Major lower limb amputations in the elderly observed over ten years: the role of diabetes and peripheral arterial disease

GA Carmona¹, P Hoffmeyer¹, FR Herrmann², J Vaucher¹, O Tschopp¹, A Lacraz¹, UM Vischer²

SUMMARY

Background: Major amputation is a dreaded event with high mortality and morbidity. However, few studies have investigated the epidemiology of amputation in the elderly over time, in the face of evolving management and prevention efforts.

Methods: We undertook a retrospective study to determine the incidence rate, etiology and prognosis of major lower limb amputations (transfibial or higher) in elderly patients (> 65 years). Cases were identified over a 10-year period in the Geneva (Switzerland) area, where all amputations are performed in a single center and reliable demographic data are available.

Results: The rate of amputation varied from 1.8 to 11.4/10000 patients/year, increasing with age and male gender. Diabetes was present in 48% patients, and conferred a 10 times higher risk of amputation. Severe peripheral arterial disease (PAD) was present in > 94% patients. The prognosis remains poor, 47% patients had died after two years and only 53% patients could be equipped with a prosthetic limb. Over 10 years we found a progressive increase in age at amputation; this encouraging increase was mostly accounted for by diabetic patients (> 6 months per year).

Conclusions: The rate of amputation observed among elderly patients was low. Neither the rate nor the prognosis improved over the decade studied. However, the age at amputation increased by > 6 months/year, particularly in diabetic amputees, suggesting that current management successfully delays amputation. Amputations were almost exclusively performed for severe PAD. Further reduction in the rate of amputation will require progress in the prevention and management of PAD.

Key-words: Diabetes · Amputation · Peripheral arterial disease.

RÉSUMÉ

Les amputations majeures des sujets âgés et leur évolution observée sur 10 ans : impact du diabète et de l’insuffisance artérielle des membres inférieurs

Contexte : Les amputations majeures sont des événements très redoutés qui entraînent une morbidité et une mortalité importantes. Cependant peu d’études ont analysé le risque et les causes d’amputation chez les sujets âgés, et l’impact de la prise en charge et de la prévention.

Méthodes : Dans cette étude rétrospective nous avons déterminé l’incidence, les étiologies et le pronostic des amputations majeures des membres inférieurs chez les sujets de > 65 ans. Tous les cas ont été identifiés pendant 10 ans (de 1990 à 1999) à Genève (Suisse), où toutes les amputations sont effectuées dans un seul centre, et des données démographiques détaillées sont disponibles.

Résultats : L’incidence d’amputation variait de 1,8 à 11,4/10000 patients/an augmentant avec l’âge et le sexe masculin. Le diabète avait une prévalence de 48 % et conférait un risque relatif d’amputation d’environ 10. Une insuffisance artérielle des membres inférieurs (IAAMI) sévère était présente chez > 94 % des patients. Le pronostic resta mauvais, la mortalité à deux ans était de 47 % et seuls 53 % des patients ont pu être équipés d’une prothèse. En 10 ans, l’âge à l’amputation a pourtant progressivement augmenté, en particulier dans la population diabétique (> 6 mois/an).

Conclusions : L’incidence d’amputation majeure dans notre population âgée est faible. Ni l’incidence ni le pronostic n’ont changé sur 10 ans. En revanche, l’âge à l’amputation a nettement augmenté, en particulier chez les diabétiques, suggérant que la prise en charge actuelle retarde efficacement les amputations. La quasi-totalité des amputations sont justifiées par une IAMAI sévère. Dans le futur, la réduction du risque d’amputation passera par des progrès dans la prévention et la prise en charge de l’IAAMI.

Mots-clés : Diabète · Amputation · Insuffisance artérielle des membres inférieurs.
Lower limb amputation is a dreaded event associated with significant morbidity and mortality, a high risk of secondary amputations and enormous costs [1, 2]. The actual incidence of amputation, in particular in relationship with diabetes, is difficult to ascertain, and may vary with the area, the ethnic group, age, gender, and local medical resources. Incidence rates also depend on the levels of amputation considered in any given study [3, 4]. Few studies have specifically looked at the features of elderly patients requiring a lower limb amputation.

The prevention of amputation is a major goal in public health, above all in diabetes care. In 1990, the Saint-Vincent declaration set the ambitious goal of reducing the rate of diabetes-related lower limb amputations by one half in five years [5]. Surprisingly few studies have documented the evolution in the rate of amputation over time. We therefore undertook this retrospective study to investigate the incidence, etiologies and prognosis of all major amputations in the Geneva (Switzerland) area, and to study changes in practice over a ten-year period. We took advantage of the fact that in Geneva all major amputations are performed in a single center, allowing reliable identification of all amputations performed. Our state office publishes yearly demographic reports allowing the calculation of reliable incidence rates. Already in the seventies and eighties, Geneva undertook major efforts in the treatment and prevention of diabetic foot ulcers [6]. In the department of Orthopaedic surgery, any elective amputation is preceded by a multidisciplinary audit, where the options of revascularization or conservative management (e.g. non-surgical, antibiotic treatment of osteomyelitis) are systematically discussed, with a strong conservative bias [7]. We thus undertook the following analyses to determine: 1) The age- and gender-specific incidence rate of major amputation and their evolution over ten years in elderly patients (> 65 years old). 2) The etiology underlying the decision to amputate. 3) The prognosis and mortality risk factors after major amputation.

Patients and methods

Patients

We conducted a systematic search of all major amputations performed on patients aged > 65 years in the Department of Orthopaedic Surgery, University Hospitals, Geneva (Switzerland) from January 1st, 1990 to December 31st, 1999. Major amputations were categorized as transtibial, through knee disarticulation, transfemoral or through hip disarticulation. Forefoot amputations were not included. Subjects were identified by searching for a diagnosis of major amputation on the discharge summary. We also checked the personal files of the rehabilitation personnel. Mortality data were obtained from State registries, and when necessary by direct contact with the general practitioner.

Diagnostic criteria

Severe Peripheral Arterial Disease (PAD) was defined as a typical foot gangrene in the context of either previous angioplasty, arterial reconstruction or sympathectomy; or a characteristic non-invasive arterial evaluation (ankle-brachial index < 0.6, ankle pressure < 80 mmHg or a transcutaneous PO₂ < 40 mmHg). Likely PAD was defined as a clinical diagnosis of severe PAD (usually with gangrene), used by the orthopedic team in the decision to perform the amputation, but without previous surgery or when a non-invasive arterial evaluation was not available. Cases were categorized as “no PAD” when FAD was not relevant to the decision to amputate (e.g. tumor or trauma). Acute lower limb ischemia was abstracted as a clinical diagnosis from the patients’ charts.

We recorded the presence/absence of any wound (ischaemic, “diabetic”, excluding traumatic or surgical wounds). We also transcribed the clinical diagnosis of “diabetic plantar ulcer” or “diabetic foot” made by the surgical team.

Diabetes was defined as a clinical diagnosis on the admission medical record or as the use of insulin or oral hypoglycaemic agents. The following conditions were extracted from the medical or nursing records: hypertension (defined by the presence of prescribed anti-hypertensive medication), congestive heart failure, atrial fibrillation (verified on the pre-operative EKG), obesity (body mass index > 30 kg/m²), previous stroke (excluding transient ischemic attack), obstructive lung disease, active smoking, hemodialysis, drug-treated depression, dementia or neoplasia.

Statistical analysis

Age- and gender-specific amputation rates calculation were established on yearly updated demographic statistics from the Geneva Population Statistics Office. Comparison of relative risk between groups was based on Poisson’s 95% confidence interval evaluation.

The Kaplan-Meier method was applied to quantify survival following amputation. Follow-up (measured in days and expressed as years and person-years) started on the date of amputation and continued until death or censoring. Censoring event was defined as being alive after the last contact or on the date of survival data collection closure (December 31st, 2000). Survival curves were compared using the log-rank test. Cox proportional hazards model was used to estimate the influence of patients’ characteristics on mortality. Independent variables evaluated were gender, age, amputation levels and other co-morbidities. Statistical analyses and 95% confidence intervals computations were performed using the STATA program, Release 8.2. (Stata Statistical Software: Release 8.2 [program], College Station, Texas, USA: Stata Corporation, 2003).
Results

The epidemiology of amputation

During the 10-year period under examination we identified 262 major amputations in 209 patients. Twenty three patients were re-amputated at a higher level on the same limb, and 31 underwent bilateral amputations. These amputations were performed on 116 (55.5%) men and 93 (44.5%) women, with an age range of 65-96 years (mean 78.0 ± 7.5, median 77.5). The average incidence rate was 4.18 amputations/year/10000 inhabitants (95 % CI 3.66-4.76), but varied from 1.79 to 11.41 amputations/year/10000 inhabitants, depending on age and gender (Table I). There was a statistically significant increase in the rate of amputations with age, with the highest rate observed in men > 85 years old (11.41 amputations/year/10000). The risk of amputation was 2-2.7 fold higher in men than in women throughout the age groups.

Diabetes was present in 48% of patients. Assuming an average prevalence of diabetes of 10% [8], the yearly incidence of amputation can be estimated at 19.9/10000/year for diabetic (95% CI 16.4-24.0) and 1.8/10000/year among non diabetic (95% CI 1.5-2.2).

The rate of amputation did not vary significantly over the 10-year observation period. However, the age at amputation increased from 76.9 years in 1990 to 82.7 years in 1999, an increase of almost 6 months per calendar year (0.49 years, 95% CI 0.15-0.83, P = 0.004). After breaking down this analysis by diabetes status, this trend was exclusively observed among diabetic patients and exceeds 8 months per year (0.69 years, 95% CI 0.27-1.10, P = 0.001). Age at amputation was not influenced by previous arterial reconstructive surgery (P = 0.452). Almost half the amputations were transtibial, and the remaining amputations were through knee disarticulations or transfemoral. Only one patient underwent through hip disarticulation (Table II). There was a tendency for increasing age with higher amputation levels. 23/262 (8.7%) operations were second amputations at higher levels on the same limb performed after 40.5 days (median 29.5, range 6-210). 31/262 (11.8%) operations were second amputations on contro-lateral limb, performed after 34.5 months (median 5.9, range 0.0 – 485.9). 112/209 (53.6%) patients could be equipped with a prosthetic limb during the same hospital stay.

Etiology of amputation: the role of PAD and diabetes

Severe PAD was by far the most common cause for amputation. On a total of 229 admissions for amputations, arterial disorders were present in 216 (94.3%). Likely or certain severe PAD was present in 198/229 (86.5%) admissions. Acute arterial occlusion was the admitting diagnosis for amputation in 26/229 (11.4%) admissions. Acute arterial occlusion occurred in the setting of pre-existent severe PAD in 8/26 patients. 49% patients had previous arterial reconstructive surgery or sympathectomy, and 31 % were directly transferred from the Department of Cardio-Vascular Surgery. Non-arterial conditions were the main cause for amputation in only 13/229 (5.7%) admissions; these included tumors (4/229), trauma (3/229), open fractures complicated by osteomyelitis (3/229) and others (3/229).

Only 32/229 amputations were classified as due to diabetic plantar ulcers by the surgical team, but these patients had features distinct from plantar neuropathic ulcers. 22 of these 32 cases had multiple wounds, affecting toes and heels in addition to the plantar area. All 32 patients had certain (29/32) or likely (3/32) severe PAD.

Prognosis

Only 61.7% patients survived one year after major amputation. 10.5% (22/209) died during the initial hospital stay. Survival was 47.9% after 2 years, 22.6% after 5 years and 13.7 % after 10 years. Survival was somewhat better after transtibial than higher level amputations (Figure 1). Thus, 2-year survival was 59% after transtibial amputation, and 39% after through knee or transfemoral amputation (P = 0.02). This difference remains significant after adjusting for age in a Cox regression model. The one-year survi-

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Incidence (Amput./year/10000)</th>
<th>95 % CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>1.79</td>
<td>[1.21-2.56]</td>
</tr>
<tr>
<td>75-84</td>
<td>3.47</td>
<td>[2.48-4.73]</td>
</tr>
<tr>
<td>85</td>
<td>5.84</td>
<td>[4.02-8.20]</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>4.83</td>
<td>[3.70-6.21]</td>
</tr>
<tr>
<td>75-84</td>
<td>6.84</td>
<td>[4.95-9.21]</td>
</tr>
<tr>
<td>85</td>
<td>11.41</td>
<td>[7.15-17.28]</td>
</tr>
</tbody>
</table>

Table I
Incidence of major amputations by age and gender.

<table>
<thead>
<tr>
<th>Amputations (number)</th>
<th>Amputation percentage</th>
<th>Age at amputation (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transtibial</td>
<td>123</td>
<td>47.0</td>
</tr>
<tr>
<td>Through knee amputation</td>
<td>79</td>
<td>30.2</td>
</tr>
<tr>
<td>Transfemoral</td>
<td>59</td>
<td>22.5</td>
</tr>
</tbody>
</table>

Table II
Distribution of amputations according to section level (N = 262, 1 patient with hip disarticulation excluded).
val did not vary over time during the decade under study (not shown).

We addressed the possible influence of co-morbidities on survival after amputation. Twelve conditions were extracted from the medical or nursing record, in addition to gender and age. These conditions together with their frequencies are listed in Table III.

In univariate analysis, only four co-morbidities besides male gender were associated with higher mortality after amputation: congestive heart failure (Hazard ratio (HR) = 2.1, P = 0.001), atrial fibrillation (HR = 2.3, P = 0.003), obesity (HR = 1.9, P = 0.01) and dementia (HR = 1.91, P = 0.02). Diabetes and hypertension did not emerge as prognostic factors.

In a full Cox regression model including all 14 variables (Tab III) the gender effect disappears and age, diabetes and dialysis become significant in addition to the previous co-morbidities.

Discussion

Both the methods of case identification and the demographic data are critical for the validity of our analysis. We believe that our case identification was quite complete. Indeed, major amputations are performed in a single center, and the information from discharge coding could be completed by examination of the files of the rehabilitation personnel. Interestingly, almost a third of the cases identified would have been missed by discharge summaries alone. Because of insurance coverage, it is highly unlikely that Geneva patients were operated elsewhere; no patients were admitted from outside areas; thus the population attended to by our orthopedic service is indeed the same than described in the local demographic statistics.

We observed a global incidence rate of major amputation of 4.18/10000 patients/year, ranging from 1.8 to 11.4/10000 patients/year depending on gender and increasing age (Tab I). The incidence among diabetic

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Prevalence (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>55.5</td>
<td>1.05</td>
<td>0.90</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.02</td>
<td>0.75-1.39</td>
<td>1.04</td>
</tr>
<tr>
<td>Diabetes</td>
<td>48.3</td>
<td>1.07</td>
<td>1.49</td>
</tr>
<tr>
<td>Obesity</td>
<td>41.2</td>
<td>1.85</td>
<td>1.49</td>
</tr>
<tr>
<td>CHF</td>
<td>41.6</td>
<td>2.08</td>
<td>1.49</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>28.2</td>
<td>2.25</td>
<td>1.49</td>
</tr>
<tr>
<td>Dementia</td>
<td>15.8</td>
<td>1.91</td>
<td>1.49</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>4.8</td>
<td>1.64</td>
<td>1.49</td>
</tr>
<tr>
<td>Hypertension</td>
<td>47.8</td>
<td>1.10</td>
<td>1.49</td>
</tr>
<tr>
<td>Stroke</td>
<td>8.1</td>
<td>1.54</td>
<td>1.49</td>
</tr>
<tr>
<td>Obstructive lung disease</td>
<td>12.4</td>
<td>1.14</td>
<td>1.49</td>
</tr>
<tr>
<td>Smoking</td>
<td>22.5</td>
<td>0.71</td>
<td>0.82</td>
</tr>
<tr>
<td>Depression</td>
<td>15.8</td>
<td>1.35</td>
<td>1.52</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>13.9</td>
<td>1.21</td>
<td>1.23</td>
</tr>
</tbody>
</table>

Figure 1
Survival according to amputations levels (upper curve=transtibial, lower curve higher levels).

Table III
Prevalence of co-morbidities in patients undergoing major amputation and factors associated with mortality (N = 209).
patients is 20/10000 patients/year, with a relative risk of approximately 10 compared to the non-diabetic population. This figure is an estimate based on diabetes prevalence data from the Verona study (Italy), where clinically identified diabetes was present in approx 10% of the population > 65 year (8-12%, depending on age and gender) [8]. However, it is unlikely to represent an underestimate. In our population the repeated medical interventions preceding amputation likely maximize the identification of diabetes, leading to a relative overestimation of the contribution of diabetes among amputees. Our rate of amputations is low, considering that our analysis included amputations for trauma and all reamputations. Our global incidence rates for major amputations are 3-4 times lower than reported from the Tayside registry [9]. A population-based study in Eastern Finland has also reported amputation rates 2-4 times higher than ours, whether in the general or the estimated diabetic population, with incidence rates in elderly (> 65 years) diabetic patients ranging from 43 to 123/10000 patients/year depending on gender and age [10]. A retrospective cohort study in diabetic patients (including younger patients) from the Rochester area indicates an incidence rate of 39/10000 patients/year, a number likely underestimated by the case identification system. A study on diabetic patients from the Veterans’ administration also reports an incidence of major amputations of approx. 40-50/10000 patients/year in patients > 65 years old [11]. Thus, we believe that our global rate of major amputations among elderly patients is low in the general and diabetic populations, in comparison with other reports.

Although we found no evidence for a decrease in amputation rates over the decade under study, the age at amputation increased progressively, suggesting improved management and delayed amputation. Importantly, the increase in age at amputation was almost entirely accounted for by the diabetic sub-population. In 1990, the Saint-Vincent declaration called for a reduction in the incidence of amputations among diabetic subjects by half [5]. Clearly this objective was not achieved. Already in the seventies, Geneva undertook major efforts in the treatment and prevention of diabetic foot ulcers [6]. Any elective amputation is preceeded by a multidisciplinary audit, where the options of revascularization or conservative management are discussed [7]. It is likely that these efforts, preceding the St-Vincent Declaration, had already allowed a decrease in “easily avoidable” amputations before 1990. Encouragingly, the progressive increase in age at amputation suggests further progress in the management of high-risk diabetic patients.

The cause for amputation was severe PAD in the vast majority of elderly patients. Indeed, after exclusion of trauma or tumors, severe PAD was present in almost all patients. It is remarkable that bone deformation or infection were never a cause of amputation in the absence of severe PAD. In the Tayside study [9], approx. 60% of amputations were performed for severe PAD, the remaining etiologies being mainly infections and bone deformities. In the Rochester study [12], > 20% of amputations were performed because of infection or non-healing wounds. In these studies the prevalence of non-PAD amputations may be partly accounted for by the inclusion of minor amputations and younger patients. Charcot’s arthropathy, a rare cause of major amputation, is usually diagnosed at a younger age and therefore absent form this population of elderly patients. Nonetheless, our local practice of aggressive, non-surgical management of infected wounds or osteomyelitis likely accounts for the absence of amputations for infectious reasons [7].

The prognosis after amputation remains poor. The high incidence of diabetes, hypertension and obesity confirms that amputated patients present with the high cardiovascular risk of the metabolic syndrome and/or already suffer from its complications. Indeed, the high mortality is likely explained by the high incidence of severe PAD and other mostly vascular co-morbidities such as congestive heart failure, atrial fibrillation, stroke, dementia and hemodialysis.

This study has the limitations inherent to retrospective studies. The decision to amputate is influenced by local, partly subjective practices or attitudes. In particular in the later stages of life, patients and physicians may prefer conservative, palliative management of pain and infection. Conversely, amputation itself may be seen as part of a palliative care approach, improving the patients’ symptoms (e.g. ischemic pain) and simplifying nursing. Thus, the incidence rates of major amputations among elderly patients are not a sufficient indicator of the quality of care. The lack of consensual criteria for amputations is a problem in most publications in this field. One essential, unanswered question is whether delaying amputations improves the quality of life or just prolongs the pre-amputation period of active wound care and morbidity (e.g. pain). This question will only be answered by a prospective study using pre-defined criteria for amputation and evaluation of quality of life before and after amputation [13]. Nonetheless, the unchanged prognosis over time suggests that amputations were not simply performed later in the course of the underlying disease.

One important insight from our study is that severe PAD is the almost exclusive etiology of major amputation, whether in the presence or the absence of diabetes. Future reductions in the rate of amputation will require progress in the management of PAD. More aggressive and more distal surgical revascularization could further delay amputations. Early prevention of PAD by the management of cardiovascular risk factors, such as smoking in all patients and glycemic control in diabetic patients [14-16], are essential for the prevention of amputations in elderly patients.
References


