Morbidity and mortality of infected diabetic foot managed in general surgical department

La morbidité et la mortalité du pied diabétique infecté pris en charge dans un service de chirurgie générale

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RÉSUMÉ

Introduction : Les ulcères du pied diabétique sont des complications qui surviennent dans 10% à 25% des cas. Ils représentent une cause importante de morbidité et de mortalité liée au diabète. Cette étude rétrospective a pour but d'évaluer, à l'aide d'une base de données administrative, le risque de morbidité et de mortalité des pieds diabétiques infectés.

Méthodes: Il s'agit d'une étude rétrospective colligeant des patients diabétiques opérés entre le 1er Janvier 2012 et le 31 Décembre 2016 dans le service de chirurgie B de l'hôpital Charles Nicolle. La régression logistique a identifié des facteurs indépendants prédictifs d'amputation majeure, de morbidité et de mortalité.

Résultats: Cette étude rétrospective, colligeant 644 patients diabétiques, a montré que l'insuffisance cardiaque (OR=5.00, IC 95% [1.08-23.25], p=0.039), l'admission en réanimation durant les 48 premières heures (OR=12.76, IC 95% [4,92-33,33], p<0,001) et l'amputation majeure (OR=6,40, IC 95% [2,41-16,94], p<0,001) étaient prédictifs de mortalité.

Concernant la morbidité, l'insuffisance cardiaque (OR=0,163, IC95% [0,055-0,479], p=0,001) et la défaillance d'un organe à l'admission (OR=0,017, IC 95% [0,004-0,066], p=0,017) étaient des facteurs prédictifs d'admission en milieu de réanimation pendant les 48 premières heures. En outre, l'âge avancé (OR=1.033, IC à 95% [1.014-1.052], p=0.001), le séjour préopératoire (OR=1.093, IC à 95% [1.039-1.151], p=0.001) et l'admission en réanimation pendant les 48 premières heures (OR = 0,142, IC 95% [0,071-0,285], p <0,001) étaient des facteurs prédictifs d'amputation majeure. De plus, l'insuffisance cardiaque (OR=0,517, IC 95% [0,298-0,896], p=0,019), l'admission en réanimation pendant les 48 premières heures (OR=0,176, IC 95% [0,088-0,354], p<0,001) et le séjour pré-opératoire (OR=1,083, IC 95% [1,033-1,134], p=0,001) étaient des variables prédictives des complications post-opératoires. L'admission en réanimation pendant les 48 premières heures (OR=0.140, IC 95% [0.48-0.405], p <0.001), l'amputation majeure (OR=0.170, IC 95% [0.76-0.379], p <0.001) et le nombre de séjours en réanimation (OR=3,334, IC à 95% [1,558-7.164], p=0,002) étaient des facteurs prédictifs de complications médicales. La durée du séjour pré-opératoire (OR=1,091, IC 95% [1,038-1,147], p=0,001) était prédictif de réintervention.

Conclusions: Notre étude rétrospective a montré que le taux de mortalité était moindre quand le patient n'avait pas eu d'amputation de jambe, de complications post-opératoires ou de réintervention. La principale limite de notre étude était la forme rétrospective.

Mots-clés

Pied diabétique, infection, amputations, mortalité

SUMMARY

Background: Foot ulcers are diabetes-related complications which occur in 10%-25% in diabetic patients. They are an important cause of morbidity and mortality in diabetes. This retrospective study aimed to assess, using an administrative database, the morbidity and the mortality risk of infected diabetic ulcers.

Methods: It's a retrospective study enrolling 644 patients operated on for a diabetic foot between January 1st, 2012 and December 31st, 2016 in the surgical department B of Charles Nicolle's Hospital. Logistic regression identified independent predictive factors of major amputation, morbidity and mortality.

Results: This retrospective study showed that "Cardiac failure" (OR=5.00, 95%CI [1.08-23.25], p=0.039), "Admission in the ICU in the first 48h" (OR=12.76, 95%CI [4.92-33.33], p<0.001) and "Major amputation" (OR=6.40, 95%CI [2.41-16.94], p<0.001) were considered as independent predictive factors of mortality. As concerns morbidity, Cardiac failure (OR=0.163, 95%CI [0.055-0.479], p=0.001) and organ failure at admission (OR=0.017, 95%CI [0.004-0.066], p=0.017) were predictive factors of admission in the ICU during the first 48 hours. Besides, advanced age (OR=1.033, 95%CI [1.014 -1.052], p=0.001), Pre-operative stay (OR=1.093, 95%CI [1.039-1.151], p=0.001) and admission in the ICU during the first 48 hours (OR=0.142, 95%CI [0.071-0.285], p<0.001) were predictive factors of major amputation. Moreover, Cardiac failure (OR=0.517, 95%CI [0.298-0.896], p=0.019), admission in the ICU during the first 48 hours (OR=0.176, 95%CI [0.088-0.354], p<0.001) and Pre-operative stay (OR=1.083, 95%CI [1.033-1.134], p=0.001) were predictive variables of complicated post-operative course. Admission in the ICU during the first 48h (OR=0.140, 95%CI [0.48-0.405], p<0.001), major amputation (OR=0.170, 95%CI [0.76-0.379], p<0.001), and number of ICU stays (OR=3.341, 95%CI [1.558-7.164], p=0.002) were predictive factors of medical complications. Preoperative stay (OR=1.091, 95%CI [1.038-1.147], p=0.001) was predictive of reintervention.

Conclusions: Our retrospective study assessed that mortality rate was inferior when the patient didn't have amputation, no post-operative complications and no reintervention. The main limitation of our study was the retrospective design.

Key-words

Diabetic foot, infection, amputations, mortality

INTRODUCTION

Diabetes is a major public health problem. Foot ulcers are diabetes-related complications. They occur in 10%-25% in diabetic patients [1]. They are an important cause of morbidity and mortality for diabetic patients [1].

Diabetic foot treatment is either medical or surgical. Medical treatment consists on a broad spectrum antibiotic therapy. Surgical treatment consists on either a major amputation, performed through the leg or the thigh, or a minor amputation involving the toes or the foot [2]. Amputation of the lower limb represents the ultimate solution for a peripheral arterial occlusive disease caused by diabetic foot. Amputation is still widely performed despite all measures that have been performed to manage diabetes and its complications. Major amputation's mortality ranged between 13.3% and 17.8% and minor amputation's mortality was varying from 5.2% to 12% according to series [3,4].

When we consulted Medline database with the key words 'diabetic foot ulcers', we noticed that the articles concerning diabetic foot ulcer increased from 307 in 1998 to 822 articles in 2016.

This retrospective study, using an administrative database, aimed to assess the morbidity and mortality risk of infected diabetic ulcers.

METHODS

This retrospective study enrolled consecutive patients admitted for an infected diabetic foot between January 1st, 2012 and December 31st, 2016 in the surgical department B of Charles Nicolle's Hospital.

Eligibility criteria:

We included patients from 18 years old and above, admitted for an infected diabetic foot, in the surgical department B of Charles Nicolle's hospital, whatever their gender, past medical history, emergency context and the surgery carried out.

Non eligibility criteria:

We did not include neither the non-diabetic patients, nor foot ulcer due to reasons other than diabetes mellitus.

Surgical approach:

Major amputation: We defined a major amputation as an amputation performed above the ankle through the tibia or the femur [2].

Minor amputation: We defined a minor amputation as an amputation involving the toes or the foot (at the ankle's level and below) [2].

Data collection:

Were culled the following variables: age, gender, comorbidities (Diabetes, hypertension/cardiac failure, renal failure), previous surgery, American Society of Anaesthesiologists (ASA) classification, admission in an intensive care unit (ICU) during the first 48 hours, intervention, anaesthesia type (general/loco regional), level of amputation (major/ minor/excision), operator (senior/resident), median operative time, transfusions, post-operative course, medical complications which correspond to extra surgical site complications, resuscitation, respiratory assistance, reintervention, mortality, post-operative stay, hospital stay duration.

Outcome measures:

The main outcome measure was mortality, defined as death that occurred during the hospital stay or within 30 days after surgery [4].

The secondary outcome measures were: 1/ Admission in the ICU during the first 48 hours, 2/ Major amputation, 3/ Operative time, 4/ Reintervention, 5/ Post-operative complications defined as complications that occurred during the hospital stay, which may be related to the comorbidities or to the performed surgery. The types of complications analyzed were: medical complications, surgical complications and mortality [4]. 6/ Post-operative hospital stay

Statistical analysis:

Data were analyzed with SPSS® software (Statistical Package for the Social Science, SPSS®, Inc; version 23.0).

Descriptive analysis reported the baseline characteristics of all patients and the subgroup of operated patients. Qualitative variables were mentioned with its counts and percentages. Continuous variables were mentioned by means and standard deviations when the distribution was normal and by median values accompanied with interquartile ranges (IQR) and ranges when the distribution was not normal.

Bivariate analysis was performed with the chi-square test and Fisher's exact test for qualitative variables and the Student-t-test for quantitative variables. When the distribution was not Gaussian, the Mann-Whitney U test was used. All variables with a p value ≤ 0.05 were introduced into a logistic regression model. For predictive continuous variables, we applied receiving operating characteristic (ROC) curve to identify the cut-off point with the best couple sensitivity and specificity. We calculated the area under the curve with its $^{95\%}$ Confidence Interval.

Ethical considerations: All information of each patient was collected through a retrospective medical record review. All these informations were confidential.

Conflicts of interests: None.

RESULTS

Descriptive analysis:

Four hundred seventy two men (73.3%) and 172 women (26.7%) met eligibility criteria. The mean age (± standard) was 61.28±12.28 years. The majority of patients were classified by the American Society of Anaesthesiologists (ASA) as ASA II in 395 cases (76.4%). Three hundred sixty eight patients (57.1%) had hypertension or a cardiac failure. Intervention was performed for 544 patients (84.5%). One hundred and fourteen patients underwent major amputation (21%). Post-operative course was uneventful for 465 patients (85.5%). Global mortality rate was 4.3%. Median value of the post-operative stay duration was two days [0-76] IQR [1-4] (Table 1).

Admission in an ICU* during the first 48 hours:

Bivariate analysis showed that fourty two patients were admitted in the ICU during the first 48 hours. Thirty eight patients (90.5%), who were hypertensive or had a cardiac failure, were admitted in the ICU during the first 48h (Admitted) versus 330 patients (54.8%) who were not admitted in the ICU during the first 48h (Non-Admitted) with a statistically significant difference (p<0.001). Fifty three patients (8.8%), who had renal failure, belonged to the Non-Admitted group versus eight patients (19%) belonged to the Admitted group (p=0.049).

Five hundred and five patients (83.9%) were operated on in the Non-Admitted group versus 39 patients (92.9%) in the Admitted group with a non-statistically significant difference (p=0.121).

The median operative time for the Non-Admitted group versus Admitted group was statistically significant 0h30 [0h10-4h15] versus 1h22 [0h10-4h00], respectively (p<0.001).

Post-operative course was uneventful for 444 patients (87.9%) in the Non-Admitted group comparing to 20 patients (51.3%) in the Admitted with a statistically significant difference (p<0.001). Post-operative mortality rate was inferior in the Non-Admitted group comparing to the Admitted group (2.4% versus 41%, p<0.001). Median post-operative duration in the Non-Admitted group was inferior comparing to the Admitted group (2 [0-62] versus 4 [0-76] days, respectively, p< 0.001).

Table 1: Baseline characteristics of patients: Univariate analysis (N= 644)

Variables (N=644)	n (%) or median [range]
Demographics	
Mean Age ±SD (years)	61.28±12.28
Gender, male	472 (73.3%)
Comorbidities	640 (99.4%)
Diabetes	644 (100%)
Hypertension, Cardiac failure	368 (57.1%)
Renal failure	61 (9.5%)
ASA (missing 127)	
I	20 (3.9%)
II	395 (76.4%)
III	95 (18.4%)
IV	5 (1%)
V	2 (0.4%)
Previous surgery	421 (65.4%)
Organ failure at admission	15 (2.3%)
Admission in an ICU* during the first 48 hours Medical complications	42 (6.5%) 51 (7.9%)
Respiratory assistance (days) median [range] (n=18)	3 [1-50]
Mortality	28 (4.3%)
Number of ICU stays median [range]	0 [0-6]
ICU stay duration (days) median [range]	0 [0-75]
Variables (N=544)	**n (%) or median [range]**
Operation variables	
Intervention (yes)	544 (84.5%)
General anesthesia (missing 103)	388 (71.7%)
Major amputation	114 (21%)
Operator (resident) (missing 102)	484 (89.3%)
Median Operative time [hours] (missing 119)	0.30 [0.10- 4.15]
Transfusions median [Range]	2 [1-5]
Post-operative course	
Uneventful	465 (85.5%)
Complications	52 (9.5%)
Mortality	27 (5%)
Reintervention	56 (10.3%)
Pre-operative stay (median [ ] IQR [ ])	1 [0-42] IQR** [0-2]
Post-operative stay (median [ ] IQR [ ])	2 [0-76] IQR** [1-4]
Hospital stay duration (median [ ] IQR [ ])	3 [0-77] IQR** [1-7]

ICU*: Intensive care unit, IQR**= Interquartile range

A multivariate analysis showed that patients who didn't have "Cardiac failure (No)" (OR=0.163, 95%CI [0.055 0.479], p=0.001) and those who didn't have "Organ failure at admission (No)" (OR=0.017, 95%CI [0.004 0.066], p=0.017) had less risk to be admitted in the ICU during the first 48 hours.

Operated / Non-operated patients:

Bivariate analysis revealed that fifteen patients (15%), who had renal failure, belonged to the Non-Operated group versus 46 patients (8.5%) belonged to the Operated group with a statistically significant difference (p=0.040). Seventy four patients (74%) had previous surgery in the

Non-Operated group versus 347 patients (63.8%) in the Operated group with a statistically significant difference (p=0.049). Mortality rate in the Non-Operated group was inferior comparing to the Operated group (1% versus 5%, p=0.105).

In our study, operated patients had often no renal failure (OR=1.910, 95%CI [1.021 3.575], p=0.043).

Global Mortality factors:

A bivariate analysis allowed us to identify predictive factors of mortality. These mortality factors were age (p=0.058), male gender (p=0.048), hypertension and cardiac failure (p<0.001), organ failure at admission (p<0.001), admission in the ICU during the first 48 hours (p<0.001), medical complications (p<0.001), resuscitation (p<0.001), number of ICU stays (p<0.001), ICU stay duration (p<0.001) (Table 2). Logistic regression revealed that "Cardiac failure (Yes)" (OR=5.65, 95%CI [1.26 25], p=0.023) and "Admission in the ICU in the first 48h (Yes)" (OR=21.24, 95%CI [8.92 50], p<0.001) are considered as the predictive pre-operative independent variables associated to mortality. When we included pre and intra operative variables in the logistic regression model, we identified "Cardiac failure (Yes)" (OR=5.00, 95%CI [1.08 23.25], p=0.039), "Admission in the ICU in the first 48h (Yes)" (OR=12.76, 95%CI [4.92 33.33], p<0.001) and "Major amputation (Yes)" (OR=6.40, 95%CI [2.41 16.94], p<0.001) as the predictive pre-operative and intra-operative independent variables associated to mortality.

Medical complications:

Bivariate analysis showed that the mean age (± standard) of patients who didn't have medical complications was 61.00±12.26 years versus 64.53±12.24 years for patients who had medical complications, with a statistically significant difference (p=0.053). Three hundred and twenty three patients (54.5%), who were hypertensive or had cardiac failure, didn't have medical complications versus 45 patients (88.2%) had medical complications with a statistically significant difference (p<0.001). Fifty one patients (8.6%), who had renal failure, didn't have medical complications versus 10 patients (19.6%) had medical complications with a statistically significant difference (p=0.021). Of the 15 patients who had organ failure at admission, six patients (1%) didn't have medical complications versus 9 patients (17.6%) had medical complications with a statistically significant difference (p<0.001). The median operative time for those who didn't have medical complications versus those who had medical complications was statistically significant 0h30 [0h10-4h15] versus 1h20 [0h10-3h40], respectively (p<0.001). Post-operative course was uneventful for 452 patients (90.4%) who didn't have medical complications comparing to 13 patients (29.5%) who had medical complications with a statistically significant difference (p<0.001). Mortality rate was greater in the group who had medical complications (0.2% versus 59.1%, p<0.001). Median post-operative duration for those who didn't have medical complications was inferior to those who had medical complications (2 [0-62] versus 6 [0-76] days, respectively, p<0.001).

Logistic regression revealed that patients who were not admitted in the ICU during the first 48 hours (No)" (OR=0.140, 95%CI [0.48 0.405], p<0.001) and those who didn't have "Major amputation (No)" (OR=0.170, 95%CI [0.76 0.379], p<0.001) had less risk to have medical complications. On the other hand, each patient who had

Table 2: Global mortality factors: Bivariate analysis (N= 644)

Variables (N=644)	Alive (n=616)	Deceased (n=28)	p
Demographics			
Mean Age ±SD (years)	61.06±12.19	66.00±13.66	**0.058**
Gender, male	456 (74%)	16 (57.1%)	**0.048**
Comorbidities	612 (99.4%)	28 (100%)	1.000
Hypertension, Cardiac failure	342 (55.5%)	26 (92.9%)	**<0.001**
Renal failure	56 (9.1%)	5 (17.9%)	0.173
Previous surgery	405 (65.7%)	16 (57.1%)	0.349
Organ failure at admission	9 (1.5%)	6 (21.4%)	**<0.001**
Admission in an ICU* during the first 48 hours	26 (4.2%)	16 (57.1%)	**<0.001**
Medical complications	24 (3.9%)	27 (96.4%)	**<0.001**
Respiratory assistance (days) median [range]	-	3 [1-50]	-
Resuscitation	14 (2.3%)	24 (85.7%)	**<0.001**
Number of ICU stays median [range]	0 [0-6]	1 [0-2]	**<0.001**
ICU stay duration (days) median [range]	0 [0-35]	3 [0-75]	**<0.001**

ICU*: Intensive care unit

one more stay in the ICU had 3.341 times risk to have medical complications (OR=3.341, 95%CI [1.558 7.164], p=0.002).

Major amputation:

Bivariate analysis revealed that patients who had major amputation were older than those who didn't have major amputation (p<0.001). Two hundred and thirty patients (53.5%), who were hypertensive or had a cardiac failure, didn't underwent major amputation versus 78 patients (68.4%) underwent major amputation with a statistically significant difference (p=0.004). Fifteen patients (3.5%) of the Non-Major amputation group were admitted in the ICU during the first 48 hours versus 24 patients (21.1%) of the Major amputation group with a statistically significant difference (p<0.001). The median operative time for those who didn't have major amputation versus those who had major amputation was statistically significant 0h25 [0h10-2h30] versus 1h30 [0h30-4h15], respectively (p<0.001). Post-operative course was uneventful for 378 patients (87.9%) of the Non-Major amputation group comparing to 87 patients (76.3%) of the Major amputation group with a statistically significant difference (p<0.001). Mortality rate in the Non-Major amputation group was inferior comparing to those of the Major amputation group (1.6% versus 17.5%, p<0.001). Median post-operative duration in the Non-Major amputation group was inferior to the Major amputation group (1 [0-76] versus 3 [0-45] days, respectively, p< 0.001) (Table 3).

Logistic regression showed that "Age" (OR=1.033, 95%CI [1.014 1.052], p=0.001) and "Pre-operative stay" (OR=1.093, 95%CI [1.039 1.151], p=0.001) increased the risk of major amputation. However, patients who were not admitted in the ICU during the first 48 hours (No) (OR=0.142, 95%CI [0.071 0.285], p<0.001) had less risk to have major amputation. The area under the curve of the "Age" (AUC) was 0.610 95%CI [0.553 0.666], p<0.001.

Mortality of operated patients:

A bivariate analysis allowed us to identify predictive factors

Table 3: Major Amputation: Bivariate analysis (N= 544)

Variables	Non-Major amputation (n=430)	Major amputation (n=114)	p
Demographics			
Mean Age ±SD (years)	60.40±12.63	65.41±11.49	**<0.001**
Gender, male	313 (72.8%)	84 (73.7%)	0.849
Comorbidities	427 (99.3%)	113 (99.1%)	1.000
Hypertension, Cardiac failure	230 (53.5%)	78 (68.4%)	**0.004**
Renal failure	34 (7.9%)	12 (10.5%)	0.371
Previous surgery	261 (60.7%)	86 (75.4%)	**0.004**
Organ failure at admission	4 (0.9%)	9 (7.9%)	**<0.001**
Admission in an ICU* during the first 48 hours	15 (3.5%)	24 (21.1%)	**<0.001**
Operation variables			
General anesthesia	290 (67.9%)	98 (86%)	**<0.001**
Operator (resident)	389 (90.7%)	95 (84.1%)	**0.043**
Median Operative time [Range] (hours)	0.25 [0.10-2.30]	1.30 [0.30-4.15]	**<0.001**
Post-operative course			
Uneventful	378 (87.9%)	87 (76.3%)	**<0.001**
Complicated	45 (10.5%)	7 (6.1%)	
Mortality	7 (1.6%)	20 (17.5%)	
Medical complications	14 (3.3%)	30 (26.3%)	**<0.001**
Resuscitation	10 (2.3%)	22 (19.3%)	**<0.001**
Number of ICU stays median [range]	0 [0-5]	0 [0-6]	**<0.001**
ICU stay duration (days) median [range]	0 [0-75]	0 [0-35]	**<0.001**
Reintervention	49 (11.4%)	7 (6.1%)	0.101
Pre-operative stay (median [range])	1 [0-42]	1 [0-34]	**<0.001**
Post-operative stay (median [range])	1 [0-76]	3 [0-45]	**<0.001**
Hospital stay duration (median [range])	2 [1-77]	6 [0-47]	**<0.001**

ICU*: Intensive care unit

of mortality for patient who were operated for an infected foot ulcer. These mortality factors were male gender (p=0.037), hypertension and cardiac failure (p<0.001), organ failure at admission (p<0.001), admission in the ICU during the first 48 hours (p<0.001), medical complications (p<0.001), resuscitation (p<0.001), number of ICU stays (p<0.001), ICU stay duration (p<0.001), general anaesthesia (p=0.004), major amputation (p<0.001), operative time (p<0.001) and complicated post-operative course (p<0.001) (Table 4).

Complicated post-operative course:

Bivariate analysis showed that two hundred and fifty patients (53.8%), who were hypertensive or had a cardiac failure, didn't have complicated post-operative course versus 58 patients (73.4%) had complicated post-operative course with a statistically significant difference (p=0.001). Five patients (1.1%), who had organ failure at admission, didn't have complicated post-operative course versus 8 patients (10.1%) had complicated post-operative course with a statistically significant difference (p<0.001).

The median operative time for those who didn't have complicated post-operative course versus those who had complicated post-operative course was statistically significant 0h30 [0h10-4h15] versus 0h45 [0h10-3h40], respectively (p=0.004). Thirteen patients (2.8%) didn't have medical complications versus 31 patients (39.2%) had medical complications with a statistically significant difference (p<0.001). Mortality rate when the patient didn't have complicated post-operative course was inferior comparing to those who had post-operative course (0% versus 34.2%, p<0.001). Median post-operative duration for those who didn't have complicated post-operative course was inferior comparing to those who had complicated post-operative course (1 [0-62] versus 6 [0-76] days, respectively, p< 0.001).

Logistic regression revealed that patients who didn't have "Cardiac failure (No)" (OR=0.517, $^{95\%}$CI [0.298 0.896], p=0.019) and those who were not admitted in the ICU during the first 48 hours (No) (OR=0.176, $^{95\%}$CI [0.088 0.354], p<0.001) had less risk to have complicated post-operative course. On the other hand, those who had longer "Pre-operative stay" (OR=1.083, $^{95\%}$CI [1.033 1.134], p=0.001) had a higher risk to have complicated post-operative course.

Table 4: Post-operative mortality: Bivariate analysis (N= 544)

Variables	Alive (n=517)	Deceased (n=27)	p
Demographics			
Mean Age ±SD (years)	61.22±12.46	65.85±13.89	0.062
Gender, male	382 (73.9%)	15 (55.6%)	**0.037**
Comorbidities	513 (99.2%)	27 (100%)	1.000
Hypertension, Cardiac failure	283 (54.7%)	25 (92.6%)	**<0.001**
Renal failure	41 (7.9%)	5 (18.5%)	0.068
Previous surgery	332 (64.2%)	15 (55.6%)	0.361
Organ failure at admission	7 (1.4%)	6 (22.2%)	**<0.001**
Admission in an ICU* during the first 48 hours	23 (4.4%)	16 (59.3%)	**<0.001**
Operation variables			
General anesthesia	362 (70.4%)	26 (96.3%)	**0.004**
Major amputation	94 (18.2%)	20 (74.1%)	**<0.001**
Operator (resident)	461 (89.5%)	23 (85.2%)	0.517
Median Operative time [Range] (hours)	0.30 [0.10-4.15]	1.00 [0.10-3.40]	**<0.001**
Post-operative course			
Complicated	52 (10.1%)	27 (100%)	**<0.001**
Medical complications	18 (3.5%)	27 (96.3%)	**<0.001**
Resuscitation	9 (1.7%)	23 (85.2%)	**<0.001**
Number of ICU stays median [range]	0 [0-6]	1 [0-2]	**<0.001**
ICU stay duration (days) median [range]	0 [0-35]	3 [0-75]	**<0.001**
Reintervention	51 (9.9%)	5 (18.5%)	0.187
Pre-operative stay (median [range])	1 [0-42]	1 [0-12]	0.241
Post-operative stay (median [range])	2 [0-62]	3 [0-76]	0.117
Hospital stay duration (median [range])	3 [1-64]	7 [0-77]	0.151

ICU*: Intensive care unit

Reintervention:
A bivariate analysis revealed less resuscitation in the No-reintervention group comparing to the Reintervention group. The number of ICU stays in the No-reintervention group versus the Reintervention group was statistically non-significant 0 [0-6] versus 0 [0-2], respectively (p=0.060). The ICU stay duration in the No-reintervention group versus the Reintervention group was statistically non-significant 0 [0-25] versus 0 [0-75], respectively (p=0.068). Post-operative course was uneventful for 462 patients (94.7%) versus 3 patients (5.4%) in the Reintervention group (p<0.001).
Mortality rate in the No-Reintervention group was inferior comparing to the Reintervention group (4.6% versus 8.9%, p<0.001).
Median post-operative duration for the No-Reintervention group was inferior to the Reintervention group (1 [0-62] versus 7 [0-76] days, respectively, p<0.001).
Logistic regression revealed that patients who had a longer "Pre-operative stay" (OR=1.079, 95%CI [1.030 1.132], p=0.002) had more risk to undergo a reintervention.

Summary of the independent predictive variables of the different outcome measures:
Table 5 showed all independent predictive variables of the different outcomes.
In practice, we can only control the variable 'pre-operative stay' to reduce major amputations, post-operative complications and the number of reinterventions.

DISCUSSION

This retrospective study showed that "Cardiac failure (Yes)" (OR=5.00, 95%CI [1.08 23.25], p=0.039), "Admission in the ICU in the first 48h (Yes)" (OR=12.76, 95%CI [4.92 33.33], p<0.001) and "Major amputation (Yes)" (OR=6.40, 95%CI [2.41 16.94], p<0.001) were identified as independent predictive factors of mortality.
As concerns morbidity, Cardiac failure (OR=0.163, 95%CI [0.055 0.479], p=0.001) and organ failure at admission (OR=0.017, 95%CI [0.004 0.066], p=0.017) were predictive factors of admission in the ICU during the first 48 hours. Besides, advanced age (OR=1.033, 95%CI [1.014 1.052], p=0.001), Pre-operative stay (OR=1.093, 95%CI [1.039 1.151], p=0.001) and admission in the ICU during the first 48 hours (OR=0.142, 95%CI [0.071 0.285], p<0.001) were predictive factors of major amputation. Moreover, Cardiac failure (OR=0.517, 95%CI [0.298 0.896], p=0.019), admission in the ICU during the first 48 hours (OR=0.176, 95%CI [0.088 0.354], p<0.001) and Pre-operative stay (OR=1.083, 95%CI [1.033 1.134], p=0.001) were predictive variables of complicated post-operative course. Admission in the ICU during the first 48h (OR=0.140, 95%CI [0.48 0.405], p<0.001), major amputation (OR=0.170,

Table 5 : independent predictive variables of the different outcome

Predictive variables	Admission in the ICU during the first 48h	Operated patients	Major amputation	Global mortality	Complicated post-operative course	Medical complications	Reintervention
Age			√				
Pre-operative stay			√		√		
Cardiac failure	√			√	√		
Renal failure		√					
Organ failure at admission	√						
Admission in the ICU during the first 48h			√	√	√	√	
Major amputation				√		√	
Number of ICU stays						√	

95%CI [0.76 0.379], p<0.001), and number of ICU stays (OR=3.341, 95%CI [1.558 7.164], p=0.002) were predictive factors of medical complications. Preoperative stay (OR=1.091, 95%CI [1.038 1.147], p=0.001) was predictive of reintervention.

This study was based on variables enrolled from administrative database which is defined as 'large computerized data files generally compiled in billing for health care services such as hospitalizations' [5]. As stated by Guller [6], surgical outcomes research based on administrative data should be viewed as being complementary and not inferior to randomized clinical trial. Comparing to randomized clinical trials, administrative data are less expensive and time consuming [6]. Besides, administrative database allows the performance of descriptive analysis [7] and permits researchers to answer questions that can't be answered through a randomized clinical trial because of its complexity, its high price and some ethical problems [8].

Six hundred and forty four patients were included in this study, from which 472 men (73.3%) and 172 women (26.7%). We found some similarities with other medical articles. Brechow reported 69% of male [9], Nazi reported 147 male (67.4%) [10], Won reported 128 male (74%) [11] and Icks reported 71.8% male [13]. However, Miyajima reported a lower number of men 113 (53.8%) [12]. In our study, the mean age (±standard) was 61.28±12.28 years. Other studies found the same results such as Brechow (66.3±11.0 years) [9], Nazri 60.97 (range 36–98) years [10], Won 67.5±11.4 years [11], Miyajima 64.2±9.8 years [12], Icks 69.1 years [13] and Chuan 66.96±11.96 years [14]. In our study, one hundred and fourteen patients underwent major amputation (21%). In Hambleton study, there were 82 (30%) major amputations and 123 (60%) minor amputations [2]. In Ozan study, 32 (29.8%) patients had major amputations, and 75 (70.2%) patients had minor amputations [15]. In Ploeg study, 45 major amputations (36.8%) and 77 minor amputations (63.1%) were performed in 97 patients [4]. However there were some divergences with other medical litterature. Brechow reported a lower rate of major amputation (32 patients=4.7%) [9], Nazri revealed 31 patients (14.2%) [10], Chuan reported 5.2 % major amputations and 6.8 % minor amputations [14], Won [11] reported twelve (6.9%) major amputations and forty-seven (27.1%) minor amputations and Miyajima [12] reported 45 major amputations (21.4%) and 65 minor amputations (30.9%).

Logistic regression showed that "Age" (OR=1.033, 95%CI [1.014 1.052], p=0.001) and "Pre-operative stay" (OR=1.093, 95%CI [1.039 1.151], p=0.001) increased the risk of major amputation. However, patients who were not admitted in the ICU during the first 48 hours (No) (OR=0.142, 95%CI [0.071 0.285], p<0.001) had less risk to have major amputation (Table 12). The area under the curve of the "Age" (AUC) was 0.610 [0.553 0.666], p<0.001 (Figure 1). Won revealed that ulcer severity was the only explanatory factor significantly associated with amputation (HR 3.18, 95% CI 1.53-6.59) [11]. In Miyajima study, there was no significant difference in the sex or age at diagnosis between the major amputation group and minor or non-amputation group [12]

In our study, the median operative time [range] was 0h30 [0h10- 4h15]. None of these studies analyzed the median operative time [8-14]. Re-intervention was practiced for 56 patients (10.3%). Ploeg reported the same rate of 11.7% in the minor amputation and 14.9% in the major amputation [4]. Beaulieu revealed that re-amputation occurred in 95 of the readmitted patients (95%), including limb amputation in 64 patients (64%) (Below knee in 58, through knee in 2, and above knee in 4) [16].

Major amputations are still associated with high morbidity and mortality. Indeed, fifty two patients (9.5%) had post-operative complications and 465 patients with uneventful post-operative course (85.5%) in our study. This complication rate was low compared to other series, which varied from 15 to 30% [17, 18]. However, in Ploeg study, 65 patients with a total of 107 complications were reported (67%) [4]. In our study, mortality rate was 4.3%. Brechow reported a lower mortality rate (2.5% (n=17)) [9]. Mortality rate for patients who didn't have major amputation was inferior comparing to those who had major amputation (1.6% versus 17.5%, p<0.001) in this study. Cruz reported a 30-day mortality of 12% for minor amputation and 17% for major amputation [19] and Ploeg reported 5.2% for minor amputations and 17.8% for major amputations [4]. Feinglass reported a 30-day mortality of 6.3% for minor amputations and 13.3% for major amputations [3].

Logistic regression revealed that "Cardiac failure (Yes)" (OR=5.65, 95%CI [1.26 25], p=0.023) and "Admission in the ICU in the first 48h (Yes)" (OR=21.24, 95%CI [8.92 50], p<0.001) are considered as the predictive pre-operative independent variables associated to mortality. When we included pre and intra operative variable in the logistic regression model, we identified "Cardiac failure (Yes)" (OR=5.00, 95%CI [1.08 23.25], p=0.039), "Admission in the ICU in the first 48h (Yes)" (OR=12.76, 95%CI [4.92 33.33], p<0.001) and "Major amputation (Yes)" (OR=6.40, 95%CI [2.41 16.94], p<0.001) as the predictive pre and intra-operative independent variables associated to mortality. Morbach revealed that age (HR 1.05, 95% CI 1.01--1.10), and peripheral artery disease (HR 35.34, 95% CI [4.81--259.79]) were significant predictors for the first major

amputation [20]. Ploeg study revealed cardiac origin in seven patients, sepsis occurred in five patients, two patients died of pneumonia and one patient died from end stage renal disease [4]. Morbach also reported that age (HR 1.08, 95% CI 1.06--1.10), male gender (HR 1.65, 95% CI 1.18--2.32), and peripheral artery disease (PAD) (HR 1.44, 95% CI 1.05--1.98) were significant predictors for death [20]. In Icks study, significant risk factors for mortality were age (1.05; 1.03–1.06) and amputation above the knee (1.50; 1.16–1.94) [13].

In our study, post-operative stay duration was 2 [0-76] IQR [1-4] and hospital stay duration was 3 [0-77] IQR [1-7]. Ozan reported a superior mean length of hospitalization (16.2 ± 7.35 days in minor amputations and 31.8 ± 13.6 days in major amputations, p=0.0001) [15].

The principal limitation of our study was the retrospective design. We used an administrative database, therefore we faced coding errors, some missing informations such as details about the exact kind of lesions, their location and their extension, the state of the lower limbs' pulses and the lack of radiologic exploration of lower limbs arterial axes.

A prospective prognostic study on a larger sample is mandatory to identify predictive factors of mortality and morbidity for infected diabetic foot ulcer.

CONCLUSIONS

This retrospective study, enrolling 644 patients with infected diabetic foot ulcers suggests that mortality rate was inferior when the patient didn't have amputation, no post-operative complications and no reintervention and showed that Cardiac failure, admission in the ICU in the first 48h and major amputation were independent predictive factors of mortality.

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