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

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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-acquired) 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 prosthelic valve, 7% of patients had a permanent pacemaker (PPM) and 5% of patients had implantable cardioverter 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.

Table 1

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

References

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

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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.

Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>% (N=201)</th>
<th>Variable</th>
<th>% (N=201)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean [IQR]</td>
<td>58 [45-71]</td>
<td>Microorganisms in blood cultures</td>
<td>79.1</td>
</tr>
<tr>
<td>Age ≥ 70 years</td>
<td>28.4</td>
<td>- Streptococci</td>
<td>30.3</td>
</tr>
<tr>
<td>Male sex</td>
<td>67</td>
<td>- Oral streptococci</td>
<td>15.4</td>
</tr>
<tr>
<td>1st symptoms-diagnostic ≤ 4 weeks</td>
<td>67</td>
<td>- Group D streptococci</td>
<td>5.9</td>
</tr>
<tr>
<td>Cardiac history</td>
<td>45.8</td>
<td>- Other streptococci</td>
<td>9</td>
</tr>
<tr>
<td>- No previously known heart disease</td>
<td>21.4</td>
<td>- Enterococci</td>
<td>5</td>
</tr>
<tr>
<td>- Prosthetic valve</td>
<td>32.8</td>
<td>- Staphylococcus aureus</td>
<td>22.9</td>
</tr>
<tr>
<td>- Previously known native valve disease</td>
<td>7</td>
<td>- Coagulase-negative staphylococci</td>
<td>6</td>
</tr>
<tr>
<td>- Previous IE</td>
<td>42.3</td>
<td>- Other microorganism</td>
<td>10.9</td>
</tr>
<tr>
<td>Location of IE</td>
<td>34.8</td>
<td>- ≥ 2 microorganism</td>
<td>4</td>
</tr>
<tr>
<td>- Mitral</td>
<td>8</td>
<td>- No microorganism in blood culture</td>
<td>20.9</td>
</tr>
<tr>
<td>- Aortic</td>
<td>38.3</td>
<td>- No microorganism identified</td>
<td>16.4</td>
</tr>
<tr>
<td>- Aortic and mitral</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Right-sided IE</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Bilateral</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cardiac device IE</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Unknown</td>
<td>59.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode of acquisition</td>
<td>38.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Community</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Healthcare-related</td>
<td>3.84(1.42-10.38)</td>
<td>Multivariate logistic regression OR(95%CI)</td>
<td>0.01</td>
</tr>
<tr>
<td>- Intravenous drug use</td>
<td>Age &gt; 50 years</td>
<td>3.45(1.63-7.29)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Blood culture-negative EI</td>
<td>In-hospital death</td>
<td>4.71(2.21-10.08)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cardiac Surgery</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>In-hospital death</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.
Introduction

Enterococci are the third most common causal agent of infective endocarditis (IE) worldwide and it is increasingly prevalent. 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 and American 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. However, long courses of ampicillin and aminoglycosides imply a high likelihood of renal toxicity, especially among the elderly, such as 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 short course group. Nevertheless, another difficulty, besides ampicillin nephrotoxicity, raised during the last decade in the treatment of enterococcal IE: increasing rates of high-level aminoglycosides resistance have been detected worldwide. Since the efficacy of double beta-lactam therapy was firstly described in the mid-1990s in vitro, and thereafter has been proved in animal models and in a small non-randomized clinical trial performed in Spain, this option has 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 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 26-month follow-up. Analysis was performed by an intention-to-treat basis. Demographic features, microbiological and clinical outcomes and toxicity were analysed.

References


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 (<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 in between groups.

Table 1. Epidemiological and clinical features of patients.

Table 2. Clinical profile and outcomes.

Conclusions

• Our data suggest that 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, 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.
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.

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.

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.

CONCLUSIONS

1. PET/CT seems a useful tool in the early management of IE of cardiac protheses 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

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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 these variables (r=0.088, figure).

Results

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.

Introduction

The mortality of 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 IE in one French region in 2011 (198 patients, Se 90%, PPV 87.4%). The frequency of definite IE according to Duke criteria linked to the HDD summary was 74.4%, 95% CI 67.9%-80.9%.1
- Risk factors of in-hospital mortality were estimated using logistic regression model.
- Correlation between regional frequency of surgery and regional mortality was analyzed.

Conclusions

- Risk factors of in-hospital 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.

References

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, uncontrollable infection, high risk of embolism or intra-cardiac damages [Huib 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 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.

OBJECTIVES

The aim of this study was to identify pre-operative risk factors 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

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 prosthesis valve IE. Many observational studies [Lalani 2010, Bannay 2009, Kieler 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 define these criteria and to evaluate if thrombosis 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 [Moris 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.

In-hospital mortality was 25%.

Post-operative complications in ICU 82/149 = 55% :
- ARDS, n=35
- Acute renal failure requiring dialysis, n=43
- Neurological infection, n=38
- Used a new post-cardiac surgery, n=45

Correlated with severity of patients and EuroSCORE II (table 1)
**Unique blood culture for diagnosis of bloodstream infections - A prospective multicentre study**

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**Background**

Detection of microorganisms by blood cultures (BCs) is essential in managing patients with bloodstream infection (BSI). The use of a unique blood culture (UBC) in a large volume of blood, to reduce the risk of contamination, was evaluated in a prospective multicentre study.

**Patients included**

Patients with a first set of four bottles (n=2314) in Caen (n=1551), Lille (n=461) and Rouen (n=302). Subsequent 2-bottle set not performed (n=1119) and patients with well labelled first 4-bottle set and from 1 to 3 subsequent 2-bottle sets drawn (n=1195) were included in analysis (n=826). Patients with a 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 a confirmed contaminant.

**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 cultures (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.

**Results**

UBC allowed detecting pathogens in the blood of 97.1% of patients versus 95.5% for MBC (89.8% with the first 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 a confirmed contaminant.

**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 €183,275 annually for Caen University Hospital (€193,795 in Lille and €172,571 in Rouen).

**Acknowledgements**

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Microbiological diagnosis in Cardiac Device Infections: the role of sonication


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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) 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 LLD, Spectranetics®, Colorado Springs, CO, USA), knives, laser or radiofrequency. A total of 75 collected devices (45 generators and 30 leads) 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 (BioMérieux) system was used to perform the antimicrobial susceptibility testing. For daptomycin, gradient test diffusion (E-test) was used to perform antimicrobial susceptibility. Table 1. General characteristics of study population

Table 2. Performance of sonication in the diagnosis of CDs

Table 3. Causative microorganisms of CDs

Figure 1. 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. Two independent pocket swabs were performed in 12 subjects. Leads included atrial and/or ventricular electrodes, wires.

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 as 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.