Management of patients hospitalized for diabetic foot infection: Results of the French OPIDIA study


Department of Diabetology and Nutritional Diseases, Carémeau University Hospital, place du Professeur-Robert-Debré, 30029 Nîmes cedex 9, France

Department of Bacteriology, Caremeau University Hospital, Nîmes, France

Department of Diabetology, Metabolic Diseases and Nutrition, Jeanne d’Arc Hospital, Dommartin-les-Toul, France

Department of Diabetes and Metabolic Diseases, Pitié-Salpêtrière Hospital, AP–HP, Pierre-et-Marie-Curie University, Paris, France

Department of Endocrinology and Diabetology, Robert-Debré University Hospital, Reims, France

Department of Infectious Diseases, Dron Hospital, Tourcoing, France

Received 5 May 2010; received in revised form 28 September 2010; accepted 1st October 2010

Abstract

Aim. – This study was an analysis of how diabetic patients with infected foot wounds are managed in hospital by departments specializing in diabetic foot pathology, including an evaluation of the outcome 1 year after discharge.

Methods. – This was a prospective study of a cohort of patients hospitalized for diabetic foot infection at 38 hospital centres in France and followed-up for 1 year after discharge.

Results. – Altogether, 291 patients were included (73% male; 85% type 2 diabetes; mean age: 64.3 ± 11.7 years). Most of the wounds were located on the toes and forefoot, and infection was most often graded as moderate; nevertheless, in about 50% of patients, osteomyelitis was suspected. Also, 87% of patients had peripheral neuropathy and 50–62% had peripheral artery disease. Gram-positive cocci, and Staphylococcus aureus in particular, were by far the most frequently isolated microorganisms. During hospitalization, lower-limb amputation was performed in 35% of patients; in 52%, the wound healed or had a favourable outcome. A year after discharge, 150 non-amputated patients were examined: at this time, 19% had to undergo amputation, whereas 79% had healed their wounds with no relapse. Risk factors for amputation were location (toes), severity of the wound and presence of osteomyelitis. Peripheral artery disease was associated with a poor prognosis, yet was very often neglected.

Conclusion. – In spite of being managed at specialized centres that were, in general, following the agreed-upon published guidelines, the prognosis for diabetic foot infection remains poor, with a high rate (48%) of lower-limb amputation.

© 2010 Elsevier Masson SAS. All rights reserved.

Keywords: Amputation; Diabetic foot; Infection

Résumé

Prise en charge des patients hospitalisé pour pied diabétique infecté : résultats de l’étude française OPIDIA.

Objectif. – Décrire la prise en charge des patients diabétiques hospitalisé pour plaie infectée du pied et le devenir à un an de leur plaie.

Méthodes. – Étude prospective d’une cohorte de patients hospitalisés dans 38 centres hospitaliers français avec suivi à un an.

© 2010 Elsevier Masson SAS. Tous droits réservés.
1. Introduction

Diabetic foot infection (DFI) is a common and costly [1] complication of foot ulcers in diabetic patients, and represents a major cause of morbidity and mortality. It is thought to be the most common cause of diabetes-related admission to hospital, and is one of the primary routes leading to lower-limb amputation [2–4]. As a whole, it is estimated that 15–25% of diabetics will suffer from foot ulceration at some time during their life, and between 40 and 80% of these ulcerations will become infected [5]. Moreover, it was recently reported that the risk of hospitalization and lower-extremity amputation was around 56 and 155 times greater, respectively, in diabetics with, compared with those without, a foot infection [6].

To reduce the burden of DFI, several guidelines have been published for the management of this pathology [2,7], including those recently proposed by the French Society of Infectious Disease (Société de pathologie infectieuse de langue française [SPIFLF]) [5].

However, to the best of our knowledge, no specific data on DFI and its management in France are currently available [8]. For this reason, the present study was implemented to determine precisely how DFI is managed in French hospitals and to follow-up its outcome a year later.

2. Material and methods

2.1. Study description and population

This prospective multicentre observational study was conducted from 12 January 2007 to 9 June 2009. A protocol, designed by a steering committee, was initially submitted to 51 French hospitals selected from a national list of hospitals known to manage DFI. At each hospital, the protocol was then submitted to the endocrinologists involved in diabetic foot management. Altogether, 38 endocrinologists agreed to participate in the study.

As described in the protocol, each investigator had to include the first 10 consecutive patients who met the following criteria:

(i) type 1 or 2 diabetes;
(ii) age ≥ 18 years old;
(iii) hospitalized for an infected foot wound [grades 2–4, according to the Infectious Diseases Society of America/International Working Group on the Diabetic Foot (IDSA/IWGDF) classification; see below] requiring antibiotic therapy.

As this observational study was designed to be representative of all diabetic patients with an infected diabetic foot ulceration, no exclusion criteria were applied, especially as regards to the presence of other diabetic complications (including renal failure) or co-morbidities.

2.2. Data collection

The information collected by each investigator on a case-report form during hospitalization included:

(i) baseline characteristics of the study population (sociodemographic data, and clinical data on diabetes and the wound);
(ii) methods used to investigate the infected lesion (neurological and vascular examinations, imaging, wound sampling and microbiological assays);
(iii) management of the infected wound and discharge plans.

In the case of multiple wounds on the same foot or on both feet, the investigator chose the most severe wound as the index case. Each wound was examined for local signs of inflammation and explored with a sterile blunt metal probe [9]. Methods for ulcer area measurement and wound sampling were left to the discretion of each investigator. Culture, organism identification and susceptibility testing were performed at each site laboratory. Multidrug-resistant organisms (MDROs) were defined as methicillin-resistant \textit{Staphylococcus aureus}, glycopeptide-resistant enterococci, Enterobacteriaceae species resistant to third-generation cephalosporins (extended-spectrum \(\beta\)-lactamases and derepressed cephalosporinase), ceftazidime-resistant \textit{Acinetobacter baumannii}, and \textit{Pseudomonas aeruginosa} resistant to at least two of the following antibiotics: ticarcillin, ciprofloxacin, ceftazidime and imipenem.

Neuropathy was assessed by the presence or absence of paraesthesia or cramps, dry skin or hyperkeratosis on the foot, Charcot foot, other foot deformities and protective sensation...
Peripheral artery disease (PAD) was clinically assessed by the presence or absence of suggestive symptoms, such as intermittent claudication and leg pain at rest, and signs such as cold legs or feet, pale or bluish-looking skin and foot pulses. In addition, according to the usual local practices, Doppler ultrasound, ankle–brachial pressure index (ABPI), transcutaneous oxygen pressure (TcPO₂) and great-toe systolic pressure examinations were performed, as were imaging tests (plain radiography, magnetic resonance imaging [MRI], computed tomography [CT], bone and leucocyte scintigraphy, and angiography).

Diabetes was classified into four categories:

- “type 1”, if onset was before age 30 years or if insulin treatment was initiated within 2 years of diagnosis;
- “type 2a”, if onset was after age 30 years and treatment was with oral hypoglycaemic drugs;
- “type 2a”, if onset was after age 30 years and insulin treatment was initiated more than 2 years after diagnosis;
- “other”, which included all other types of the disease.

Wound severity was assessed using the University of Texas (UT) classification system [11], and infection was graded according to the IDSA/IWGDF system [12]. In addition, the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) definition was used to assess sepsis [13].

At the end of hospitalization, patients were classified into three groups according to outcome:

(i) amputation;
(ii) stable or worsening wound;
(iii) improving or healed wound.

All patients, except those who underwent amputation, were scheduled to attend an end-of-study examination 1 year after discharge, when their outcome was then classified as:

(i) healed wound;
(ii) healed wound, but with secondary infectious relapse;
(iii) non-healed wound;
(iv) minor or major amputation, defined as amputation below or above the ankle, respectively.

2.3. Statistical methods

All data were analyzed by RCTs (Lyon, France). Statistical analyses were carried out using SAS software for Windows (Statistical Analysis System, version 9.1, SAS Institute, Cary, NC, USA). Population characteristics were expressed as means ± standard deviation (S.D.) or medians, using the first and third quartiles for quantitative variables, and percentages (%) for qualitative variables. Factors associated with amputations performed during the study period were analyzed using univariate logistic regression; statistically significant factors were entered into a multivariate logistic-regression model. All P values were two-tailed, with P < 0.05 considered statistically significant.

2.4. Ethical considerations

As this was an observational study involving no changes to the patients’ usual medical management, no study protocol had to be submitted for ethics committee approval, which is in accordance with the current French legislation. However, patients were provided with both oral and written information by the investigator, and gave their verbal consent before being included in the study. They were also informed of their rights under French information-protection laws. All questionnaire data were rendered anonymous by a procedure validated by the French Data Information Protection Commission (Commission nationale de l’informatique et des libertés).

3. Results

3.1. Baseline characteristics of the study population

Altogether, 304 patients were initially included in the present study, although 13 were excluded from the statistical analysis because of missing data. The final study population comprised 291 patients (Fig. S1; see supplementary material associated with this article online), and their demographic and clinical characteristics are presented in Table 1. Most of the included patients were male and age > 60 years; 80% were overweight or obese and 85% had type 2 diabetes. In the year prior to hospitalization, 40% of patients had a history of infected foot ulcer and, at the time of presentation, 34% had had a previous lower-limb amputation, mainly at toe level (84%).

3.2. Baseline wound characteristics

On entry into the study (Table S1; see supplementary material associated with this article online), most of the patients had a severe wound, with 56% considered grade 3 according to the UT classification system. Eight wounds were initially classified as non-infected (stage A) by the investigators but, after reviewing the data, the steering committee decided to reclassify four of the wounds from stage A to stage B, and four other wounds from stage C to stage D, as a consequence of an obvious coding error. Lesions involved mainly the toes (45%) or forefoot (34%) and, most usually, the infection was moderate, according to the IDSA/IWGDF classification. In 95% of ulcers, local inflammatory manifestations were noted. Purulent discharge was present in 62% of wounds, and sepsis in 42%. Probing the bone through the ulcer was positive in 47% of ulcers and, thus, suggestive of underlying osteomyelitis.

3.3. Assessment of neuropathy and arterial disease

Protective sensation, as assessed in 278 patients by the 10-g monofilament test, was lost in 252 patients (87%), and Charcot foot deformity was present in 39 (13%). Intermittent claudica-
Table 1
Sociodemographic and clinical characteristics of the study population (n = 291).

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Patients (n [%])</th>
<th>Mean ± S.D. [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: male/female</td>
<td>212 (72.9)/79 (27.2)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.3 ± 11.7 [23–93]</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (&gt;25 kg/m² and &lt;30 kg/m²)</td>
<td>111 (38.7)</td>
<td>29.8 ± 6.3 [15.4–60.2]</td>
</tr>
<tr>
<td>Obesity (≥30 kg/m²)</td>
<td>120 (41.8)</td>
<td></td>
</tr>
<tr>
<td>Diabetes type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>36 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Type 2a (treated by oral drugs)</td>
<td>127 (43.9)</td>
<td></td>
</tr>
<tr>
<td>Type 2b (treated by insulin)</td>
<td>120 (41.5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td></td>
<td>17.5 ± 11.1 [0–49]</td>
</tr>
<tr>
<td>Diabetes complications</td>
<td>265 (91.7)</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>159 (54.6)</td>
<td></td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>134 (46.1)</td>
<td></td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>231 (79.4)</td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>75 (25.8)</td>
<td></td>
</tr>
<tr>
<td>Nephropathy</td>
<td>119 (41.2)</td>
<td></td>
</tr>
<tr>
<td>HbA1c ≥ 7.0%</td>
<td>170 (68.8)</td>
<td>8.25 ± 2.2 [4.6–17.8]</td>
</tr>
<tr>
<td>History of infected foot ulcer</td>
<td>115 (39.5)</td>
<td></td>
</tr>
<tr>
<td>History of lower-limb amputation</td>
<td>99 (34.0)</td>
<td></td>
</tr>
<tr>
<td>Minor/major</td>
<td>91/8</td>
<td></td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>222 (76.6)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>153 (52.9)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>32 (11.0)</td>
<td></td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>125 (43.1)</td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>133 (45.9)</td>
<td></td>
</tr>
</tbody>
</table>

a Missing data: 4.

b Missing data: 2.

c Missing data: 1.

d Glomerular filtration rate <60 mL/min/1.73 m² (Modification of Diet in Renal Disease [MDRD] formula) [14].

e Within 2 months prior to inclusion.

f Within the year prior to hospitalization.

tion and leg pain at rest was reported by 8% and 7% of patients, respectively. Peripheral pulses were examined in 286 patients: dorsalis pedis and posterior tibial pulses were absent in 48% and 56% of patients, respectively, and neither pulse was palpable in 45%. ABPI was measured in only 98 patients: mean (± S.D.) was 0.92 (± 0.28) (median of first to third quartiles: 1.00; range: 0.77–1.12). ABPI values were <0.90 in 37 patients and >1.30 in four, and considered normal in 58% (57/98) of those in whom it was performed. Measurements of TcPO2 and great-toe systolic pressure were rarely performed (in 25% and 2% of patients, respectively), whereas Doppler ultrasonography was carried out in most cases (230/291 patients, 79%); waveform analysis was considered normal in only 28% (64/229) of patients.

3.4. Imaging and microbiology

Altogether, 99% of patients underwent at least one medical imaging investigation, mostly plain radiography (98%). Medical imaging to assess arterial disease (angiography, angio-MRI or angio-CT) was carried out in 21% of patients and, in particular, before amputation (25%) or because of a worsening wound (35%).

Samples for microbiological assays were taken in 86% of patients (n = 251), usually on the day of admission. Swabbing the wound was the most frequently used technique (60%). Curettage was done in 49 patients (19%), as was bone biopsy. Cultures were positive in 213 of the 251 patients (85%) from whom specimens were collected.

As a whole, 395 samples were obtained but, for technical reasons, 27 were not usable. Of the remaining 368 samples, cultures were positive in 80% (n = 294), and accounted for 351 organisms. The mean (± S.D.) number of samples per patient was 1.6 (± 0.7), and the mean number of bacteria per positive culture was 1.4 (± 0.7). Of the cultures, 68% were monomicrobial, and Gram-positive cocci were the most frequently recovered organisms, comprising 60% of all strains (Table 2). By far, S. aureus was the predominant pathogen found, accounting for 54% of all Gram-positive organisms and 32.5% of all isolates. Strep- tococcus species were the next most frequently cultured group among Gram-positive bacteria, recovered from 48 specimens.
who received topical antibiotic treatment. Median duration of (49%), or both oral and parenteral (12%), except for one patient infected wound). Antibiotic therapy was oral (39%), parenteral (28%), and conservative surgery in 70 (24%).

3.5. Wound management and treatment of infection

As shown in Table S2 (see supplementary material associated with this article online), off-loading the wound was applied in nearly all cases, and bedside debridement was frequently done. Vascular reconstruction was performed in 25 patients (9%) and conservative surgery in 70 (24%).

On the day of admission to hospital, all patients were treated with antibiotics, administered for the first time in 84% and continued in 16% (52% of patients had a history of antibiotic treatment within the previous three months, mainly for an infected wound). Antibiotic therapy was oral (39%), parenteral (49%), or both oral and parenteral (12%), except for one patient who received topical antibiotic treatment. Median duration of parenteral therapy (alone or associated with oral administration) was 10.5 days (first–third percentiles: 6–16 days); in 82% of patients receiving parenteral therapy, treatment was continued with oral agents for a median duration of 30 days (first–third percentiles: 20.5–60 days).

A total of 62 combinations of antibiotics were prescribed although, by far, the most frequently prescribed antibiotic agents were penicillin derivatives associated with β-lactamase inhibitors (amoxicillin or ticarcillin/clavulanic acid), used in 49% of cases. Fluoroquinolones were used in 32% of patients, extended-spectrum penicillins in 15%, and semisynthetic penicillinase-resistant penicillins, streptogramins (pristamycins) and aminoglycosides (mainly gentamicin) in 12%. Other agents rarely prescribed as first-line therapy included carbapenem (3%), third-generation cephalosporin (3%) and β-lactamase-sensitive penicillin (1%). In 56% of patients, the initial antibiotic regimen was changed mainly due to a mismatch in susceptibility results.

3.6. Outcome and discharge

Median hospital length of stay (LOS) was three weeks (first–third percentiles: 1.9–4.4 weeks). Lower-limb amputation was performed in 101 patients (35%) while in hospital and was mostly minor, limited to toes in 82 (81%) patients and transmetatarsal in 10 (10%). Two patients underwent a second amputation on the contralateral limb, and two others on the ipsilateral limb at a more proximal level. In 150 patients (52%), the wound improved or healed whereas, in 40 (14%), it stayed the same or worsened. Thus, the outcome was considered unfavourable in 141 patients, and a history of previous amputation together with infection was associated with the poorest outcomes (Table S3; see supplementary material associated with this article online). LOS was longer in amputated (3.9 weeks) compared with non-amputated patients regardless of whether the wounds improved or healed (2.8 weeks), or worsened or stayed the same (2.5 weeks).

At the time of discharge, 74% of patients were being treated with antibiotics, mainly β-lactams (52%) and fluoroquinolones (45%). Also, 72% of the discharged patients returned home, while 28% were transferred to another hospital department.

3.7. One-year outcome

A total of 23 (8%) patients of the 291 included in the present analysis died during the study – one while in hospital and 22 within a year of discharge. No deaths were related to the infectious process itself.

In addition, 150 (79%) of the 189 patients scheduled to attend the end-of-study examination did so. During the period between discharge and consultation, 18 patients died and 21 were lost to follow-up. Also, 28 of the 150 patients (19%) underwent amputation within a year of discharge: the amputation was minor in 15 patients and major in 13.

In 96 of the 122 non-amputated patients who attended the follow-up visit (79%), the wound had healed with no relapse; in two patients, infection recurred after initial healing and, in 23 (19%) cases, the wound remained open and infected.

Table 2

Foot ulcer characteristics in diabetic patients on entry into the study (n = 291).

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>n (%)</th>
<th>MDROs b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive aerobic cocci</td>
<td>210 (59.8)</td>
<td>29</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>114 (32.5)</td>
<td>28</td>
</tr>
<tr>
<td>Streptococcus spp.</td>
<td>48 (13.7)</td>
<td>–</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>28 (8.0)</td>
<td>1</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>16 (4.6)</td>
<td>–</td>
</tr>
<tr>
<td>Other gram-positive aerobic cocci</td>
<td>4 (1.1)</td>
<td>–</td>
</tr>
<tr>
<td>Gram-negative aerobic bacilli</td>
<td>126 (35.9)</td>
<td>12</td>
</tr>
<tr>
<td>Enterobacteriaceae spp.</td>
<td>95 (27.1)</td>
<td>6</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>17 (4.8)</td>
<td>1</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>20 (5.8)</td>
<td>1</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>17 (4.8)</td>
<td>2</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>4 (1.1)</td>
<td>–</td>
</tr>
<tr>
<td>Morganella morgani</td>
<td>15 (4.3)</td>
<td>1</td>
</tr>
<tr>
<td>Citrobacter spp.</td>
<td>4 (1.1)</td>
<td>1</td>
</tr>
<tr>
<td>Hafnia alvei</td>
<td>1 (0.3)</td>
<td>–</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>5 (1.4)</td>
<td>–</td>
</tr>
<tr>
<td>Other Enterobacteriaceae</td>
<td>2 (0.6)</td>
<td>–</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>23 (6.6)</td>
<td>6</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>3 (0.9%)</td>
<td>–</td>
</tr>
<tr>
<td>Other gram-negative aerobic bacilli</td>
<td>5 (1.4)</td>
<td>–</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>7 (2.0)</td>
<td>–</td>
</tr>
<tr>
<td>Gram-positive aerobic bacilli</td>
<td>8 (2.3)</td>
<td>–</td>
</tr>
<tr>
<td>Corynebacterium spp.</td>
<td>8 (2.3)</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>351</td>
<td>41</td>
</tr>
</tbody>
</table>

a Isolated bacteria out of all isolates (n = 351).

b Multidrug-resistant organisms, including methicillin-resistant Staphylococcus aureus, glycopeptide-resistant enterococci, Enterobacteriaceae resistant to third-generation cephalosporins (extended-spectrum β-lactamases and derepressed cephalosporinase), ceftazidime-resistant Acinetobacter baumannii and Pseudomonas aeruginosa resistant to at least two of the following antibiotics: ticarcillin, ciprofloxacin, ceftazidime and imipenem

(14% of all isolates), while Enterobacteriaceae (n = 95), enterococci (n = 28) and P. aeruginosa (n = 23) accounted for 27%, 8% and 7%, respectively, of all isolates. Only seven anaerobes were isolated, along with 41 MDROs (12% of all strains), while MDROs were present in 20% of patients whose culture was positive. In addition, 26% of P. aeruginosa and 25% of S. aureus were multidrug-resistant.
3.8. Risk factors for lower-limb amputation

Multivariate analysis showed that the risk of amputation during hospitalization and within the year following hospitalization was increased independently when:

(i) the lesion involved the toes;
(ii) the wound was graded C or D according to the UT classification system, or grade IV according to the IWGDF;
(iii) osteomyelitis was present.

On the other hand, debridement and conservative surgery during hospitalization lowered the risk of amputation. However, neither the presence of *S. aureus* nor MDROs in cultures appeared to be risk factors for amputation, although the incidence of amputation was significantly lower in patients already taking antibiotic agents when admitted to hospital. Detailed results are presented in Table S4 (see supplementary material associated with this article online).

4. Discussion

The aim of the present study was two-fold: to assess the management of DFI in French hospital units specializing in the care of patients with DFI; and to evaluate their outcomes. However, just as our study was beginning, the SPILF published its national guidelines for optimal management of DFI [5]. For this reason, it seemed logical to compare the procedures usually performed in French centres with those recommended by the SPILF.

As part of their clinical assessment, neurological (10-g monofilament test), vascular (palpation of peripheral pulses) and foot examinations had been performed in >95% of patients; however, it was surprising that non-invasive assessment of vascular status was rarely done, given the fact that peripheral ischaemia is frequently associated with DFI and constitutes a significant risk factor for lower-limb amputation [6,15–17]. Indeed, ABPI was measured in only a few patients, despite being a procedure that is inexpensive and easily performed, and an invaluable tool for PAD screening [18]. Furthermore, according to the American Diabetes Association (ADA), a screening ABPI should be performed in any diabetic patient aged >50 years [19], while the SPILF [5] recommends an ABPI in any diabetic patient with an infected foot wound. However, the high prevalence of medial artery calcification in older neuropathic diabetic patients renders the value of ABPI for diagnosing PAD less reliable than in the non-diabetic population [20], and may explain in part why ABPI was so infrequently measured. Moreover, Doppler ultrasound imaging was performed in the vast majority of patients, but not in all, as is recommended by the SPILF [5]. Indeed, it is worth noting that arterial waveform analysis revealed abnormalities in 72% of patients, emphasizing the high prevalence of PAD in patients with DFI [17]. Yet, few studies have been published on the evaluation of DFI and, as far as the present authors are aware, only one retrospective review was conducted in an inpatient setting – and emphasized the lack of detailed of lower-extremity examination. In that study, 31% of 255 patients admitted to hospital for DFI did not have their pedal pulses documented, and Doppler examination was performed in only 32% [21].

Our present study confirmed that toes are the most common site of infection, as has been previously reported [22–24]. Osteomyelitis, as diagnosed by a positive probe-to-bone test, was reported in nearly half of our patients, a prevalence rate in accordance with the findings by Lipsky [25], but far higher than is usually reported in the literature [6,23]. This may be explained by the fact that the present study included only hospitalized patients, whose infection was probably more severe than those seen in an outpatient setting. In any case, the predictive value of the probe-to-bone test has recently been challenged [26–28].

As regards to bacteriology, *S. aureus* was the most commonly isolated pathogen, and infection was often polymicrobial, as has been consistently reported in previous studies from Europe and the USA [2,5,23,24,29,30]. In the present study, this pathogen was recovered from 112 patients, and 25% of our isolated *S. aureus* were methicillin-resistant, a relatively low prevalence compared with previous studies [31–33]. This might be due to the decrease in the overall prevalence of MRSA in France, as reported by the French National Observatory for Epidemiology of Bacterial Resistance to Antimicrobials and the European Antimicrobial Resistance Surveillance System [34,35]. Moreover, the possible positive effects of the French health authorities' national campaigns promoting the more sensible use of antibiotic agents (1999) and the usefulness of hydro-alcoholic solutions for hand-washing (2001–2002) cannot be excluded [36], as such measures have been associated with reduced MRSA development and transmission [37]. In fact, although diabetic foot clinics are thought to be a major reservoir for MRSA, our present data are in accordance with a recent study suggesting that foot clinics do not play a key role in the acquisition and spread of MRSA [38].

The present study also showed that improved microbiological sampling is essential, as per the national and international recommendations for DFI. Inadequate and/or inappropriate wound sampling can result in the true pathogens responsible for infection being disregarded or the isolation of organisms not responsible for infection. For this reason, as emphasized in the SPILF recommendations [5], bacteriological sampling should be performed only if DFI has been clinically confirmed and corresponds to grade 2–4 infections, according to the International Consensus grading system. In addition, superficial swabs must not be used, as these fail to isolate aerobic bacteria and promote the isolation of colonizing flora. Indeed, the present data show that there is still much progress to be made even at specialized centres, as more than half of samples were obtained by swabbing the wound. The misuse of this sampling technique leads to lower isolation rates of the true pathogens.

Regarding DFI treatment, patients’ management was in line with the published guidelines [2,5], which include off-loading, debridement and systemic antibiotic therapy. However, the number of different protocols in use is still too large. The preferential use of penicillin/β-lactamase inhibitor congeners in our present study patients is probably due to the high prevalence of moderate-to-severe infection, and the need to cover both staphy-
loccal and streptococcal species, as emphasized by Lipsky [25], and recommended by American and French guidelines [2,5]. On admission to hospital, around one-third of our patients were taking fluoroquinolones and 12% were using aminoglycosides, whereas the SPIFLF does not recommend these agents as a first-line therapy for DFI, so the high rate of suspected osteomyelitis is probably the most likely explanation for their use. It is also worth noting the relatively high rate of pristinamycin prescription. This member of the streptogramin family is only marketed in some European countries, and has the advantages of an oral route, penetration into bone tissue and activity against multidrug-resistant *S. aureus* [39,40]. Moreover, this antibiotic agent is considered a good antistaphylococcal candidate in case of allergic sensitivity to β-lactams.

The present study also had a high rate of lower-limb amputation, with 48% of patients requiring amputation (101 while in hospital, and 28 within a year of discharge). However, minor amputations were considerably more frequent, accounting for 83% of all amputations. As suggested by multivariate analyses, the severity of infection and the frequently associated PAD were the most likely explanations for the high amputation rate, as the negative impact of PAD in association with infection has been clearly established [15,41,42]. In addition, the results of our study confirm the benefits of debridement and conservative surgery [43].

5. Conclusion

The present study showed that the overall outcome for diabetic patients hospitalized for an infected foot wound remains poor even at specialized centres. DFIs are often polymicrobial, although *S. aureus* remains the most frequently isolated aetiological agent. DFIs are often complicated by osteomyelitis, which makes treatment more difficult, while increasing the risk of lower-limb amputation. As a whole, however, the recommended guidelines have been put into practice at these centres, except for deep wound sampling and systematic screening for PAD. Although PAD appears to be a major factor associated with a poor outcome and amputation in patients with DFI, it is often overlooked. This suggests an urgent need to increase awareness of this issue among healthcare providers involved in the management of diabetic foot, and the requirement for specific guidelines for the screening and treatment of PAD in diabetic patients [44].

Conflict of interest statement

J.-L. Richard, J.-P. Lavigne, I. Got, A. Hartemann, D. Malgrange, D. Tsirtsikolou and E. Senneville have received consultants’ fees and honoraria from Merck Sharp & Dohme-Chibret for their participation in the OPIDIA study. A. Baleydier is a paid employee of RCTs, the company in charge of managing the study. In addition, the authors (i) have occasionally served as consultants to Merck Sharp & Dohme-Chibret (J.-L.R., J.P.L., I.G., A.H., D.M., D.T.), Wyeth (J.-L.R.), Pfizer (J.-L.R., A.H., D.T.), Genévrier (A.H.), Pierre Fabre (A.H.), Sanofi Aventis (D.T.), Novo-Nordisk (D.T.).

Acknowledgements

The authors wish to thank all of the hospital teams that participated in the study and, in particular, Flavien Roux (RCTs) for his help with the statistical analysis, and Fabienne Péretz (independent medical writer) for her help in preparing this manuscript.

Appendix A. Supplementary data

Fig. S1, and Tables S1–S4, associated with this article, can be found at http://www.sciencedirect.com, at doi:10.1016/j.diabet.2010.10.003.

Annexe B. Principal investigators in the OPIDIA study group

Drs Mahmoud Aich (Bobigny), Antoine Avignon (Montpellier), Annie Begey (Besançon), Adel Ben Ali (Paris), Emmanuelle Berthe (Granville), Martine Bonello-Farai (Nice), Lyse Bordier (Saint-Mandé), David Boutouille (Nantes), Blan- dine Delenne (Aix-en-Provence), Laurent Dusselier (Metz), Isabelle Got (Dommartin-les-Toul), Françoise Granier (Mantes-la-Jolie), Christian Guillelmet (La-Roche-sur-Yon), Laurent Hocqueloux (Orléans), Nathalie Jourdan (Nîmes), Marie-Pierre Larmaraud (Vienne), Philippe Lecocq (Valenciennes), Marc Lepeut (Roubaix), Taina Louissaint (Créteil), Jocelyne M’Bemba (Paris), Dominique Malgrange (Reims), Jacques Martini (Toulouse), Arnaud Monier (Le Coudray), Chantal Mounier (Lyon), Daniel Mouroux (Marseille), Marie-Pierre Muller (Grenoble), Floriane Ouliac (Marseille), Geneviève Ozenne (Bois-Guillaumette), Jean-Louis Richard (Le Grau du Roi), Béatrice Roche (Vichy), Renan Roussel (Paris), Agnès Salle (Angers), Eric Senneville (Tourcoing), Emmanuel Sonnet (Crest), Bilal Trabulsi (St-Brieux), François Truchetet (Thionville), Muriel Tschudnowsky (Dole), Nathalie Viger-Simorre (Narbonne), Julien Vuillarmet (Pierre-Bénite).

The study was supported by Merck Sharp & Dohme-Chibret, which also participated in the study design, data collection, data analysis, data interpretation and the writing of the final report. The corresponding author (J.-L.R.) had full access to all study data and was responsible for the final decision to submit the report for publication.

References