Predictive factors for major amputation of lower limb in diabetic foot: about 430 patients

Facteurs prédictifs d'amputation majeure du membre inférieur chez le diabétique: à propos de 430 patients

Mehdi Khalfallah, Esma Leila Gouta, Wejih Dougaz, Hichem Jerraya, Imene Samaali, Ramzi Nouira, Ibtissem Bouasker, Chadli Dziri

Service de chirurgie B - Hôpital Charles Nicolle / Tunis,

RÉSUMÉ

Introduction: L'amputation majeure du membre inférieur est définie par une amputation de jambe ou de cuisse.
Objectif : Identifier les facteurs prédictifs de l'amputation majeure des membres inférieurs chez les patients diabétiques admis pour des lésions du pied à l'aide d'une base de données administratives.
Méthodes: Il s'agissait d'une étude rétrospective du 1er juin 2008 au 31 décembre 2011, comprenant tous les patients hospitalisés pour un pied diabétique infecté au service de Chirurgie B de l'hôpital Charles Nicolle de Tunis. Le critère de jugement principal était l'amputation majeure du membre inférieur. Nous avons effectué une étude descriptive et comparative, avec analyse univariée et multivariée.
Résultats: Nous avons colligé 319 hommes et 111 femmes. L'âge moyen était de 60,5 ± 12 ans. Quatre-vingt-cinq patients ont eu une amputation majeure, soit 24% des cas. Les patients hospitalisés, réadmis dans un délai d'un mois après l'intervention, hospitalisés en réanimation, admis en soins intensifs dans les 48 heures suivant l'admission, l'âge supérieur à 65 ans, la présence d'une tare rénale, le séjour préopératoire et la durée de l'intervention ont été identifiés comme facteurs prédictifs d'amputation majeure dans l'analyse univariée. L'âge est la seule variable indépendante prédictive de l'amputation majeure qui est apparue dans l'analyse multivariée (p = 0,004). Le seuil d'âge ≥ 65 ans a une spécificité de 69% et une sensibilité de 47% [p = 0,004, OR = 1 971, IC 95%: 1,239-3,132].
Conclusion : L'âge est le seul facteur prédictif indépendant d'amputation majeure du membre inférieur du pied diabétique avec une valeur seuil supérieure ou égale à 65 ans. Les patients âgés de plus de 65 ans avaient 1,9 fois plus de risque de subir une amputation majeure du membre inférieur.

Mots-clés
Pied diabétique, amputation, courbe roc

SUMMARY

Background: Major amputation of the lower limb is defined by a leg or thigh amputation. The aim of our work was identifying predictive factors for lower limb major amputation in patients with diabetes admitted on for foot lesions through using an administrative data base.
Methods: It was a retrospective study ranging from June 1st, 2008 to December 31st, 2011, which included all the patients admitted on for an infected diabetic foot to the surgery unit B of Charles Nicolle hospital in Tunis. The main judgement criterion was the major amputation of the lower limb. We have done a descriptive and a comparative study, with univariate and multivariate analysis.
Results: We have enrolled 319 men and 111 women. The average age was 60.5 ± 12 years. Ninety five patients (24%) had a major amputation. Former inpatient, patient readmitted within one month post-operatively, stay in intensive care, admission in intensive care within 48hours after admission, age ≥ 65 years, presence of kidney problem, preoperative stay and length of intervention were identified as predictive factors of major amputation in the univariate analysis. Age was the only independent variable predictive for major amputation which appeared from the multivariate analysis (p=0.004). The age cut-off ≥ 65 years has a specificity of 69 % and a sensitivity of 47% [p=0.004, OR=1.971, IC 95%: 1.239-3.132].
Conclusions: Age was the only independent predictive factor for major amputation of the lower limb in the diabetic foot with a threshold value higher or equal to 65 years. Patients aged more than 65 had 1.9 time more risk to undergo major amputation of the lower limb.

Key-words
Diabetic foot, amputation, roc curve

Diabetic foot lesions are a real public health problem. Actually, 15% of patients with diabetes will develop foot lesions during their life (1), and 85% of lower limb amputations are related to foot lesions in patients with diabetes (1). Moreover, the risk of lower limb amputation is 15 to 46 times higher in patients with diabetes than in general population (1-4).

Major amputation of the lower limb is defined by a leg or thigh amputation. Major amputation of the lower limb is sometimes the only curative treatment in patients with diabetes, in case of advanced lesions of wet gangrene and /or lower limb arteriopathy (5). An american study reported a prevalence of 623 000 cases of major amputations in 2005 and expects two million major amputations of lower limbs in 2050, notably with population ageing (6).

Major amputation of the lower limb in patients with diabetes is burdened with a high death rate, ranging between 6 and 29% according to series (7-12). Recognizing preoperative predictive factors of lower limb major in patients with diabetes would enable surgeons selecting patients at high risk for major amputation and thus address preoperative factors. Consequently, this could allow reducing the rate of major amputation and the mortality resulting from foot lesions in patients with diabetes.

The aim of our work was identifying predictive factors for lower limb major amputation in patients with diabetes admitted on for foot lesions through using an administrative data base.

METHODS

Type and duration of study:

It was a retrospective study ranging from June 1st, 2008 to December 31st, 2011.

Criteria of inclusion:

All the patients admitted on for an infected diabetic foot to the surgery unit B of Charles Nicolle hospital in Tunis have been included, whatever their age, sex, past medical history, emergency context and the surgery carried out.

Criteria for judgement:

The main judgement criterion was the major amputation of the lower limb which was defined by an amputation of leg and /or thigh.

The secondary judgement criteria were the post-operative mortality, post-operative morbidity as well as the intensive care stay.

Data collection:

A table has been developed including mainly administrative and medical data. these variables numbered 111 shared out into demographic variables : age, sex, defects, physical status score ASA, NYHA score, preoperative variables including the time of surgery, the type of emergency (trauma or not), the patient's condition upon arrival, the diagnoses, variables relating to the intraoperative period including the surgeon (senior doctor or medical resident), the operating room (aseptic or septic), the technique of anesthesia, prophylactic antibiotic treatment, the approach, the order of going to the operating room and the various operating procedures. Variables have been collected during the post-operative period: simple, complicated postoperative course, surgical complication with reintervention, surgical complication without reintervention, medical complications, the different resuscitation services, deaths and patients delivered into the custody of their relatives as well as other variables devoted to reinterventions.

Statistical Analysis:

Descriptive study:

All the data have been entered into a statistical software SPSS® (Statistical Package for the Social Science version 23.0). The qualitative variables have been expressed by their percentages, the quantitative variables by the average and the standard deviation when the distribution was Gaussian through the median and the extremes otherwise.

Comparative study:

We have carried out an univariate analysis through comparing the « major amputation» group and the group of «minor amputation and /or excision and/or not operated». We did not include patients without surgery in the comparative analysis. The variables with a percentage ≤ 0.05 have been inserted in a logistic regression model so as to identify the independent variables predictive of major amputation. We have also developed a ROC curve to determine the threshold values of continuous variables retained after multivariate analysis.

RESULTS

Descriptive analysis:

Epidemiology:

We have enrolled 319 men and 111 women, with a sex ratio of 2.9. The average age was 60.5±12 years [extremes: 24-90 years]. One hundred and fifty patients were aged 65 or more which was 34.9%. In 184 cases, it was a former inpatient, which was 42.8%. The patient had been re-admitted in the post-operative month in in 39 cases (9%). It was an outpatient in seven cases (1.6%).

Two hundred and twenty six patients had a heart condition (52.6%), five patients had a respiratory condition (1.2%), 48 patients had a kidney condition (11.2%), 212 patients were obese (49.3%) and six patients were on steroids (1.4%). No patient was cirrhotic.

We have collected no case of pregnancy and no case of varicose veins or phlebitis of the lower limbs.
Two hundred and thirteen patients (49.5%) were classified ASA I, one hundred and fifty patients (34.9%) were ASA II and 67 patients (15.6%) were ASA III.
Three hundred and six patients were classified NYHA I that was 71.2%, 111 patients NYHA II that was 25.8% and 13 patients NYHA III that was 3%. Five patients were in a state of vital distress upon admission, which was 1.2% of cases. Twenty four patients (5.6%) have been admitted on to intensive care within 48 hours after admission. Forty three patients have stayed in intensive care that is 10%: 36 patients have stayed there once, six patients twice and one patient three times.
The surgery was performed in emergency for 379 patients (88.1%), in elective surgery for 17 patients (4%) and 34 patients (7.9%) have not been operated. Non-operated patients have all received empiric antibiotic therapy as well as daily local health care.

Intra-operative data
The surgical operation was performed in the septic block for 394 patients (99.5%) and in the aseptic block for two patients (0.5%). The surgeon was a senior one in 26 cases (6.6%) and a medical resident in 370 cases (93.4%). The intervention was performed under general anesthesia in 253 patients that is 63.9% of cases and loco-regional anesthesia (spinal anesthesia or peripheral blocks) in 143 patients (36.1%). Four patients have been transfused intra-operatively, that is 0.9% of cases. Ninety five patients (24%) had a major amputation. The median duration of the operation was 37 minutes [extremes: 30 minutes - 3 hours].

Post-operative data:
The operating follow up were uneventful in 330 patients that is 89.5 % of cases. Thirty seven patients have been operated again during the same hospitalization, which means a rate of re-intervention of 9.3%. Thirty eight patients (9.3%) had medical complication. We noted 23 deaths (5.3%). Seventeen patients (4%) have developed a health-care associated infection.

Comparative study:
Univariate Analysis
The univariate analysis data are summed up in table I.
Multivariate analysis with logistic regression: Age was the only independent variable predictive for major amputation which appeared from the multivariate analysis (p=0.004). The ROC curve of the age variable allowed us to retain a cut-off at 65 years [area under the curve = 0.585, p=0,012, IC 95%: 0.519-0.650] (figure n°1). The age cut-off ≥ 65 years has a specificity of 69 % and a sensitivity of 47% [p=0.004, OR=1.971, IC 95%: 1.239-3.132]. The patients aged more than 65 had 1.9 time more risk to undergo major amputation of the lower limb.

Table 1: Univariate analysis comparing the «major amputation» group to the minor amputation and /or excision and/or not operated on » one

Variable	Minor amputation and/or excision and/or non operated	Major amputation	p
Former patient (no/yes)	203/132	43/52	0.008
Readmission with in PO* month (no/yes)	310/25	81/14	0.029
Patient (inpatient/outpatient)	329/6	94/1	0.616
Intensive care stay (no/yes)	314/21	73/22	0.000
Intensive care Admission within48 hours after admission (no/yes)	323/12	83/12	0.001
Sex (woman, man)	88/247	23/72	0.686
Past medical history (no/yes)	7/328	1/94	0.509
Cardiac problem (no/yes)	182/153	44/51	0.167
Respiratory problem (no/yes)	332/3	93/2	0.332
Kidney problem (no/yes)	306/29	76/19	0.002
Under steroids (no/yes)	330/5	94/1	0.747
Distress upon arrival (no/yes)	332/3	93/2	0.306
Operating room **(aseptic, /septic)	1/300	1/94	0.423
Surgeon **(senior/resident)	17/284	9/86	0.189
Anesthesia ** (general/locoregional	188/113	65/30	0.291
Reintervention (no/yes)	301/34	92/3	0.032
Medical Complication of operated patients** (no/yes)	281/20	77/18	0.000
Health-care associated infection (no/yes)	328/7	85/10	0.000
Death (no/yes)	325/10	82/13	0.002
Age	59.7 ± 11.9	63.3 ± 11.7	0.01
Age ≥ 65 years (no/yes)	230/105	50/45	0.004
BMI*** (kg/m2)	25.6 ± 4.5	23.8 ± 4.7	0.257
Median duration of intervention (min)	20 [5-90]	75 [15-180]	0.000
Median preoperative stay (days)	0.7 [0-12]	1 [0-66]	0.000
Median post-operative stay (days)	1 [0-40]	3 [0-96]	0.006
Total median stay (days)	2 [0-42]	5 [1-47]	0.000

*PO: post-operative
** : total number of patients in the group stands at 301 because 34 patients have not been operated.
***BMI: BODY MASS INDEX

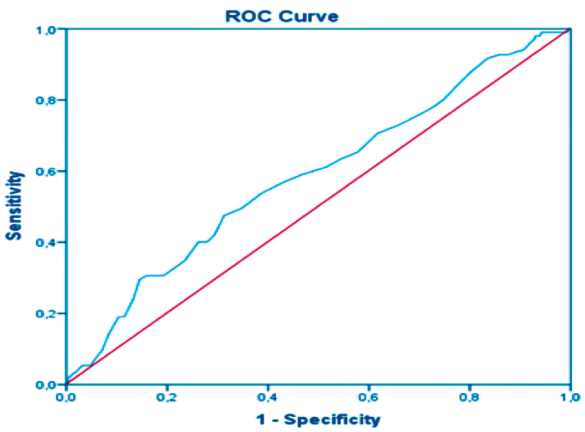

Figure 1 : ROC curve of the age [area under the curve = 0.585, p=0,012, IC 95%: 0.519-0.650]

DISCUSSION

Our study, through a univariate analysis, has allowed us to identify the following factors as being predictive for major amputation of the lower limb in patients with diabetes admitted for foot lesions: former inpatient, patient readmitted within one month post-operatively, stay in intensive care, admission in intensive care within 48 hours after admission, age ≥ 65 years, presence of kidney problem, preoperative stay and length of intervention.

In the multivariate analysis, only the age appears as an independent factor predictive for major amputation of the lower limb in the diabetic foot. Actually and after achieving a ROC curve, the threshold value of age retained was an age higher or equal to 65 years [area under curve = 0.585, p=0.012, CI 95%: 0.519-0.650] with a sensitivity of 47% and a specificity of 69% the cut-off age ≥ 65 years has a specificity of 69 % and a sensitivity of 47% [p=0.004, OR=1.971, CI 95%: 1.239-3.132]. Patients aged more than 65 had 1.9 time more risk of having major amputation of the lower limb. Other factors predictive for major amputation of the lower limb in the diabetic foot have been reported in the literature. Nelson has identified, by means of a univariate analysis, thrombopenia < 150 000 elements/mm3, INR 1.3, elevated creatinine > 1.2 mg/l and albumin levels < 34g/l as being predictive for major amputation of lower limb (5). Yesil has identified, in multivariate analysis, the following factors as being predictive for major amputation of the lower limb in the diabetic foot: ischemia of the lower limb [OR: 15.136, p=0.001, 95% CI: 2.852 – 80.321], osteomyelitis [OR: 4.546, p=0.004, 95% CI: 1.605 – 12.871] and a sedimentation rate higher than a standard deviation [OR: 3.513, p=0.013, 95% CI: 1.289 – 9.608] (13). The main judgement criterion in the series of literature was hospital mortality which was statistically higher in the '"lower limb major amputation group", as in our study (5,13,14).

We have noted some limits and shortcomings in our work, namely the lack of biology data, the lack of details about the exact kind of lesions, their location and their extension, the state of the pulses of lower limbs and finally the lack of radiologic exploration of lower limbs arterial axes. These limits are due to the fact that we have use an administrative data base in this study which gathered administrative and medical variables, especially useful to calculate health care cost. A prospective multicentre study on a larger scale seems necessary to identify the predictive factors for major amputation of the lower limb in the diabetic foot.

CONCLUSION

A former inpatient, a patient readmitted within one month post-operatively, a stay in intensive care, an admission to intensive care within 48 hours after admission, age ≥ 65 years and the existence of a kidney problem have been identified as predictive for major amputation of the lower limb in patients with diabetes admitted for foot lesions. Age is the only independent predictive factor for major amputation of the lower limb in the diabetic foot with a threshold value higher or equal to 65 years [p=0.001, OR=1.026 ,CI 95%: 1.006-1.047) with a sensitivity of 47% and a specificity of 69%. The age cut-off ≥ 65 years has a specificity of 69 % and a sensitivity of 47% [p=0.004, OR=1.971, CI 95%: 1.239-3.132]. Patients aged more than 65 were 1.9 times more likely to undergo major amputation of the lower limb.

REFERENCES

1. Jeffcoate WJ, Harding KG. Diabetic foot ulcers. Lancet 2003;361:1545-51.
2. 1999 Consensus Development Conference on Diabetic Foot Wound Care: 7-8 April 1999, Boston, Massachusetts. American Diabetes Association. Diabetes Care 1999;22: 1354-60.
3. Armstrong DG, Lavery LA, Quebedeaux TL, Walker SC. Surgical morbidity and the risk of amputation due to infected puncture wounds in diabetic versus nondiabetic adults. South Med J 1997;90:384-9.
4. Lavery LA, Ashry HR, van Houtum W etal.Variation in the incidence and proportion of diabetes-related amputations in minorities. Diabetes Care 1996;19: 48-52.
5. Nelson MT, Greenblatt DY, Soma G et al. Preoperative factors predict mortality after major lower-extremity amputation. Surgery 2012;152:685-96.
6. Ziegler-Graham K, MacKenzie EJ, Ephraim PL, Travison TG, Brookmeyer R. Estimating the prevalence of limb loss in the United States: 2005 to 2050. Arch Phys Med Rehabil 2008;89:422-9.
7. Feinglass J, Pearce WH, Martin GJ, Gibbs J, Cowper D, Sorensen M, et al. Postoperative and late survival outcomes after major amputation: findings from the Department of Veterans Affairs National Surgical Quality Improvement Program. Surgery 2001;130:21-9.
8. Belmont PJ Jr, Davey S, Orr JD, Ochoa LM, Bader JO, Schoenfeld AJ. Risk factors for 30-day postoperative complications and mortality after below-knee amputation: a study of 2,911 patients from the National Surgical Quality Improvement Program. J Am CollSurg 2011;213: 370-8.
9. Hasanadka R, McLafferty RB, Moore CJ, Hood DB, Ramsey DE, Hodgson KJ. Predictors of wound complications following major amputation for critical limb ischemia. J VascSurg 2011;54:1374-82.
10. Lim TS, Finlayson A, Thorpe JM, Sieunarine K, Mwipatayi BP, Brady A, et al. Outcomes of a contemporary amputation series. ANZ J Surg 2006;76:300-5
11. Moxey PW, Hofman D, Hinchliffe RJ, Jones K, Thompson MM, Holt PJ. Epidemiological study of lower limb amputation in England between 2003 and 2008. Br J Surg 2010;97:1348-53.
12. Eskelinen E, Lepantalo M, Hietala EM, Sell H, Kauppila L, Mäenpää I, et al. Lower limb amputations in Southern Finland in 2000 and trends up to 2001. Eur J Vasc Endovasc Surg 2004;27:193-200.
13. Yesil S , Akinci B , Yener S , Bayraktar F et al. Predictors of amputation in diabetics with foot ulcer: Single center experience in a large Turkish cohort HORMONES 2009;8:286-95.
14. Moxey PW, Hofman D, Hinchliffe RJ et al. Delay Influences Outcome after Lower Limb Major Amputation. European Journal of Vascular and EndovascularSurgery 2012;44:485-90.