Perioperative mortality in diabetic patients after non traumatic lower extremity amputations in Madrid from 1997 to 2005

Mortalidad perioperatoria en pacientes diabéticos sometidos a amputación no traumática de miembros inferiores en la Comunidad de Madrid de 1997 a 2005

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Abstract
Introduction: Chronic diabetic complications greatly affect the cost in health, economic productivity, with an emphasis on diabetic foot. Objectives: Analysis of mortality trends and related factors associated with LEA. Material and methods: A retrospective observational study of LEA in Madrid between 1997 and 2005. Documentary source: MBDS (discharge minimum basic data set). We selected cases that included an 84.1X procedure and 250.XX diagnosis (ICD-9-CM). Minor amputation was defined as distal to the ankle joint and a perioperative death that occurred during hospitalization. The trend of mortality was assessed using joinpoint regression analysis and expressed as percentage of annual change (PAC). We studied the risk of death by multivariate logistic regression using the independent variables age, sex, type of amputation and diabetes. Results: During the study period there were 278 deaths (7.3%) in diabetic patients. Mortality trends: PAC 1.99% (–2.7 to 6.9) was not significant. Risk of death (OR; 95%CI), patients over 65 years old (3.16; 2.03-4.91; p= 0.0001) and major LEA (2.75; 2.08-3.64; p= 0.0001). Conclusions: The perioperative mortality of LEA remains high and showed no downward trend during the study period with an increased risk of death for adults over 65 years and major LEA.

Keywords: mortality, amputation, diabetes.

Resumen
Introducción: Las complicaciones crónicas de la diabetes condicionan los costes relacionados con la salud, la productividad y la economía, entre las que destacan el pie diabético. Objetivos: Análisis de la tendencia y los factores relacionados con la mortalidad por amputación no traumática de miembros inferiores (AMI). Material y método: Estudio observacional retrospectivo de las AMI ocurridas en Madrid entre 1997 y 2005. Fuente documental: Conjunto Mínimo Básico de Datos. Se seleccionaron las altas con un procedimiento 84.1X y un diagnóstico 250.XX (CE-9-MC). Se definió amputación menor como distal a la articulación tarsometatarsiana. La tendencia de la mortalidad se evaluó mediante modelos segmentados de regresión de Poisson y se expresó como porcentaje anual de cambio (PAC). Se estudió el riesgo de muerte mediante regresión logística multivariante para las siguientes variables independientes: edad, sexo, tipo de amputación y diabetes. Resultados: Se produjeron 278 muertes en diabéticos (7,3%). En la evolución de la mortalidad se obtuvo un PAC del 1,99% (intervalo de confianza del 95%: –2,7 a 6,9), no significativo. El riesgo de mortalidad (odds ratio; intervalo de confianza del 95%) fue en mayores de 65 años de 3,16 (2,03-4,91; p= 0,0001) y en la AMI mayor de 2,75 (2,08-3,64; p= 0,0001). Conclusiones: La mortalidad perioperatoria de la AMI permanece elevada y no muestran tendencia descendente en el período de estudio con un mayor riesgo para los mayores de 65 años y AMI mayor.

Palabras clave: mortalidad, amputación, diabetes.

Date received: April 15th 2009
Date accepted: June 5th 2009

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List of acronyms quoted in the text:
ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; LEA: non traumatic lower extremity amputations; MBDS: Minimum Basic Data Set.
Introduction
The diabetes mellitus has been named the epidemic of the XXI century due to the large number of affected individuals and the sanitary and socio-economical consequences. It is the most frequent endocrinopathy, with effects in almost all the systems and organs of the body, placing itself in most of the developed countries among the ten first causes of death, with worrying projections.\(^1\)\(^2\) This increase in the incidence and prevalence of the diabetes might suggest an increase in the number of diabetic persons with chronic complications, and it is foreseeable that it occurs at earlier ages. The prevalence of the foot ulcer is of 4-10% in diabetic patients, and 40-60% of all the non-traumatic lower extremity amputations (LEA) occur in diabetic persons followed with ulcer in 85% of the cases. The diabetic foot affects more than 2 million of individuals per year in the United States and supposes a huge social and economic cost both for the health systems and for the patient and family.\(^3\) The polyneuropathy, the peripheral vascular disease and the infections are the factors that condition the diabetic foot in different proportions; all of them very frequent complications in diabetes and responsible of the foot ulcer, that does not heal, leading to the amputation in the worse of the cases and to death in some occasions. Objectives and declarations have been stated worldwide leading to reduce the amputations rates, and the declaration of Saint Vincent of 1989 was left behind.\(^4\) First, the efforts have to be directed to the optimization of the metabolic control and of the associated cardiovascular risk factors, to the health education of the patient and persons who take care, and to the adoption of specific measures addressed towards the prevention of the amputation, in other words, towards comprehensive programs on the diabetic foot assistance.\(^5\)\(^6\) The basis of these programs has to be the monitoring of the indicators by means of the development of adequate and feasible information systems.\(^7\) In this sense, the evolution of the rates of amputations or mortality due to amputation are indicators that have been incorporated in many health services\(^8\) as it has to do with sentinel events of great clinical-epidemiological interest and accessible by means of non-specific record systems, as it takes place under hospitalization regime.

In view of the above, it seems to be of great interest to know which has been the trend of the hospital mortality related to the LEA in diabetic patients in the environment of the Community of Madrid during the last decade, as well as the related factors.

Material and methods
An observational and retrospective study has been designed in which all the recorded admissions at public hospitals of the Community of Madrid have been analyzed regarding to the period comprised between January 1\(^{st}\) 1997 and June 30\(^{th}\) 2005, with the aim of identifying all patients who underwent a LEA. The file of the Minimum Basic Data Set (MBDS)\(^9\) has been used as source, which has been delivered to the central services of the extinct In-salud by all the hospitals appointed to its network and after the transfers as regards to health matter to the Health Counsel of the Community of Madrid. Such files contain up to 13 diagnosis fields and up to 21 related to surgical procedures, codified by means of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).\(^10\) The records that included the procedural codes 84.1X have been chosen and the subgroup of diabetic patients have been included if the code 250.x was in any of the diagnosis fields. Moreover, the traumatic and neoplastic amputations have been excluded. The methodology of Global Lower Extremity Amputation Study Group\(^11\) has been used in the definition of amputations: lower LEA has been considered the distals to the tarsometatarsian and the rest greater LEA. The trend of the mortality in the studied period was evaluated with segmented regression models of Poisson by means of the software Jointpoint of the Surveillance Research Program of the US National Cancer Institute.\(^12\) For the evaluation of the association among category variables, the test of the $\chi^2$ has been used considering the statistically relevant differences by an alpha mistake lower than 5%. The mortality risk was analyzed through logistics regression models, considering the death as dependent variables and being older than 65 years of age as independent variables as well as the sex, the type of amputation (higher or lower) and the presence of diabetes (codified as dichotomy variables). A multivariate model has been designed with the mentioned variables that showed a statistically relevant association with the dependent variable ($p <0.05$) in the bivariant analysis and the interaction terms >65 years/diabetes and higher/diabetes LEA, through the statistical package SPSS\(^\circledast\) version 12.0; those that did not show statistical relevance were excluded.

Results
Table 1 depicts the casuistry description. During the study period, 555 deaths occurred in patients who underwent LEA (9%), 278 occurred in diabetic patients (7.3%)
versus 277 (11.8%) in non-diabetic persons (p <0.0001), 221 (11.2%) in women versus 334 (8%) in men (p <0.001), 485 (10.7%) in persons older than 65 years of age versus 70 in persons under 65 years of age (4.3%) (p <0.001) and 434 (12.7%) in those who underwent upper LEA versus 121 (4.4%) of those submitted to lower LEA versus (p <0.001). In the patients who underwent upper LEA, the mortality was of 11.3% in the diabetic patients versus 14.4% in the non-diabetic patients (p <0.001), and in case lower LEA the mortality was of 3.7 versus 6.3%, respectively (p <0.005).

Table 1. Description of the population admitted by LEA

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Diabetes</th>
<th>Non-diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>6,154</td>
<td>3,805 (65.3)</td>
<td>2,349 (34.7)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>70.4 (13.7)</td>
<td>70.8 (13.4)</td>
<td>69.9 (16.6)</td>
</tr>
<tr>
<td>&lt;65 years, n (%)</td>
<td>1,634 (26.6)</td>
<td>982 (25.6)</td>
<td>652 (27.8)</td>
</tr>
<tr>
<td>&gt;65 years, n (%)</td>
<td>4,520 (73.4)</td>
<td>2,823 (74.2)</td>
<td>1,697 (72.2)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>1,974 (32.1)</td>
<td>1,321 (34.7)</td>
<td>653 (27.8)</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>4,180 (67.9)</td>
<td>2,484 (65.3)</td>
<td>1,696 (72.2)</td>
</tr>
<tr>
<td>LEA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower, n (%)</td>
<td>2,742 (44.6)</td>
<td>1,992 (52.4)</td>
<td>750 (31.9)</td>
</tr>
<tr>
<td>Greater, n (%)</td>
<td>3,412 (55.4)</td>
<td>1,813 (47.6)</td>
<td>1,599 (68.1)</td>
</tr>
</tbody>
</table>

LEA: non traumatic lower extremity amputations; SD: standard deviation.

In the multivariant analysis, a model has been obtained with the variables age over 65, larger amputation and absence of diabetes, as prognosis factors of mortality; the gender has been excluded due to the loss of statistical meaning (table 2). In the final model, the interaction over 65 years and diabetes has been included as well as the interaction greater AMI and diabetes due to statistically meaning.

In any case, as it can be observed at the bottom of the table, the explaining power of the logistics model is very limited (determination coefficient). When analyzing exclusively the discharges of the diabetic patients we obtain regression equations with identical variables (gender is also excluded), though in the diabetic patients the OR for the age and the type of amputation is greater, in other words, the association between >65 years of age and suffer a greater amputation and die during admission is greater (table 3). Consider that in table 2 the last interaction or effect modification has been excluded (higher/diabetes LEA) when losing the statistical meaning in the multivariant model (p >0.05).
Discussion

The diabetic patients who underwent LEA show a high mortality related to the great associated comorbidity (brain vascular disease, heart disease, chronic renal disorder, etc.). The amputation is a good marker of the advanced microvascular and macrovascular diabetes disease and, therefore, an unfavourable prognosis sign.

Among the works that study the hospital mortality due to LEA in diabetic patients in our environment we point out the Alcalá Martínez et al.\textsuperscript{15} (Murcia), with a mortality of 2% for lower LEA and 10% in case of greater LEA (global mortality of 5.8%) or the one of Almaraz et al.\textsuperscript{16} (Malaga) with a 3.6% of total LEA. The mortality in the diabetic patients of our study was of 7.3% of 11.3% for greater LEA and 3.7% for the lower LEA, slightly greater than in the two mentioned studies.

In the study about the mortality performed at Tayside (Scotland)\textsuperscript{17} between the years 1992 and 1998, a mean survival is described after the LEA of 27.2 months for the diabetic patients, and after 12 years the survival was of 25%; the values for the non-diabetic patients was of 46.7 months and 7.4% respectively. In both cases, the greater amputations are analyzed. Greater perioperative mortality has been reported when the amputation is proximal. Thus, Subramaniam et al.\textsuperscript{18} (Boston, United States) obtained between 1990 and 2001 mortality after 30 days of a LEA over the knee of 17.5% and below the knee of 4.2%, with a total mortality of 7.4%. The diabetes mellitus in the logistics regression study was not related to a higher risk of perioperative death nor to a lower survival after 3 years, though in fact after 10 years. Our work is not designed for the survival study after the patient’s discharge; in fact, the follow-up is circumscribed to the admission events and all the deaths occurred outside admission that includes amputation, though the obtained perioperative mortality (intra-event) is practically identical to the one analyzed in the article of Sunramaniam, with an equal methodology. Our diabetic patients shown a death OR of 0.4 (CI of 95%: 0.24-0.67) lower than 0.76 and the same occurs with the amputation level, with an OR of 2.64 (CI of 95%: 2.13-3.26) for greater LEA versus 4.35 in the work that we compare, though such authors consider proximal amputation the one practiced over the knee, which might explain these differences. Probably we might have obtained similar results as regards to the mortality at mean term if we could have studied it, but what is stated in the high perioperative mortality for the greater amputations. It has to be considered that the number of lower LEA exceeds the greater one in men but exactly the opposite happens in women, which together with the distribution explains its highest mortality (it has to be reminded that the gender variable is excluded from the regression equation in the multivariant adjustment). The age is also an independent death risk factor, which also modifies the diabetes effect, which seems logical when preventing a higher prevalence of the comorbidities, as the cardiovascular and renal disease. In Europe, different observational studies of similar design, as the one performed in Greece\textsuperscript{19} and in the United Kingdom,\textsuperscript{20} obtained perioperative mortalities of 14.7% in diabetic patients versus 21.3% in non-diabetic in the first one and 5.9 versus 9.1% in the second one, without the differences resulting statistically relevant and likewise a higher death risk associated to the amputation level and the age.

However, we could not demonstrate any trend to the mortality reduction in the study period; probably, the intervention point has to be looked after in the prevention of the amputation.

The outstanding fact that the mortality is lower in the diabetic patients than in the non-diabetic might be attributed considering that the first LEA occurs at earlier ages in diabetic patients and that in them the diabetes control as well as the modifiable cardiovascular risk factors is stricter during the last decade;\textsuperscript{19} moreover, the differences attributable to a different comorbidity and etiological composition of amputations in diabetic patients cannot be excluded. The limitations of our observational and retrospective design, as well as the used document

| Table 3. Death risks (multivariant logistics regression). Diabetic and non-diabetic patients |
|------------------------------------------|------------|---------|-----------------|
|                                         | p         | OR     | CI of 95% of OR |
| Diabetes                                |           |        |                 |
| Age: >65 years old                      | 0.0001    | 3.16   | 2.03-4.91       |
| LEA: greater                            | 0.0001    | 2.75   | 2.08-3.64       |
| Non-diabetes                            |           |        |                 |
| Age: >65 years old                      | 0.0001    | 1.8    | 1.3-2.52        |
| LEA: greater                            | 0.0001    | 2.34   | 1.68-3.25       |

CI: confidence interval; LEA: non traumatic lower extremity amputations; OR: odds ratio or advantages reason.
source, difficult the evaluation of certain factors, as the associated morbidity, mainly the cardiovascular disease and the nephropathy, or the presence of infections of ulcers related to the mortality, as well as the death cause. As we have already mentioned, the neuropathy and the vasculopathy are the main causes of amputation and the prevention should be the intervention point to reduce the high number of associated deaths.

To conclude, we believe that the use of general systematic records, as the MBDS might be useful as basis with a low cost, for the record of the events of great impact in diabetology as the LEA and the mortality due to LEA; fact that will be also useful to improve the quality of such records.

Conclusions
We have to conclude that the rates of mortality related to the hospitalization due to LEA are high in the Community of Madrid, higher than the ones reported by other groups of our environment, and have not shown a decreasing trend during the 9 years of study. The advanced age and the proximal association are associated to a higher mortality. ■

Declaration of potential conflict of interests
Á.M. Molino, P. de Miguel, A. Albarracín, R. Patiño and A. Fernández-Cruz state that there are no conflicts of interest as regards to the content of this article.

References
11. Decreto 89/1999, de 10 de junio, por el que se regula el Conjunto Mínimo Básico de Datos (CMBD) al alta hospitalaria y cirugía ambulatoria, en la Comunidad de Madrid. BOCM n.° 145, 22-6-1999.