients died in hospital and 21 (42.9%) were dead after a median follow-up of 28.8 months (IQR 4.6–51.2). Two (3.9%) were lost to follow-up.

Conclusions: In New Caledonia, IE afflicts relatively young patients with rheumatic heart disease, and carries high complication and mortality rates. Access to heart surgery remains relatively limited in this remote archipelago.

KEY MESSAGES

What is already known about this subject?
► There have been major changes in the characteristics and epidemiology of infective endocarditis over the past three decades in North America and Europe.
► Cardiac surgery is part of the management of infective endocarditis, with increasing data that favours early intervention from studies conducted in tertiary centres.

What does this study add?
► We provide contemporary data on the characteristics, access to treatment and long-term outcomes of infective endocarditis in a remote Pacific Island.
► Rheumatic heart disease remains the main underlying predisposing factor in a young Oceanic population.
► Access to early heart valve surgery is limited to a fraction of patients in whom surgery was indicated.
► Outcomes remain poor with over 40% mortality at approximately 2 years of follow-up.

How might this impact on clinical practice?
► Prevention of underlying aetiologies such as rheumatic heart disease should lessen the burden of infective endocarditis in Oceanic populations.
► Early diagnosis and early referral to overseas cardiac surgery facilities may improve outcomes.

INTRODUCTION

Infective endocarditis (IE) is a rare but severe infectious disease that has been extensively described in western countries. The epidemiology of IE has significantly changed across North America and Europe in recent years by affecting an increasing ageing population with comorbidities. Presentation is often acute nowadays, and characterised by a high rate of *Staphylococcus aureus* infection, cardiac complications and embolic events.[1–3] Early surgery has become a mainstay in the treatment of IE.[4–7] Series originate mainly from referral centres where access to urgent surgery is readily available,[1 6 8 9] and expertise may significantly impact on outcomes.[10] However, management and outcomes of IE in general hospitals located in remote settings may be drastically different, and have been scarcely explored so far.

CrossMark

We describe, by means of a general hospital-based retrospective study, the clinical characteristics, treatment and long-term outcomes of IE in New Caledonia, a high-income and remote South-Pacific archipelago.

METHODS
Objectives
The main objective was to describe the clinical characteristics of patients admitted with IE in New Caledonia, their treatment and long-term outcomes.

Settings
New Caledonia, located in the southwest Pacific Ocean, is a special collectivity of France, with a population of approximately 250 000 inhabitants.[11] Rheumatic heart disease remains prevalent among indigenous populations, with incidence in Oceanic populations, including Melanesians and Polynesians, being as high as 9.5 per 1000 schoolchildren, according to data obtained by means of a systematic echocardiography-based surveillance programme.[12] The Centre Hospitalier Territorial de Nouvelle Calédonie is the only centre providing cardiology and infectious disease care in the archipelago. Air transport for urgent referral for remote communities is widely available within the archipelago. The New Caledonian social security system provides free-of-charge access to good-quality medicine, imaging and microbiological diagnostic testing. Nouméa, the capital city, can be reached by a 3 h flight from Sydney, Australia, the closest cardiac surgery centre. Patients in need of heart valve surgery are referred to neighbouring Australia by medical air transportation at no additional cost to the patient. Patient management is systematically discussed between the cardiologists and infectious disease specialists.[13]
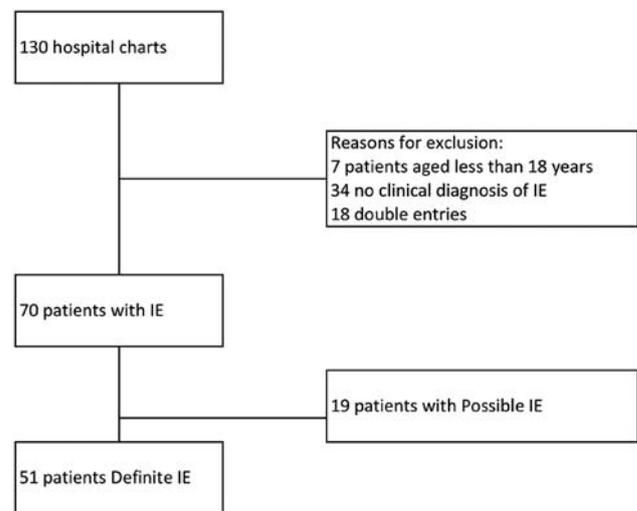
Patients
Patients aged over 18 years, admitted from 1 January 2005 to 31 December 2010 to the Centre Hospitalier Territorial de Nouvelle Calédonie with definite IE according to the modified Duke criteria were included in the study.[14]

Data collection
Hospital records of individuals with a primary or secondary International Classification of Diseases 10th revision (ICD 10) separation diagnosis of IE (ICD I33.0) were selected. One hundred and thirty hospital charts were retrospectively reviewed, with a final definite IE diagnosis in 51 patients (figure 1). In case of IE reinfections or relapses, the first IE episode during the study period was considered for inclusion.

The following data were collected: demographics; comorbidities assessed by the Charlson score[15]; underlying heart valve disease; history of cardiac surgery; IE characteristics (microbiological and echocardiographic findings); origin of bloodstream infection (as previously described);[16] IE complications as *per* previously

Figure 1 Flow chart of the study (IE, infective endocarditis).

published guidelines[5] and surgical treatment. Theoretical indication for surgery was also collected according to guidelines in use at the time of admission.[17] Patients with left-sided and right-sided IE were assigned to the left-sided group. Those with native valve IE and prosthetic valve IE were assigned to the latter.

Outcome measures were: in-hospital mortality, relapse/reinfection and long-term mortality. Relapse referred to a repeat episode of IE caused by the same microorganism within the first 6 months, while reinfection included IE with a different microorganism or beyond 6 months after the first episode.[5] Follow-up was undertaken as a cross-sectional study by contacting the patient or his/her next of kin in January 2013. Patients who could be joined were asked their New York Heart Association class (NYHA) functional status and occupation (employed or student, retired, unemployed), and whether they presented with fatigue or memory loss.

Statistical methods
The results are reported as median and IQR or as numbers and percentages. Categorical variables were compared using χ^2 test or Fisher's exact test, and continuous variables using Student t test or Wilcoxon rank-sum test. Factors associated with long-term mortality were analysed using a Cox proportional hazard model, with binomial CIs. For the analysis of the overall population, time to death was calculated as time from hospital admission to death or last follow-up. Significance was defined as p values less than 0.05. Statistical analyses were performed using STATA software, version SE/12.1 (StataCorp LP, College Station, Texas, USA). Patients were asked to give oral consent to be enrolled in the study at the time of follow-up.

RESULTS
Clinical characteristics at admission
Fifty-one patients with definite IE were included in the study (figure 1). Patient characteristics are depicted in

table 1. Median age was 52.4 years (IQR 33.0–70.0). Thirty-one patients (60.8%) were men. Forty-three patients (84.3%) were Oceanic (including 33 indigenous Melanesians and 10 Polynesians) and 8 were non-Oceanic (11.8%) (6 European and 2 of other ethnic backgrounds). Overall, left-sided IE accounted for 47 (92.2%) cases: native valve IE in 34 (66.7%) and prosthetic valve IE in 13 (25.5%) patients. Four (7.8%) patients experienced pacemaker lead IE. Underlying heart disease included: rheumatic valve disease in 19 (37.3%), degenerative heart valve disease in 12 (23.5%), congenital heart disease in 6 (11.8%), functional in 2 (3.9%) and of unknown or unspecified origin in 12 (23.5%) patients. Four (7.8%) patients had a history of IE in keeping with reinfection, the first episode was before 2005. Significant comorbidities (Charlson's score >3) were observed in 20 patients (39.2%).

IE was community acquired in 43 cases (84.3%), healthcare-related nosocomial in 7 cases (13.7%) and healthcare-related non-nosocomial in 1 case (2.0%).[16] There were no intravenous drug users or patients with HIV infection. Pathogens identified by blood cultures were: *S. aureus* in 16 (31.4%) patients, of whom 1 had a methicillin-resistant strain and 15 had methicillin-susceptible strains; *Streptococcus* spp in 15 (29.4%) patients, of whom 8 had *S. viridans* (15.7%); *coagulase-negative*

Staphylococcus in 7 (13.7%) patients; *Enterococcus* spp in 2 (3.9%) patients; Gram-negative bacteria (*Citrobacter kosei, Actinobacillus*) in 2 (3.9%) patients; *S. pneumoniae* in 1 (2.0%) patient; and *Corynebacterium diphteriae* in 1 (2.0%) patient. Microbiology was negative in seven patients (13.7%); three had received antibiotics before blood cultures were drawn. Primary site of infection in patients was dental in 7 (13.7%), cutaneous in 6 (11.8%), intravenous line/device related in 5 (9.8%), other in 5 (9.8%) and unknown in 27 (52.9%) patients. No patient with negative blood cultures who subsequently underwent surgery had PCR performed on the valve specimen.

Median time from first symptoms to admission was 3 days (IQR 2–29). Median time from hospital admission to IE diagnosis was 3 days (IQR 0–9).

Complications, investigations and treatment
Complications were noted in 33 patients (64.7%) and included: acute heart failure in 17 cases (33.3%), severe valve regurgitation in 15 cases (29.4%); neurological event (including symptomatic or asymptomatic stroke, haemorrhage, or encephalopathy) in 23 cases (45.1%); shock in 7 cases (13.7%); and conduction abnormalities in 2 cases (3.9%). Five patients (9.8%) presented with local complications (abscess, and/or fistula) on echocardiogram.

Table 1 Characteristics by in-hospital mortality

Factor	All patients N=51	Discharged alive N=40	Died in-hospital N=11	Univariate analysis p value*
Age ≥53 years, n (%)	24 (47.1)	16 (40.0)	8 (72.7)	0.05
Male, n (%)	31 (60.8)	26 (65.0)	5 (45.5)	0.24
Oceanic†, n (%)	43 (84.3)	34 (85.0)	9 (81.8)	0.80
Charlson's score >3, n (%)	20 (39.2)	13 (32.5)	7 (63.4)	0.08
Chronic renal replacement therapy, n (%)	3 (5.9)	2 (5.0)	1 (9.1)	0.61
Left-sided IE, n (%)	47 (92.2)	37 (92.5)	10 (90.9)	0.86
Native valve IE, n (%)	34 (66.7)	27 (67.5)	7 (63.6)	0.81
Aetiology of valve disease, n (%)				0.17
Rheumatic heart disease	19 (37.2)	17 (42.5)	2 (18.2)	
Degenerative	12 (23.5)	7 (17.5)	5 (45.5)	
Congenital	6 (11.8)	5 (12.5)	1 (9.1)	
Functional	2 (3.9)	2 (5.0)	0	
Healthcare-related IE, n (%)	8 (15.7)	6 (15.0)	2 (18.2)	0.80
Microbiology, n (%)				
Streptococcus spp	15 (29.4)	12 (30.0)	3 (27.3)	0.86
Staphylococcus aureus	16 (31.4)	12 (30.0)	4 (36.4)	0.69
Acute heart failure, n (%)	17 (33.3)	13 (32.5)	4 (36.4)	0.81
Severe valve regurgitation, n (%)	15 (29.4)	13 (32.5)	2 (18.2)	0.33
Neurological complication, n (%)	23 (45.1)	18 (45.0)	5 (45.5)	0.87
Shock, n (%)	7 (13.7)	2 (5.0)	5 (45.5)	<0.01
Vegetation length ≥15 mm, n (%)	10 (19.6)	7 (17.5)	3 (27.3)	0.39
Perivalvular abscess‡, n (%)	5 (9.8)	4 (10.0)	1 (9.1)	0.94
Cardiac surgery, n (%)	22 (43.1)	20 (50.0)	2 (18.2)	0.06
Cardiac surgery denied§, n (%)	19 (37.3)	12 (30.0)	7 (63.8)	0.04

*Comparison of patients discharged alive versus patients who died during their first hospital admission.
†Includes indigenous Melanesians and Polynesians.
‡On echocardiography.
§In spite of at least one indication according to guidelines at the time of treatment.
IE, infective endocarditis.

All patients underwent transthoracic echocardiography and blood cultures. Echocardiographic characteristics are depicted in table 2. Among 23 (45.1%) patients with neurological complications, 17 underwent a brain CT scan (of whom 13 had subsequent MRI) and 4 underwent brain MRI alone. Neurological complication was clinically silent in 3 of 23 patients.

Hospital length of stay was a median of 55 days (IQR 37–79). Median duration of intravenous antibiotic regimen was 42 days (IQR 30–45). Antibiotic regimens included: (1) a combination of amoxicillin and gentamycin in 12 of 15 cases with streptococcal infection, amoxicillin alone in 1 case, penicillin G and gentamycin in 1 case, and vancomycin and gentamycin in 1 case; (2) oxacillin and gemamycin in 9 of 14 cases with *S. aureus* methicillin-susceptible cases, oxacillin alone in 2 cases, oxacillin and amikacin in 1 case, oxacillin and rifampicin in 1 case, and cefotaxime and gentamycin in 1 case; (3) vancomycin and fosfomycin in 1 case of *S. aureus* methicillin-resistant case; and (4) a variety of regimens in negative blood cultures IE (amoxicillin and gentamycin in 2 cases, vancomycin and gentamycin in 1 case, ceftriaxone and gentamycin in 1 case, vancomcyin alone in 1 case, amoxicillin–clavulanate and gentamycin in 1 case, and ceftriaxone and gentamycin in 1 case). Twenty-four patients (47.1%) were admitted to the intensive care unit. Cardiac surgery was performed in 22 of 40 patients with a theoretical indication at a median 24 days (IQR 14–44) after IE diagnosis. None underwent emergent cardiac surgery (ie, first 24 h); 2 (3.9%) were operated within 7 days; and 11 (21.5%) between 8 and 30 days. The remaining nine (17.6%) patients were operated on after completion of antibiotic treatment. Eighteen

(34.0%) patients did not undergo surgery in spite of theoretical indications. Reasons for denying surgery were available in 11 cases: underlying comorbidities in 4 (36.3%); neurological complications in 3 (27.3%); combination of comorbidities and neurological complications in 2 (18.2%); multiorgan failure including neurological complication in 1 (9.1%); and patient's refusal in 1 (9.1%) case.

Outcomes: in-hospital mortality and long-term outcomes

Eleven (21.6%) patients died in hospital after a median hospital stay of 25 days (IQR 16–43). Factors associated with in-hospital mortality on univariate analysis were: shock (p<0.001); and medical treatment alone in spite of surgical indications in 19 patients (p=0.04; table 1). Overall, 21 (42.9%) were dead at median 28.8-month follow-up (IQR 4.6–51.2); 2 (3.9%) were lost to follow-up (figure 2). Factors associated with long-term mortality on univariate analysis were: age (p=0.001); comorbidities by the Charlson score>3 (p<0.01); streptococcal IE (p<0.001); *S. aureus* IE (p=0.01); and cardiac surgery (p=0.02; table 3). The mortality rate was 57.1% (16/28) for patients treated medically compared to 23.8% (5/21) of those who underwent cardiac surgery (p=0.02). Among the 11 patients who died during the first hospital admission, the cause of death was documented in 10: 3 died from neurological complications of IE, 3 from heart failure or cardiogenic shock, 2 from septic shock at the acute phase of IE and 2 from underlying comorbidities. Among the remaining patients discharged alive and who subsequently died, cause of death could be collected in 3 of 10 cases: 1 died from heart failure, 1 from brain haemorrhage after the resolution of the IE episode under oral anticoagulant treatment and 1 from new sepsis. There were two (3.9%) relapses and two (3.9%) reinfections. Three patients (5.9%) needed redo surgery during the follow-up period.

Among the 28 patients joined at follow-up (87.5% of survivors), 19 (67.9%) were in NYHA I, 9 (32.1%) in

Table 2 Echocardiographic findings

| Echocardiography	All 51 IE cases
Transthoracic echocardiography, n (%)	51 (100)
Transoesophageal echocardiography, n (%)	34 (66.7)
Vegetation, n* (%)	39 (76.5)
Vegetation size ≥10 mm†	25 (49.0)
Vegetation size ≥15 mm†	13 (25.5)
Mobile vegetation‡	39 (76.5)
Severe aortic regurgitation, n§ (%)	7 (13.7)
Severe mitral regurgitation, n§ (%)	8 (15.7)
Perivalvular abscess, n (%)	5 (9.8)
Fistula, n§ (%)	1 (2.0)
Valvular obstruction, n¶ (%)	7 (13.7)
New abscess or fistula on serial echocardiography, n** (%)	5 (9.8)
Increased severity in valvular regurgitation on serial echocardiography, n** (%)	7 (13.7)

*Missing data in two cases.
†Missing data in 11 cases.
‡Missing data in nine cases.
§Missing data in one case.
¶Missing data in three cases.
**Missing data in four cases; no pseudoaneurysm was noted.
IE, infective endocarditis.
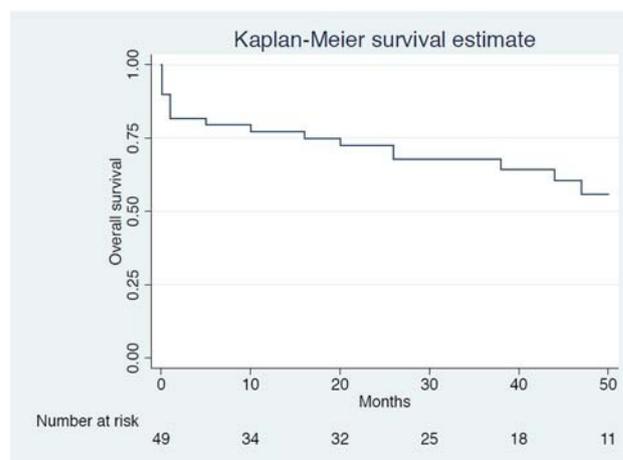
Figure 2 Kaplan-Meier survival estimates. Missing data for two patients.

Table 3 Characteristics by long-term mortality (missing data for 2 patients)

Factor	Alive at FU N=28	Dead at FU N=21	Univariate HR (95% CI)	p Value
Age ≥53 years, n (%)	9 (32.1)	15 (71.4)	1.22 (0.25 to 2.20)	0.01
Male, n (%)	19 (67.9)	11 (52.4)	−0.60 (−1.48 to 0.28)	0.18
Oceanic*, n (%)	24 (85.7)	17 (81.0)	−0.20 (−1.30 to 0.90)	0.73
Charlson's score >3, n (%)	4 (14.3)	16 (76.2)	1.54 (0.52 to 2.55)	<0.01
Chronic renal replacement therapy, n (%)	0	3 (14.3)	−0.56 (−2.58 to 1.47)	0.55
Left-sided IE, n (%)	25 (89.3)	20 (95.2)	0.15 (−1.88 to 2.18)	0.89
Native valve IE, n (%)	20 (71.4)	12 (57.1)	0.57 (−0.53 to 1.63)	0.31
Aetiology of valve disease, n (%)†			−0.65 (−1.67 to 0.36)	0.21
Rheumatic heart disease	12 (42.9)	5 (28.8)		
Degenerative	3 (10.7)	9 (42.9)		
Congenital	4 (14.3)	2 (9.5)		
Functional	1 (3.6)	1 (4.8)		
Healthcare-related IE, n (%)	1 (3.6)	7 (33.3)	0.61 (−0.35 to 1.58)	0.21
Microbiology, n (%)				
Streptococcus spp	11 (39.3)	2 (9.5)	−35.45 (−3.9×10⁷ to 3.9×10⁷)	0.001
Staphylococcus aureus	4 (14.3)	12 (57.1)	1.11 (0.21 to 2.00)	0.01
Acute heart failure, n (%)	9 (32.1)	7 (33.3)	−0.28 (−1.24 to 0.69)	0.58
Severe valve regurgitation, n (%)	10 (35.7)	4 (19.0)	−0.82 (−1.93 to 0.29)	0.15
Neurological complication, n (%)	13 (46.4)	10 (47.6)	0.04 (−0.83 to 0.92)	0.92
Shock, n (%)	2 (7.1)	5 (23.8)	−	−
Vegetation length ≥15 mm, n (%)	5 (17.9)	5 (23.8)	−0.12 (−1.94 to 0.85)	0.81
Perivalvular complications‡, n (%)	2 (7.1)	3 (14.3)	−0.91 (−2.94 to 1.11)	0.38
Cardiac surgery, n (%)	16 (57.1)	5 (23.8)	−1.29 (−2.33 to −0.25)	0.02

*Indigenous Melanesians and Polynesians.
†Analysis of RHD versus other aetiologies.
‡Abscess or fistula on echocardiogram (no pseudoaneurysm noted). FU.
IE, infective endocarditis; FU, follow-up; RHD, rheumatic heart disease.

NYHA II and 2 (7.1%) in NYHA III. Thirteen (46.4%) reported about fatigue and 10 (35.7%) experienced concentration problems and memory loss. Sixteen patients (31.1%) were either employed or studying at follow-up.

DISCUSSION

We present original data on IE, with long-term outcome measures, in a group of islands in the Pacific. The main underlying heart condition was rheumatic heart disease. The majority of patients presented with complicated IE. Barely half the surgical candidates were deemed fit for surgery. Access to emergent or urgent surgery is limited in this remote area. Mortality was extremely high (>40%) at long-term follow-up ~2.5 years.

Clinical characteristics

Patterns of IE in New Caledonia, a high-income country, resemble those of many emerging market-economies with an on-going epidemiological transition.[18][19] Although we focused our study on adults, patients were relatively young (mean age ~53 years). Our patients are younger by 10 years when compared to a recent survey conducted in France.[2] In the USA, patients with IE are increasingly older; 36% of patients are over 69 years of age.[3]

As in Europe and North America, the most frequent pathogen in IE was *S. aureus*.[1–3] However, *S. viridans* remains the second leading pathogen in our series (15.7%), whereas it has almost disappeared in the USA.[3][20] In our study, the microbiological profile reflects the emergence of healthcare-related bacteraemia and the persistence of poor dental health.[18] Healthcare-associated IE was, however, present in a minority of our patients (13.7%). This finding differs from the epidemiology of IE in Western countries, where healthcare-associated IE accounts for over a third of cases.[21]

Rheumatic heart disease remains a major predisposing factor of IE, the condition being highly prevalent among Oceanic populations in New Caledonia.[12] Although rheumatic heart disease still prevails in most of the developing countries and among indigenous populations,[22] the importance of rheumatic heart disease as an underlying condition for IE is highly variable across other tropical or subtropical countries. The disease remains the main predisposing factor for IE in countries where a large proportion of the population lives in poverty,[19] whereas its significance has diminished elsewhere over the past decade.[18]

Investigations, complications, treatment

Blood cultures and echocardiography were performed in all patients. However, advanced techniques for the diagnosis of blood culture negative endocarditis were not systematically performed.[4] As in other series, approximately one-third of patients presented with heart

failure and/or severe valve regurgitation,[2] with neurological complications collected in almost half the cases,[23] and a significant proportion (~50%) being admitted to the intensive care unit.[24]

Management of IE is challenging,[25] especially in nonsurgical centres. Access to surgery, in our study, was relatively limited since barely 55% of patients with a theoretical indication for surgery were deemed fit for intervention.[17] Of note, no patient underwent emergency surgery and only a minority of surgical candidates (3.9%) had surgery within 7 days after admission. Although comorbidities and neurological complications accounted for main reported reasons for denying surgery, no contraindications were identified in the remaining 7 of 18 surgical candidates not operated on. Remoteness may have contributed to favour medical treatment in patients with theoretical indications other than heart failure. Our study highlights the difficulties in applying current guidelines in remote locations,[5] which may be even greater in poorly resourced settings.[26] Of note, underuse of heart valve surgery is not restricted to IE or remote locations.[27]

Outcomes

Although the crude in-hospital case fatality rates observed are apparently similar to other reports, our patients were markedly younger.[2 28] Early mortality was mostly IE related due to cardiogenic shock and/or neurological complications. Mortality almost doubled at long-term follow-up, reaching 42.9%. These findings highlight the severity of the condition and the need for longer follow-up periods to estimate the true impact of the disease.[29] Factors associated with in-hospital and long-term mortality varied, as previously described by Bannay et al.[29] Previously described factors, such as older age,[30 31] comorbidities,[32] microorganisms (*S. aureus* infection being of poor prognosis)[31 33] and use of cardiac surgery,[6] were associated with long-term outcomes in our study. The mortality rate is extremely high considering the young and relatively comorbid-free population affected by IE in our series. In addition, the rate of complications was similar to what has been described elsewhere.[1 2 24] Reportedly, only patients admitted to intensive care experience higher case fatality rates after a similar follow-up period.[34] Several hypotheses can be raised to explain our findings. Rapid diagnosis is key to early antibiotic treatment that impacts on the advent of complications, especially neurological emboli.[35] Time from onset of symptoms to hospital admission varied, and there may still be room for improvement in the rapid diagnosis of IE through early referral from primary care centres. The higher than expected in-hospital mortality in our study may also be potentially and partly explained by the difficulties to access urgent cardiac surgery (ie, within the first 7 days), especially for those in cardiogenic shock.

Almost 1 of 10 patients experienced a relapse or reinfection during the follow-up period. This finding is a novelty in the field, seldom reported in the literature.[10]

In addition to high case fatality rates, only a third of survivors resumed their normal activities, albeit the majority did not experience cardiovascular symptoms. Of note, the mean unemployment rate in New Caledonia is 6%.[11] Our results suggest that IE, a curable disease, may lead to long-term individual loss of income.

Ways of reducing the burden and mortality of IE

Prevention of rheumatic heart disease may diminish the incidence of IE in our population.[22] Our findings should also promote periodontal health. Prophylaxis before oral procedures should be addressed in countries where the incidence of streptococcal IE remains high.[36] Urgent referral to the hospital with echocardiography facilities may reduce the delay between the onset of symptoms and diagnosis, thereby preventing the advent of complications. Access to urgent heart surgery should be facilitated to prevent complications and decrease early mortality in patients with IE in countries with no on site surgical facilities.

Strengths and Limitations

This is, to the best of our knowledge, the first report on IE from a tropical Pacific Island. Our study suffers, however, from several limitations. It lacked power to assess factors associated with long-term outcomes given the sample size precluding multivariate analysis. Survivor selection bias prevents from drawing conclusions from the higher fatality rates among patients treated medically. Our results should foster further prospective studies to confirm our findings, find ways to increase access to surgery, and guide prevention programmes.

Conclusion

In New Caledonia, a high-income country located in the Pacific, IE still remains a disease of relatively young patients with underlying rheumatic heart disease. Almost half the surgical candidates are not deemed fit for cardiac surgery, and long-term mortality remains dramatically high. Ways to decrease the burden of IE and improve its management in remote locations need further assessment.

Author affiliations
[1]INSERM U970, Paris Cardiovascular Research Centre—PARCC, Paris, France
[2]Université Paris Descartes, Sorbonne Paris Cité, Paris, France
[3]Cardiology Department, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris, France
[4]Cardiology Department, Hôpital Territorial de Nouvelle Calédonie, Nouméa, New Caledonia
[5]Department of Internal Medicine and Infectious Disease, Hôpital Territorial de Nouvelle Calédonie, Nouméa, New Caledonia
[6]Department of Bioinformatics, Hôpital Territorial de Nouvelle Calédonie, Nouméa, New Caledonia
[7]Cardiology Department, Hôpital Bichat and Paris Diderot University, Paris, France

Contributors MM designed and supervised the study, analysed the data and wrote the manuscript. RA, PBM and HC collected the data and provided critical review of the manuscript. FL, BN, JR, MN and CB provided critical review of the manuscript. SG provided the list of patients eligible to the study and provided critical review of the manuscript. EM, BI and XJ were involved in the design of the study, undertook critical review of the data analysis and provided critical review of the manuscript.

Competing interests None declared.

Ethics approval Ethical clearance was provided by the Ethical Review Committee of the Institut National de la Santé et de la Recherche Médicale (French Institute of Health and Medical Research), Paris, France (IRB 00003888FWA00005831).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Technical appendix is available by emailing MM (mariana.mirabel@inserm.fr).

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES

1. Murdoch DR, Corey GR, Hoen B, *et al*. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Int Med* 2009;169:463–73.
2. Selton-Suty C, Celard M, Le Moing V, *et al*. Preeminence of staphylococcus aureus in infective endocarditis: a 1-year population-based survey. *Clinl Inf Dis* 2012;54:1230–9.
3. Bor DH, Woolhandler S, Nardin R, *et al*. Infective endocarditis in the U.S., 1998–2009: a nationwide study. *PLoS ONE* 2013;8:e60033.
4. Thuny F, Grisoli D, Collart F, *et al*. Management of infective endocarditis: challenges and perspectives. *Lancet* 2012;379:965–75.
5. Habib G, Hoen B, Tornos P, *et al*. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for infection and cancer. *Eur Heart J* 2009;30:2369–413.
6. Kang DH, Kim YJ, Kim SH, *et al*. Early surgery versus conventional treatment for infective endocarditis. *NEJM* 2012;366:2466–73.
7. Erwin JP, Otto CM. Infective endocarditis: old problem, new guidelines and still much to learn. *Heart* 2014;100:996–8.
8. Thuny F, Beurtheret S, Gariboldi V, *et al*. Outcome after surgical treatment performed within the first week of antimicrobial therapy during infective endocarditis: a prospective study. *Arch Cardiovasc Dis* 2008;101:687–95.
9. Thuny F, Beurtheret S, Mancini J, *et al*. The timing of surgery influences mortality and morbidity in adults with severe complicated infective endocarditis: a propensity analysis. *Eur Heart J* 2011;32:2027–33.
10. Botelho-Nevers E, Thuny F, Casalta JP, *et al*. Dramatic reduction in infective endocarditis-related mortality with a management-based approach. *Arch Int Med* 2009;169:1290–8.
11. ISEE. http://www.isee.nc/population/telecharpdf/4page-rpnc09.pdf (accessed 1 Aug 2014).
12. Mirabel M, Fauchier B, Bacquelin R, *et al*. Echocardiography screening to detect rheumatic heart disease A cohort study of schoolchildren in French Pacific Islands. *Int J Cardiol* 2015;188:89–95.
13. Chambers J, Sandoe J, Ray S, *et al*. The infective endocarditis team: recommendations from an international working group. *Heart* 2014;100:524–7.
14. Li JS, Sexton DJ, Mick N, *et al*. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;30:633–8.
15. Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
16. Friedman ND, Kaye KS, Stout JE, *et al*. Health care-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. *Ann Int Med* 2002;137:791–7.
17. Baddour LM, Wilson WR, Bayer AS, *et al*. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation* 2005;111:e394–434.
18. Ferreiros E, Nacinovich F, Casabe JH, *et al*. Epidemiologic, clinical, and microbiologic profile of infective endocarditis in Argentina: a national survey. The Endocarditis Infecciosa en la Republica Argentina-2 (EIRA-2) Study. *Am Heart J* 2006;151:545–52.
19. Gupta A, Gupta A, Kaul U, *et al*. Infective endocarditis in an Indian setup: are we entering the 'modern' era? *Ind J Crit Care Med* 2013;17:140–7.
20. Desimone DC, Tleyjeh IM, Correa de Sa DD, *et al*. Incidence of infective endocarditis caused by viridans group streptococci before and after publication of the 2007 American Heart Association's endocarditis prevention guidelines. *Circulation* 2012;126:60–4.
21. Benito N, Miro JM, de Lazzari E, *et al*. Health care-associated native valve endocarditis: importance of non-nosocomial acquisition. *Ann Int Med* 2009;150:586–94.
22. Marijon E, Mirabel M, Celermajer DS, *et al*. Rheumatic heart disease. *Lancet* 2012;379:953–64.
23. Klein I, Iung B, Labreuche J, *et al*. Cerebral microbleeds are frequent in infective endocarditis: a case-control study. *Stroke* 2009;40:3461–5.
24. Sy RW, Kritharides L. Health care exposure and age in infective endocarditis: results of a contemporary population-based profile of 1536 patients in Australia. *Eur Heart J* 2010;31:1890–7.
25. Bolger AF. The special challenge of left-sided endocarditis. *Heart* 2011;97:1117–18.
26. Zuhlke L, Mirabel M, Marijon E. Congenital heart disease and rheumatic heart disease in Africa: recent advances and current priorities. *Heart* 2013;99:1554–61.
27. Mirabel M, Iung B, Baron G, *et al*. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? *Eur Heart J* 2007;28:1358–65.
28. Curlier E, Hoen B, Alla F, *et al*. Relationships between sex, early valve surgery and mortality in patients with left-sided infective endocarditis analysed in a population-based cohort study. *Heart* 2014;100:1173–8.
29. Bannay A, Hoen B, Duval X, *et al*. The impact of valve surgery on short- and long-term mortality in left-sided infective endocarditis: do differences in methodological approaches explain previous conflicting results? *Eur Heart J* 2011;32:2003–15.
30. Lopez J, Revilla A, Vilacosta I, *et al*. Age-dependent profile of left-sided infective endocarditis: a 3-center experience. *Circulation* 2010;121:892–7.
31. Hill EE, Herijgers P, Claus P, *et al*. Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. *Eur Heart J* 2007;28:196–203.
32. Sy RW, Chawantanpipat C, Richmond DR, *et al*. Development and validation of a time-dependent risk model for predicting mortality in infective endocarditis. *Eur Heart J* 2011;32:2016–26.
33. Lopez J, Fernandez-Hidalgo N, Revilla A, *et al*. Internal and external validation of a model to predict adverse outcomes in patients with left-sided infective endocarditis. *Heart* 2011;97:1138–42.
34. Mirabel M, Sonneville R, Hajage D, *et al*. Long-term outcomes and cardiac surgery in critically ill patients with infective endocarditis. *Eur Heart J* 2014;35:1195–204 .
35. Dickerman SA, Abrutyn E, Barsic B, *et al*. The relationship between the initiation of antimicrobial therapy and the incidence of stroke in infective endocarditis: an analysis from the ICE Prospective Cohort Study (ICE-PCS). *Am Heart J* 2007;154:1086–94.
36. Parrish A, Maharaj B. Prevention of infective endocarditis in developing countries—justifiable caution? *S Afr Med J* 2012;102:652–4.