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Relative mortality and long term survival for the non-diabetic lower limb amputee with vascular insufficiency

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Abstract

On a well defined non-diabetic amputation group with vascular insufficiency consisting of 10,191 amputations during the period 1982 to 1992 the Standard Mortality Rate (SMR) and the long term survival (Kaplan-Meyer) were analysed. The SMR for the total group was 8.6 (8.4-8.9) times the expected mortality the first year after amputation, decreasing to 3.2 (3.3-3.4) the second year. SMR in relation to age, gender and level of amputation was analysed. In the long term survival studies the median survival time (50% survival) for the total group was 1.8 years. Significant relation was found between the long term survival and gender, age and level of amputation.

Introduction

Lower limb amputation in patients with critical ischaemia because of non-diabetic arteriosclerotic manifestations, and amputation in diabetic patients has often been analysed as one group in epidemiological studies. Together these two amputation groups constitute more than 90% of all amputations in the western world (Pohjolainen and Alaranta, 1988; Ebskov, 1991; Rommers *et al.*, 1997; Stewart and Jain, 1993; Eneroth 1997). However the causal pathway (Pecoraro *et al.*, 1990) leading to amputation in these two populations is not identical. The clinical manifestations, the treatment and the epidemiology are different in several aspects. In two recent studies on relative mortality and long term survival the author (Ebskov, 1996; Ebskov 1998) has focused on diabetic amputations. The object of this paper was to analyse the relative mortality and survival in an isolated non-diabetic vascular insufficiency group. The survival figures from Denmark are compared to other studies. Further similarities and differences in some central epidemiological parameters between diabetic and non-diabetic amputations are discussed.

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Material and methods

Since 1978 the Danish Amputation Register (DAR) has based its statistics on data from the National Patient Register. The reliability of this database has been found adequate for epidemiological studies by several authors (Andersen *et al.*, 1987; Madsen *et al.*, 1990; Schmidt *et al.*, 1989; Seidelin and Eickhoff, 1995). Diagnoses are recorded according to WHO's International Classification of Diseases (ICD). Detailed information on the infrastructure of DAR has previously been published (Ebskov, 1977; Ebskov, 1986).

Information concerning date of death from the Central Bureau of Personal Registration (CBPR), in which all Danish residents are recorded by means of a personal identification number was also used. The DAR and the CBPR have been linked using the personal identification number to identify the amputees who died during the observation period (January 1982 to December 1993).

The material includes 10,191 non-diabetes mellitus vascular insufficiency (NDMVI) primary lower limb amputations performed during the period January 1982 to December 1992.

None of the patients had suffered a major amputation before entering the study in 1982.

Definitions

Primary amputation: the first admission of a

person for amputation of the lower limb excluding toes.

Following amputations: any admission for amputation of the limb, ipsi- or contralateral, after the primary amputation. Approximates to 1.3 per patient.

Amputation levels included: transmetatarsal level or more proximal.

Assumptions

The rationale for exclusion of the toe amputations in this study is primarily that NPR data only include information concerning patients admitted to a hospital, whereas information from out-patient clinics, where some of the toe amputations are carried out, is not registered in the NPR.

Data concerning previous vascular surgery are at present not available. It is assumed that about 40-50% of the amputations are performed after failed vascular reconstruction (Thomsen *et al.*, 1995).

Statistical methods

Whenever appropriate 95% confidence intervals (CI) were used. In calculating the relative mortality (Standard Mortality Ratio, SMR) the Danish population was used as the reference population. The long term survival analyses (absolute mortality) is calculated according to Kaplan-Meyer statistics. Log-rank test and Cox-analysis were used when comparing survival figures. As level of significance 1% was chosen.

Results

Standard mortality ratio

The SMR for the NDMVI group (n=10,191) shows a mortality averaging 8.6 (95% CI 8.4-8.9) times the expected mortality in the first postoperative year. In the second year the mortality is 3.2 (95% CI 3.0-3.4) times the expected mortality. From the third year the variations are insignificant ranging from 2.9 to 3.3.

Figure 1a shows the SMR in the NDMVI group for men and women respectively. The tendency is obviously that the female group has the highest relative mortality in year 0 (9.5 with 95% CI 9.1-9.9) versus males (7.9 with 95% CI 7.6-8.2). From year 1 and in the rest of the period a high degree of accordance between the genders was found.

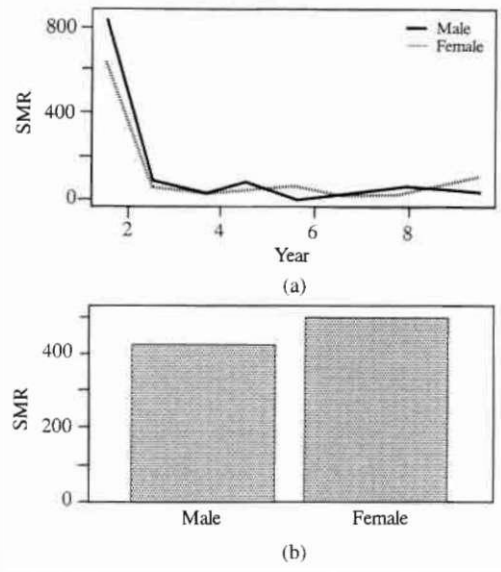

Fig. 1. (a) The relative mortality (SMR) of men and women for each year in the observation period. (b) SMR overall values for men and women.

Figure 1b shows the overall values for the period, thus emphasising the higher SMR in the female group (500) versus the male group (425).

Figure 2a shows the SMR in the different age groups i.e. 0-59 years, 60-69 years, 70-79 years, 80 years and older. As expected there seems to

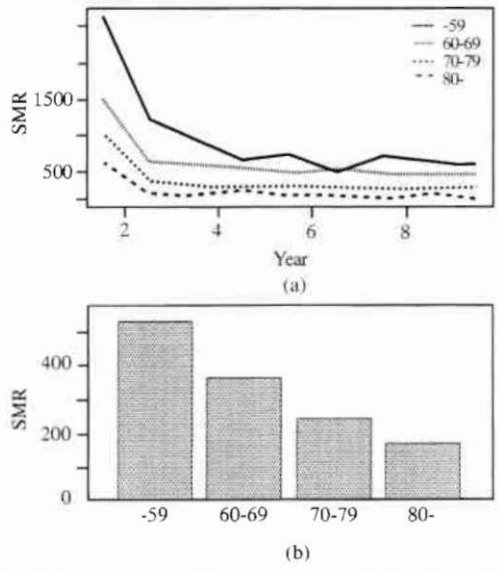

Fig. 2. (a) The relative mortality (SMR) of the age groups: ≤59 yrs; 60-69 yrs; 70-79 yrs and ≥80 yrs during the period. (b) SMR overall values for the different age groups.

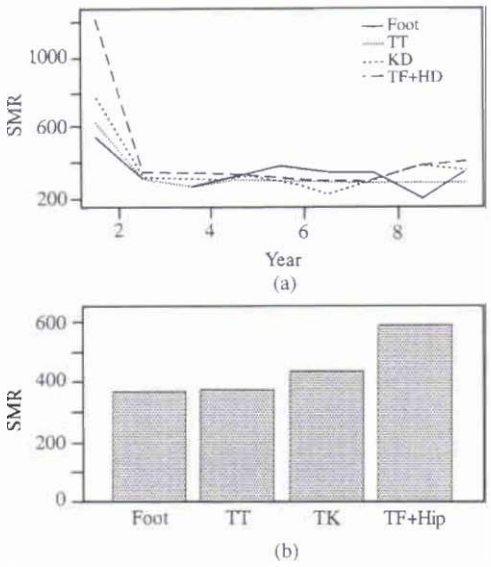

Fig. 3. (a) The relative mortality (SMR) for the level groups: foot (excl. toes); trans-tibial (TT); knee disarticulation (KD) and trans-femoral (TF) and hip disarticulation (HD). (b) SMR overall values for the level groups.

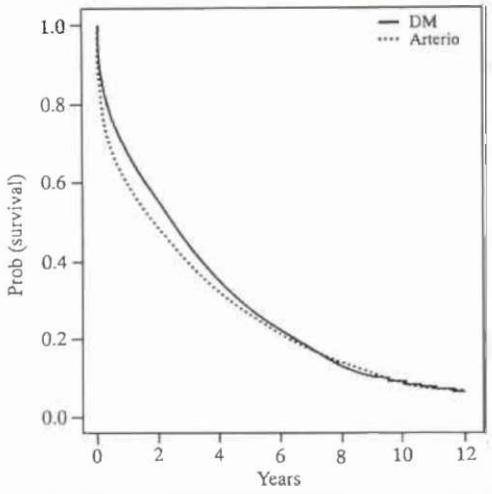

Fig 4. The long term survival (a.m. Kaplan-Meyer) with 12 years observation period for amputees with NIDDM (10,191) and DM (n=3516).

be an inverse relation between age and the SMR i.e. the youngest amputees have the highest relative mortality and the oldest amputees have the lowest relative mortality. Figure 2b shows the overall values for the period.

Figure 3a shows the relation between the relative mortality and the level of amputation. In year zero the relative mortality is significantly related to the level of amputation so that amputation at foot level implies the smallest SMR (5.5, 95% CI 4.57-6.36), trans-tibial amputation has a significantly higher relative mortality (6.4, 95% CI 6.07-6.74), knee disarticulation (7.8, 95% CI 7.0-8.6) and trans-femoral amputation (including hip disarticulation) (12.2, 95% CI 11.7-12.8). This strong relation between level of amputation and SMR in year zero is much less pronounced in the remaining period. The overall values (Fig. 3b) shows the differences for the period in total.

Table 1 shows the SMR for NDMVI group compared to the figures from the DM group (Ebskov, 1996).

Long term survival

Figure 4 shows the long term survival for the NDMVI amputations (and the DM group). The median survival time (50% survival) for the non-

Table 1. The relative mortality (SMR) in relation to gender, age and level of amputation for the NIDDM group compared to the DM group.

		Year			
		0	1	2	≥3
Total material		8.6/8.4	3.2/4.1	2.9/4.3	3.1/4.3
Gender	males	7.9/7.5	3.1/3.8	2.9/3.5	3.1/3.9
	females	9.5/9.7	3.3/4.6	2.9/5.5	3.2/4.8
Age	-59	26.3/19.9	12.3/12.7	9.5/11.3	6.5/10.8
	60-69	15.2/12.4	6.3/7.2	5.9/8.5	5.1/5.5
	70-79	10.3/8.9	3.7/3.9	3.0/3.6	3.0/3.9
	≥80	6.5/6.1	2.1/2.6	1.9/2.8	1.9/2.2
Level	Foot	5.5/5.4	3.2/4.1	2.8/4.1	3.3/3.8
	TT	6.4/7.6	3.1/4.1	2.6/4.4	2.9/4.3
	KD	7.8/11.7	3.1/2.9	2.9/3.8	3.2/4.6
	TF+Hip	12.2/12	3.5/4.9	3.3/4.8	3.4/5.8

diabetic amputees is about 1.8 years. After one year about 60% of the amputees were alive, after 2 years 49%, 40% after 3 years and 26% after 5 years. In the DM group the median survival time is about 2.4 years. After one year about 68% of the amputees were alive, after 2 years 55%, 45% after 3 years and 28% after 5 years.

Analysis of the long term survival in the NDMVI group for men versus women is shown in Figure 5. The women tend to have a lower percentage of survival. According to a log-rank test the difference is significant (p=0.008). The median survival time for men is 2.3 years, for women 1.7 years.

There are significant (p=0.00001) differences between the long term survival for the different age groups as seen in Figure 6. The median survival time in the age group younger than 60 years is 6.3 years, in the age group 60-69 years the median survival is 3.2, in the age group 70-79 years the median survival is 1.85, whereas the median survival time in the age group older than 80 years is about 0.9 years.

Log-rank test applied to survival figures concerning level of amputation (Fig. 7) shows strongly significant differences between the **levels of amputation (p=0.00001). The median survival time for the foot amputees is 3.7 years; for the TT amputees 2.6 years, for KD 2.3 years and for TF and HD amputees only 1 year.**

Analysis of the survival for the patients amputated in the period 1982-1987 compared to patients amputated in the period 1988-1992 (Fig. 8) showed borderline significant difference (p=0.01). Further it has been possible to detect significant differences (p=0.00001) in long term survival between the 3 different types of departments in Denmark where amputations are performed i.e. specialised orthopaedic departments, general surgical departments and

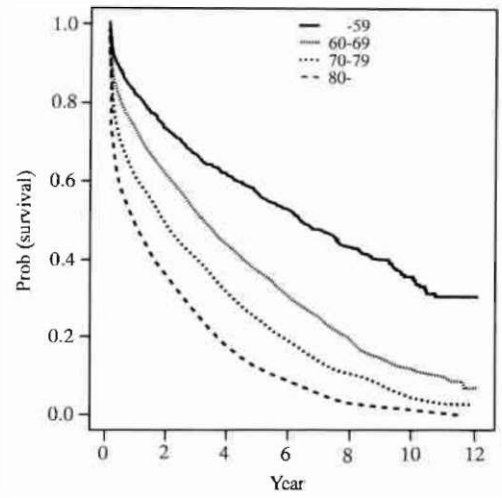

Fig. 6. The long term survival for NIDDM patients for the age groups ≤59 yrs; 60-69 yrs; 70-79 yrs and ≥80 yrs. Log rank test (p=0.001)

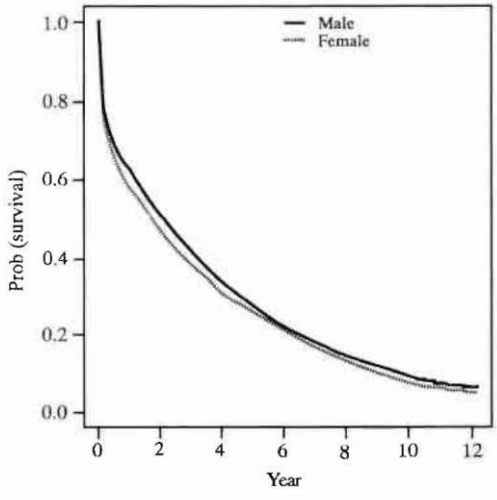

Fig. 5. The long term survival for men and women (NIDDM). Log rank test (p=0.0001).

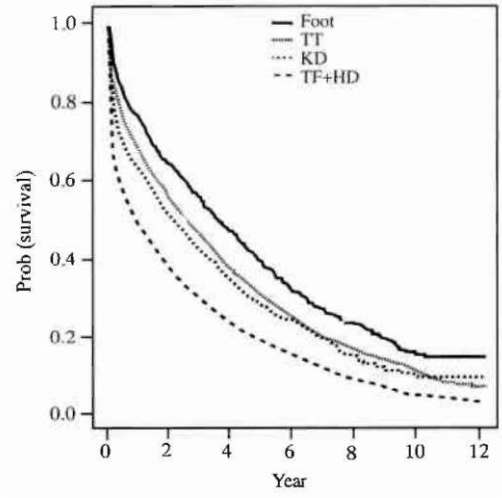

Fig. 7. The long term survival for NIDDM patients primary amputated at foot, trans-tibial level (TT), knee disarticulation (KD) and trans-femoral (TF) including hip disarticulation (HD). Log rank test (p=0.0001).

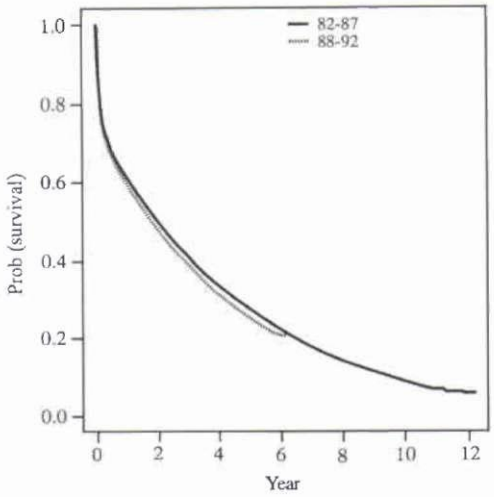

Fig. 8. The long term survival for NIDDM patients amputated in the period 1982-87 compared to patients amputated in the period 1988-92.

non-specialised departments with medicine and surgery (Fig. 9).

A Cox multivariate analysis for the isolated NDMVI group shows that when all the confounders i.e. gender, level of amputation, age, year of admission, type of department are included in the statistical calculations 3 factors i.e. the level of amputation, age and gender show significant influence on long term survival.

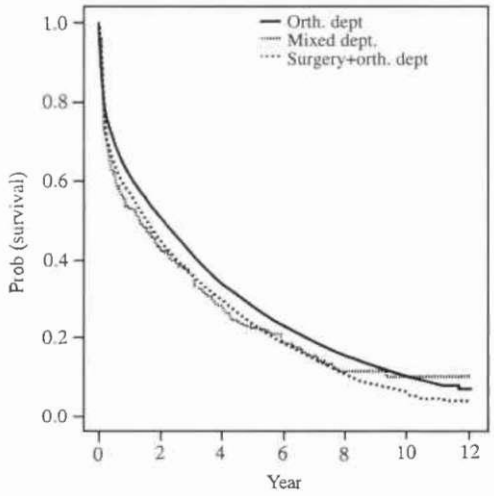

Fig. 9. The long term survival in relation to specialisation i.e. specialised orthopaedic departments versus mixed departments (internal medicine+surgery+orthopaedic surgery and surgery+orthopedic surgery.

Discussion

The primary aim with this study was to analyse the SMR and the long term survival for the NDMVI group. The SMR (Table 1) and long term survival figures are compared with the figures from the DM group, which have been separately analysed by the author in two recent publications (Ebskov, 1996; Ebskov, 1998). It is important to emphasise that several different methods in analysing the mortality/survival have been used. As mentioned by Larsson (1994) comparison between studies with different methods is invalid. In this study two well established methods were used i.e. the SMR to analyse the relative mortality and Kaplan-Meyer statistic to analyse the absolute mortality.

Some of the figures in Table 1 have to be discussed. First it should be mentioned that no significant difference between NDMVI and DM could be found when analysing total material, gender, age and level of amputation. The tendency that DM amputees have a slightly higher (but non-significant) relative mortality when analysing the total material could be because of the lower median age in the DM group (NDMVI: median age 76.1 years; DM: median age 72.9 years; Kruskal-Wallis p=0.000001). A very high SMR for both NDMVI and DM in the age group less than 69 years was observed especially in the first postoperative year. This may be because the expected longevity in the normal population for this age group is relatively high in combination with the fact that amputation in these relatively young patients is the result of severe arteriosclerosis with generalised manifestations. As a general rule the SMR decreases in a relatively uniform pattern with increasing age and increasing period after amputation. In the analysis of amputation level it seems that the SMR for the DM patients having a KD amputation is remarkably high compared to SMR for the NDMVI. This may be a consequence of a high complication ratio in this particular group (Baumgartner, 1983; Stirnemann and Althus, 1983).

Contrary to the SMR studies where no comparable studies have been found, it was possible to compare the long term mortality with several other authors (Larsson, 1994; Hansson, 1964; Mandrup-Poulsen and Jensen, 1982; Pohjolainen *et al.*, 1989; Cossart *et al.*, 1983;

Kolind-Sørensen, 1974; Stewart *et al.*, 1992; Helm *et al.*, 1986). Before discussing long term survival for NDMVI it is interesting to compare the curves with the normal population. For the normal population (age correlated) the median survival is about 8 years. Tibell (1971) analysed the long term survival for patients with arteriosclerosis obliterans or with DM (first admission between 1949 and 1965). The 50% survival in the arteriosclerosis obliterans group was about 2.2 years. The 50% survival in the DM group was a little higher averaging 3 years. Comparison of the 3 different conditions: the normal individual, the arteriosclerotic individual (with or without DM) and finally the amputee (with or without DM) indicates that survival/mortality after amputation is multifactorial and that the amputation as an isolated factor seems to be less important than the aetiological cause of amputation i.e. arteriosclerosis with its generalised manifestations affecting the brain, heart and kidneys.

Stewart *et al.* (1992) analysed long term survival for DM patients versus non-diabetic vascular insufficiency patients. They found a significant ($p<0.006$) difference between the groups in favour of the non-diabetic group. The author has found the opposite with a significantly better survival for the DM group even though the curves converge after about 7 years. On the other hand the 50% survival (i.e. mean survival) found by Stewart *et al.* (1992) is much better than the survival found in this study. Actually the 50% survival for both NDMVI and DM (total materials) is less than the 50% survival among TF amputees in Dundee in the period 1970 to 1979 found by Stewart *et al.* (1992). A survival which they actually have doubled for the period 1980-89 to about 6 years. Bodily and Burgess (1983) found a 50% survival of about 3.5 years (n=55, combined NDMVI and DM). Rasmussen *et al.* (1982) found a 50% survival averaging 20 months (n=58, NDMVI). Mandrup-Poulsen and Jensen (1982) found (n=310, combined NDMVI and DM) a 50% survival of about 2 years and 7 months. Helm *et al.* (1986) found (n=257, combined material with NDMVI, DM and 7 trauma) a 50% survival of about 2 years. Larsson (1994) found a 50% survival in diabetics (n=220) of about 3 years (after major amputation). Hansson (1964) found a 50% survival of about 1 year (combined DM and NDMVI).

Increase in survival over time has been analysed by Harris *et al.* (1988) who compared the period 1970-1979 (116 cases) with the period 1980-1989 (189 cases) (3 years 2 months versus 3 years 11 months) and found no statistically significant improvement, even though the tendency was positive. As mentioned above, Stewart *et al.* (1992) found an impressive improvement in long term survival. With the more limited time interval the author could not find the same positive tendency in Denmark; on the contrary it seems that the survival has been decreased.

The literature review shows a quite clear picture concerning survival after amputation. The tendency is that specialised orthopaedic centres seem to achieve better survival as compared to figures from larger areas where the data include figures from departments with less routine experience in amputation surgery. On the assumption that the materials (Dundee versus present) are comparable one of the explanations for the better survival figures is the superiority of centralisation and Stewart and Jain (1993) believed that an integrated approach to amputation and subsequent rehabilitation is obviously an advantage. This point of view is supported by the fact that a significant difference (log rank test, $p<0.00001$) was found between the 3 types of departments which actually are engaged in amputation surgery in Denmark (Ebskov, 1992).

As indicated by the Cox analysis and the log rank test level of amputation is an important factor as regards long term survival. Level of amputation is influenced by several factors i.e. the experience of the surgeon, the possibility to perform level selection by paraclinical tests (skin perfusion etc) and the impact of vascular surgery. As regards the two first mentioned factors it seems obvious that these factors are enhanced by centralisation. The influence of vascular surgery on the epidemiology of amputations is well-documented (Holstein, 1996; Ebskov *et al.*, 1994; Eickhoff, 1993; Pedersen *et al.*, 1994; Mattes *et al.*, 1997) but the epidemiological interactions in relation to level of amputation (and long term survival) are less simple and are controversial (Burgess and Marsden, 1974; Sethia *et al.*, 1986; Tsang *et al.*, 1991; Gregg, 1985; Kazmers *et al.*, 1980; Evans *et al.*, 1990; Dardik *et al.*, 1982). Stewart *et al.*

(1993) found that 54% of the vascular cases in Dundee Limb Fitting Centre had a history of vascular surgery prior to amputation and that failed vascular surgery deteriorates the TT/TF ratio. The frequency of post revascularisation amputations is not higher than 50% in Denmark (Thomsen *et al.*, 1995). However the TT/TF ratio in the Dundee Limb Fitting Centre is more favourable (primary amputations 2.6, post-revascularisation amputations 1.8) than in the present study (total material 1.06).

The relation between long term survival and level of amputation has been described by other authors (Pohjolainen and Alaranta, 1988; Larsson, 1994; Mandrup-Poulsen and Jensen, 1982).

SMR and long term survival are important epidemiological factors. The present study demonstrates that continuous surveillance is important and should be performed to detect differences between geographical areas with different organisations. The study indicates it may be possible to improve survival after amputation in Denmark.

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