Short and Long Term Mortality Rates after a Lower Limb Amputation

L.V. Fortington [a,*], J.H.B. Geertzen [a], J.J. van Netten [b], K. Postema [a], G.M. Rommers [a], P.U. Dijkstra [a,c]

[a] Department of Rehabilitation Medicine, University of Groningen, University Medical Center Groningen, Groningen, Netherlands
[b] Department of Surgery, Hospital Group Twente, Almelo, Netherlands
[c] Department of Oral and Maxillofacial Surgery, University Medical Center Groningen, Groningen, Netherlands

WHAT DOES THIS STUDY ADD TO THE EXISTING LITERATURE AND HOW WILL IT INFLUENCE FUTURE CLINICAL PRACTICE?

This study adds prognostic information for a well-defined population of people with a first amputation at or proximal to a transtibial level, due to a vascular or infection related cause. Mortality rates were 22% at 30 days, 44% at 1 year and 77% at 5 years. Median survival was 20.3 months. The importance of defining the population when reporting and using mortality rates in people with amputation is discussed.

Objective: To determine mortality rates after a first lower limb amputation and explore the rates for different subpopulations.

Methods: Retrospective cohort study of all people who underwent a first amputation at or proximal to transtibial level, in an area of 1.7 million people. Analysis with Kaplan-Meier curves and Log Rank tests for univariate associations of psycho-social and health variables. Logistic regression for odds of death at 30-days, 1-year and 5-years.

Results: 299 people were included. Median time to death was 20.3 months (95%CI: 13.1; 27.5). 30-day mortality = 22%; odds of death 2.3 times higher in people with history of cerebrovascular disease (95%CI: 1.2; 4.7, $P = 0.016$). 1 year mortality = 44%; odds of death 3.5 times higher for people with renal disease (95%CI: 1.8; 7.0, $P < 0.001$). 5-years mortality = 77%; odds of death 5.4 times higher for people with renal disease (95%CI: 1.8; 16.0, $P = 0.003$). Variation in mortality rates was most apparent in different age groups; people 75–84 years having better short term outcomes than those younger and older.

Conclusions: Mortality rates demonstrated the frailty of this population, with almost one quarter of people dying within 30-days, and almost half at 1 year. People with cerebrovascular had higher odds of death at 30 days, and those with renal disease and 1 and 5 years, respectively.

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INTRODUCTION

Mortality rates after lower limb amputation (LLA) are notoriously high. This is attributed to the population being comprised of old and medically frail people at the time of undergoing a major surgical procedure. Older age, proximal amputation levels and multi-morbidity, particularly renal disease, are all associated with a higher rate of mortality after amputation.[1–4] Despite this acceptance of a high risk of mortality after LLA, reported rates are wide-ranging. Differences are largely explained by variation in inclusion criteria. As an example, 1 year after amputation, mortality rates as low as 22% have been reported in a population that included partial foot amputation.[5] Focusing only on transtibial and more proximal levels, mortality rates can reach as high as 52% at 1 year.[6,7] Additional factors, such as the inclusion of only people undergoing their first amputation or also subsequent amputations, different causes of amputation, or the source used for death registration can also influence these rates. Unfortunately, this information is not always clear, limiting our ability to make valid comparisons across studies.

With treatment options for wound care and at-risk limbs continually changing[8] the mortality risk and profile of people with amputation is also likely to differ. From the perspective of planning and providing rehabilitation services, the characteristics of the population surviving to different time points can provide valuable insight. Understanding the timing and reasons for mortality after amputation in different subgroups may also help to identify specific risk factors and open new ideas for pre- and post-

* Corresponding author. L.V. Fortington, Department of Rehabilitation Medicine, University Medical Center Groningen, Postbox 30.001, 9700 RB Groningen, Netherlands. Tel.: +31 (0) 50 36 18042; fax: +31 (0) 50 36 11708.

E-mail addresses: l.v.fortington@umcg.nl; Lauren.fortington@gmail.com (L.V. Fortington).

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operative care. The aims of this study were to determine 30-day, 1-year, and 5-year mortality rates after a first amputation, at or proximal to transtibial level in our region. Differences by population characteristics including level of amputation, age groups and diabetes status are explored, along with major co-morbidities, medical and surgical history, and admission and discharge settings.

MATERIALS AND METHODS

The medical ethics committee of the University Medical Centre Groningen ruled that a formal approval was not required for this retrospective medical record review.

Setting and population

The study was conducted in all 14 hospitals of the three Northern provinces of the Netherlands: Groningen, Friesland and Drenthe. This region had a total population of approximately 1.7 million people in the inclusion period, with around 14% aged over 65 years in the study period.[9]

Each hospital compiled a list of all people who had an amputation at a transtibial level or proximal, in 2003 or 2004. Changes to recording of data were instigated in 2005 which affected the reliability of data in the years following. With this in mind, and to allow for a sufficient follow up time, the period 1 January 2003 to 31 December 2004 was chosen. The incidence of amputation in this setting was reported previously at 8.8 per 100,00 person-years.[10]

Medical records for all cases were reviewed between August 2010 and June 2011. People who had undergone amputation at transtibial level or proximal, on either limb, before 1 January 2003 were excluded. People with a previous amputation distal to, and including, ankle disarticulation were included. Where multiple amputations occurred within the study period (either re-amputation to a higher level or a bilateral amputation), the date of the first amputation was used to calculate time to death. Amputations that were the result of trauma, cancer, complex regional pain syndrome or congenital causes were excluded, thus leaving a cohort with amputation resulting from vascular disease, infection and/or diabetes. Amputation date, side and level (unilateral TT, unilateral proximal (KD or TF), or bilateral) were recorded for the study period, as well as any amputations performed in the years following.

Variables

The primary dependent variable was time to death. The date of death was recorded from hospital records, or general practitioners were contacted for an updated status (alive or date of death) in August 2011.

Characteristics of the population included as independent variables were: age; sex; marital status (dichotomised as partner or alone (includes single, widowed, divorced)); living situation prior to admission for amputation (home, nursing home, other); discharge destination (home, inpatient rehabilitation centre, nursing home, supported residential home, other hospital, or died before discharge); and smoking history (ever, never). Medical diagnoses were based on a list of items from the Charlson Comorbidity Index, with the most frequent diagnoses presented under combined groups of cardiac disease, cerebrovascular disease, lung disease, renal disease, diabetes (see Appendix 1). Where a diagnosis was unclear, details (including medications) were noted and discussed with a medical specialist for clarification. In addition, it was noted if a patient had diabetes type I or type II and whether they were receiving dialysis. Surgical history was recorded and included previous peripheral vascular procedures (e.g. bypass or angioplasty) as well as any previous minor amputations.

Time to death, in months, was calculated from the date of the first amputation. The last confirmed date of contact with medical care (hospital or general practitioner) was recorded for censored data. People who had bilateral or re-amputations were combined to one category, multiple major amputation, with the underlying notion that these cases had undergone multiple hospital admissions, anaesthesia and surgery, probably giving them a different mortality risk than people with single amputations. This categorisation procedure was chosen to enable sufficient numbers in each group for analyses.

Statistical analysis

To consider differences in mortality for the different population characteristics, data were first explored for a Cox hazard model. However, the hazards were not proportional over time, and thus assumptions for using this model were not met. Instead, survival was analysed using Kaplan-Meier curves and stratified Log Rank tests to check for differences across independent and combined categories of sex, age, level of amputation and diagnosis of diabetes. Missing data were right censored at the last confirmed contact date; missing data were not imputed. Characteristics of the population who died at 30-days, 1-year and 5-year were compared to those who survived using χ^2 tests for categorical variables and *t*-test for age (normal distribution). Variables with $P < 0.1$ were included in logistic regression models (stepwise backward logistic regression) with 30-day, 1-year and 5-year mortality (yes or no) as the dependent variable. Discharge destination is presented for descriptive purposes but not included in model due to overlap with the category 'death before discharge'. Statistical significance for analyses was 0.05 (two-sided). Analyses were performed using Microsoft Excel 2003 and SPSS 20.

RESULTS

Population characteristics

Of 338 cases of LLA identified, 299 were due to a vascular, infection and/or diabetes related cause and were included for analysis (Table 1). The majority of cases were men (60%), the mean age was 74.1 years and TTA was most frequent

Table 1. Characteristics of included population, with comparison of people with diabetes and people without diabetes.

Variable (*n*)	Included N = 299	Diabetes N = 150	Non-diabetes N = 149	P[a]
Level (298)	*n* (%)	*n* (%)	*n* (%)	
Transtibial	146 (49)	83 (56)	63 (42)	.020
Knee disarticulation	27 (9)	12 (8)	15 (10)	
Transfemoral	101 (34)	39 (26)	62 (42)	
Bilateral	24 (8)	15 (10)	9 (6)	
Sex (299)				
Men	178 (60)	83 (55)	95 (64)	.138
Women	121 (40)	67 (45)	54 (36)	
Age[b] (299)	Mean (sd)	Mean (sd)	Mean (sd)	
All	74.1 (11.2)	73.4 (10.5)	74.7 (11.8)	.355
Men	72.1 (10.6)	71.1 (10.8)	72.9 (10.4)	.266
Women	77.0 (11.5)	76.4 (9.5)	77.7 (13.6)	.515
Admitted from (276)	*n* (%)	*n* (%)	*n* (%)	
Home	177 (64)	90 (65)	87 (64)	.829
Care	99 (36)	49 (35)	50 (37)	
Living situation (239)				
Alone	139 (58)	79 (64)	60 (52)	.050
Partner	100 (42)	44 (36)	56 (48)	
Discharged to (294)				
Home	42 (14)	24 (16)	18 (12)	.371
Inpatient rehabilitation	40 (14)	19 (13)	21 (14)	
Care	156 (53)	82 (55)	74 (51)	
Died before discharge	56 (19)	23 (16)	33 (23)	
Medical history (299)				
Cardiac disease	114 (38)	57 (50)	57 (50)	.964
Cerebrovascular disease	44 (15)	22 (15)	22 (15)	1.000
Chronic lung disease	66 (22)	30 (20)	36 (24)	.403
Renal disease	59 (20)	39 (26)	20 (13)	.006
Smoking (228)				
Ever	137 (60)	56 (68)	81 (52)	.016
Never	91 (40)	52 (33)	39 (48)	
Surgical history (299)				
Peripheral vascular procedure	150 (50)	68 (45)	82 (55)	.093
≥1 minor amputation before major	46 (16)	48 (32)	14 (9)	<.001
>1 major (either limb)[c]	68 (23)	36 (24)	32 (22)	.351

Variable (*n*) = number of valid observations for the stated variable; medical and surgical history were yes or not recorded so calculations are based on whole population of 299.

[a] *P* is chi-square of people with diabetes compared to people without diabetes.

[b] Comparison of age by gender: with diabetes men versus women $P = 0.002$; without diabetes men versus women $P < 0.016$.

[c] Includes amputations after study period.

(49%). Most people were admitted from home (64%), with many living alone (58%). Discharge to care was most common (53%), with 19% not surviving to be discharged from the hospital.

Diabetes was diagnosed in 50% of the population. People with diabetes had twice as many TTA (56%) than TFA (26%), significantly different to people without diabetes (TTA and TFA both 42%; $P = .020$). Renal disease was more prevalent in people with diabetes (26%) than people without (13%, $P = .005$), with no differences seen between these groups for other diagnoses. Previous minor amputations were significantly more likely for people with diabetes (32%) than people without diabetes (9%, $P < .001$), whereas frequency of vascular reconstructive procedures was somewhat less in people with diabetes (45% diabetes, 55% non-diabetes, $P = 0.093$).

Mortality

Mortality data were unable to be found for 30 (10%) people. Fourteen could not be traced at all following their discharge from hospital and 16 were not known by the general practitioner listed in their file. These cases, with unknown status, were older than people with a confirmed status (known = 73.6 (11.0) years, unknown = 78.0 (12.1) years, $P = .044$). There were no significant differences in sex (% men: known status = 61%, unknown status = 48%, $P = .095$) or level of amputation (known status: TTA = 45%, TFA = 30%, unknown status: TTA = 45%, TFA = 38%).

Although death could be confirmed, the date was missing for 16 (5%) people.

The median time to death was 20.3 months (95% CI: 13.1; 27.5) (Table 2). For people with unilateral TTA, time to death was longer at 27.8 months (22.0; 33.6), and for TFA shorter at 10.6 months (1.2; 19.9) (median survival time by level, $P = 0.495$). Significant differences between median survival time were seen by age groups. People aged 85+ years survived a median 8.8 months, while the remaining younger age groups all survived 20+ months, ($P = .028$). Combining age and level, people with unilateral TFA aged 75–84 years had significantly longer survival times (22.2 months) than younger (3.4 months) and older (2.1 months) people with TFA. No differences were seen for people with or without diabetes (median (se) diabetes = 25.0 (5.8) months, non-diabetes = 20.7 (5.0), $P = 0.969$) (Fig. 1).

Twenty-two percent of the population died within 30-days. Factors significantly associated with 30-day mortality were age, location admitted from, previous peripheral vascular procedure and cerebrovascular disease (Table 3). The odds of death within 30-days were 2.3 times greater for those with cerebrovascular disease compared to those without (95% CI: 1.17; 4.68, $P = .016$) (Table 4).

After one year, 44% of the population had died. Variables associated with mortality were age, location admitted from, previous peripheral vascular procedure or previous minor amputation and a diagnosis of cerebrovascular, renal or cardiac disease. People with renal disease had 3.53 times

Table 2. Cumulative percentage of people who died at 30-day, 1-year and 5-years, and median survival estimates (months) by age, sex, level and diagnosis of diabetes.

Variable (*n*)	*N*[a]	*n* died	% Dead			Survival (months)			
			30-Day	1-Year	5-Year	Median	se	95% CI	*P*[b]
All (283)		231	22	44	77	20.3	3.7	(13.1; 27.5)	
Level (279)									
Unilateral transtibial	130	104	17	35	75	27.8	3.0	(22.0; 33.6)	.495
Unilateral transfemoral	83	69	27	54	77	10.6	4.8	(1.2; 19.9)	
Multiple major	66	57	23	45	80	16.3	6.8	(2.9; 29.7)	
Sex (283)									
Men	167	141	22	43	76	21.1	4.1	(13.0; 29.1)	.885
Women	116	90	21	42	76	25.0	7.3	(10.8; 39.2)	
Age (283)									
<65 years	59	39	19	38	65	26.7	9.9	(7.3; 46.0)	.028
65–74 years	77	64	24	45	74	21.3	7.1	(7.5; 35.2)	
75–84 years	103	87	15	38	81	25.0	4.1	(17.0; 33.1)	
85+ years	44	41	35	56	85	8.8	6.6	(0.0; 21.6)	
Diabetes (283)									
No	140	111	22	45	75	20.7	5.0	(10.9; 30.5)	.969
Yes	143	120	20	41	77	25.0	5.8	(13.6; 36.4)	
Age and level (279)									
Unilateral transtibial									
<65 years	22	15	14	24	60	30.8	10.1	(11.0; 50.5)	.041
65–74 years	32	23	16	30	71	41.2	11.2	(19.2; 63.2)	
75–84 years	51	47	12	36	82	26.6	2.7	(21.4; 31.9)	
85+ years	25	19	34	45	78	12.6	13.5	(0.0; 39.0)	
Unilateral transfemoral									
<65 years	13	10	31	62	77	8.2	4.9	(0.0; 17.9)	
65–74 years	26	23	32	64	80	3.4	1.8	(0.0; 6.9)	
75–84 years	31	21	14	35	70	22.2	21.7	(0.0; 64.7)	
85+ years	13	15	45	67	89	2.1	1.0	(0.0; 4.1)	
Multiple Major									
<65 years	20	13	21	36	68	37.9	21.4	(0.0; 79.9)	
65–74 years	19	18	27	44	72	30.8	27.3	(0.0; 84.4)	
75–84 years	21	19	24	47	94	12.8	10.5	(0.0; 33.4)	
85+ years	6	7	17	67	100	8.6	5.8	(0.0; 19.9)	

Variable (*n*) = number of valid observations for the stated variable.

[a] *N* is total number in category with confirmed status, *n* died is number with confirmed death. Not all categories add to totals stated due to missing data.

[b] *P* is log rank between categories for median survival time.

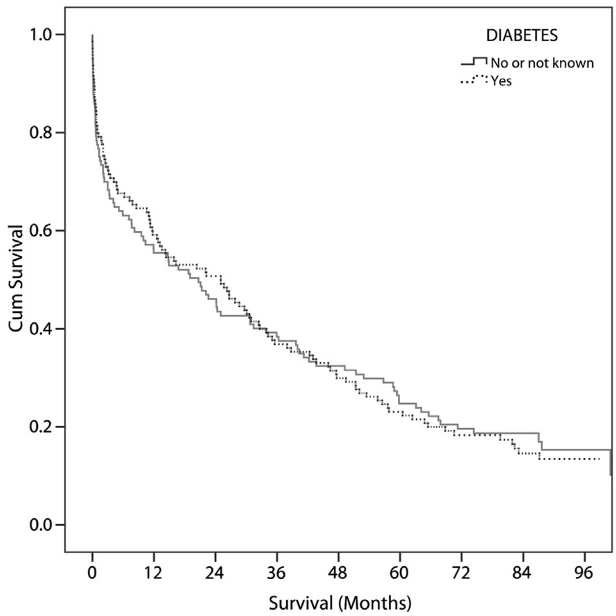

Figure 1. Kaplan Meier survival estimates after a first lower limb amputation at or proximal to transtibial level, split for status of diabetes. Based on information presented in Table 2, diabetes $n = 143$ total, 120 died; non-diabetes $n = 140$ total 111 died. Median (se) survival for people with diabetes = 25.0 (5.8) months, non-diabetes = 20.7 (5.0), $p = 0.969$.

greater odds of death at one year than people without (95% CI: 1.79; 6.96, $P < .001$) and cerebrovascular disease 2.5 times greater odds of dying than people without (95% CI: 1.21; 5.34, $P = .013$). The five-year mortality rate was 77%, with renal disease presenting 5.35 times greater odds of dying (1.79; 16.0, $P = .003$).

DISCUSSION

Against a background of changing treatment options for limb salvage, we aimed to review the effect this has on mortality rates for the population who go on to have a transtibial or proximal amputation. The mortality rates reported in this study demonstrated the frailty of the population, with 22% of people dying within 30-days. It has been suggested that LLA in people with vascular disease might be performed as pain relief at the end stages of care.[6] Our results, with a high post-operative mortality, are in line with that suggestion. Equivalent rates have been reported in Scandinavian studies with 19—30% of people dying in the first month after LLA,[1,6,7] while in other, comparable western populations this is reported to be much lower, around 10%.[3,4,11—14] Investigation of underlying influences from health services, surgical decisions and patient motivations behind decisions to amputate might help to explain some of the differences in post-operative mortality rates between studies. As an example, a poorer mortality outcome has been found when there are in-hospital delays in decision making.[15] Similarly, the health seeking behaviours of different populations should be explored for their influence on time to presentation for treatment.

For those who survive the post-operative period, mortality outcomes were more consistent with other studies. After 1 year, 44% of the population had died, falling mid-range of results in literature at 30—50%.[1,6,12,13,16] The 77% mortality rate at 5 years was higher than previous findings of 56—70%.[4,13,14] Direct comparisons of these mortality outcomes are problematic owing to the differences in populations and reporting. However, the rates do serve to highlight the variability in outcomes from reporting different populations and emphasise a need to carefully review the included population before applying results in clinical, research or other contexts.

Diabetes remains the leading cause of major lower limb amputation.[17] The disease process differs from other vascular-related causes and tends to result in transtibial or distal amputation levels. With this, the influence of diabetes on survival has been described as time-dependent, with short term rates being the same or better than people without diabetes but worse in the long term.[2,3] Other authors, including the current work, have found no difference in mortality rates for people with diabetes compared to people without diabetes at any time point.[6,18] These conflicting findings between studies of diabetes and mortality, may again arise from population differences, such as inclusion of non-vascular amputations or people undergoing (partial) foot amputation.[5] Outcomes should ideally be reported separately for both the underlying cause and level of amputation (in addition to diabetes status), to avoid the bias resultant from non-vascular and mixed-level populations. In the case of a first amputation proximal to the ankle, resulting from a vascular or infection related cause only, there was no influence of diabetes diagnosis on mortality rates.

Survival is generally described with negative wording, such as 'dismal.'[13,19] Yet, considering the population as frail and elderly, perhaps a more positive angle should be stressed; almost one quarter of our cohort survived to 5 years. There should be a focus on finding determinants of survivors to enable rehabilitation and long-term care services for this group to be well planned. Specifically, investigation of people who survived the post-operative period but died within one first year, in our case 22% of the population, could lend support to rehabilitation programs aimed at enhancing quality of life during this short time. The most important influence on mortality at 30-days was the presence of cerebrovascular disease, with renal disease having most influence after 1 and 5 years. Unfortunately, no other clear determinants of the 1-year survivors could be found but further investigation of this group is suggested, as they are potentially an important population from both surgical and rehabilitation perspectives.

Complementary to investigating determinants of survival, pre-operative care and the timing of amputation should be looked at for its influence on differing mortality rates. Less than 50% of our cohort received pre-amputation vascular intervention. In the last decade, there have been increasing possibilities for limb-salvage by means of both endovascular

Table 3. Characteristics of population who died at 30-days, 1-year and 5-years.

Variable (*n*)	Total	30-Day death	P^a	1 Year death	P^a	5-Year death	P^a
Level (266)		*n* (%)		*n* (%)		*n* (%)	
Unilateral transtibial	130	32 (25)	.194	55 (42)	.024	101 (78)	.758
Unilateral proximal	70	30 (36)		51 (61)		67 (81)	
Multiple major	66	20 (30)		33 (50)		54 (82)	
Sex (283)							
Men	167	47 (28)	.599	81 (49)	.594	131 (78)	.725
Women	116	36 (31)		60 (52)		93 (80)	
Age[b] (283)	Mean (sd)	Mean (sd)		Mean (sd)		Mean (sd)	
Died	74.1 (11.2)	75.8 (11.4)	.043	75.3 (10.8)	.015	75.0 (10.6)	<.001
Alive	65.7 (12.9)	72.8 (11.1)		72.1 (11.5)		68.8 (12.2)	
Admitted from (262)		*n* (%)		*n* (%)		*n* (%)	
Home	172	41 (24)	.045	76 (44)	.015	128 (74)	.022
Care	90	32 (36)		54 (60)		78 (87)	
Living situation (226)							
Alone	94	24 (28)	.677	44 (47)	.981	75 (80)	.399
Partner	132	37 (26)		62 (47)		99 (75)	
Discharged to (278)							
Home	41	6 (15)	<.001	14 (34)	.010	26 (63)	<.001
Inpatient rehabilitation	37	1 (3)		6 (16)		20 (54)	
Care	144	24 (17)		62 (43)		119 (83)	
Died before discharge	56	50 (89)		—	—		—
Medical history (299)							
Diabetes	143	37 (26)	.197	66 (46)	.212	113 (79)	.956
No	140	46 (33)		75 (54)		111 (79)	
Cardiac disease	104	33 (32)	.499	61 (59)	.024	91 (88)	.008
No	179	50 (28)		80 (45)		133 (74)	
Cerebrovascular disease	42	19 (45)	.014	28 (67)	.018	36 (86)	.257
No	241	64 (27)		113 (47)		188 (78)	
Chronic lung disease	61	17 (28)	.777	31 (51)	.861	52 (85)	.186
No	222	66 (30)		110 (50)		172 (78)	
Renal disease	58	19 (33)	.520	38 (66)	.007	54 (93)	.003
No	225	64 (28)		103 (46)		170 (76)	
Smoking (218)							
Ever	131	43 (33)	.234	65 (50)	.598	102 (78)	.883
Never	87	22 (25)		40 (46)		67 (77)	
Surgical history (299)							
Peripheral vasc. procedure	141	35 (25)	.097	63 (45)	.085	110 (78)	.639
None	142	48 (34)		78 (55)		114 (80)	
≥1 minor amp before major	61	13 (21)	.120	24 (39)	.065	49 (80)	.799
None	222	70 (32)		117 (53)		175 (79)	

Variable (*n*) = number of valid observations for the stated variable; medical and surgical history were yes or not recorded so calculations are based on whole population of 299. Not all variables add up to 299 (population total) due to missing data.

[a] *P* is chi-square with survivors and non-survivors.

[b] *t*-test for age with survivors and non-survivors.

and surgical techniques.[8] It remains unclear what effect these interventions may have on the population who go on to have an amputation. Along this line, the timing of amputation on both mortality and functional outcomes is also of interest. This includes consideration of patients who might benefit from having an earlier amputation or foregoing amputation entirely and choosing a palliative direction for care.[20]

A strength of this study design was the population-based setting, which covered a wide geographic region. Although the sample of people with amputation can be considered of a moderate size, some of the findings from subgroup analyses may have been due to insufficient power to detect differences. Additionally, data were retrieved directly from the medical files, giving insight to information not available in our national database.[21] However, a retrospective study presents inevitable limitations, and also includes the problem of missing data. Specifically, detailed information on the severity of disease and cause of death were not reliably available but would provide important additional information. Only co-morbidities and items that were listed in the medical files

Table 4. Final logistic regression models for variables associated with 30-day, 1-year and 5-year death.

	β (se)	*P*	OR	95% CI of OR
30-day death	−1.20 (0.17)			
Cerebrovascular disease	0.85 (0.35)	.016	2.34	1.17; 4.68
Age (centered at 70 years)	0.02 (0.01)	.070	1.02	1.00; 1.05
1-year death	−0.43 (0.18)			
Renal disease	1.26 (0.35)	<.001	3.53	1.79; 6.96
Age (centered at 70 years)	0.04 (0.01)	.002	1.04	1.02; 1.07
Cerebrovascular disease	0.93 (0.38)	.013	2.55	1.21; 5.34
Minor amputation before major	−0.70 (0.32)	.030	0.50	0.27; 0.93
5-year death	0.79 (0.19)			
Renal disease	1.68 (0.56)	.003	5.35	1.79; 16.0
Age (centered at 70 years)	0.05 (0.01)	<.001	1.05	1.02; 1.08
Admitted from care	0.62 (0.37)	.099	1.90	0.89; 3.85

Final model fit from backward stepwise LR presented.Nagelkerk R square 30-day = .050; 1-year = .143; 5 year = .159.

were recorded and therefore our results may have underestimated the prevalence of some of these. An important example is smoking, which was infrequently recorded despite its known influence on post-amputation healing and the need for revision surgeries.[14] We could not differentiate the cause beyond 'vascular or infection related' although the underlying disease processes of diagnoses differ, particularly with respect to chronic or acute limb ischaemia. Cases that had undergone multiple major amputations were combined to one group for analyses, although the mortality risk may differ for people with bilateral amputation compared to those who had a re-amputation of the one limb. However, in our national database, no differentiation between left- or right-sided amputations can be made and future work will necessitate this 'multiple-major' categorisation. Unfortunately, 10% of cases could not be traced following discharge from the hospital and a further 5% had a confirmed status but no date of death could be traced. Although unknown cases were older than confirmed cases, we expect that our estimates would not be largely affected, if anything we may have slightly underestimated mortality rates.

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CONFLICT OF INTEREST

None.

APPENDIX 1. INCLUDED DIAGNOSES, MODIFIED FROM THE CHARLSON COMORBIDITY INDEX.

ICD-code	Description
Cardiac disease	
410	Acute myocardial infarction
411	Other acute and subacute forms of ischemic heart disease
398	Rheumatic heart disease
402	Hypertensive heart disease
428	Heart failure
	History of Coronary Artery Bypass Graft (CABG)[a]
Lung disease	
491	Chronic obstructive pulmonary disease and allied conditions
492	Emphysema
493	Asthma
Cerebrovascular disease	
430	Subarachnoid hemorrhage
431	Intracerebral hemorrhage
432	Other and unspecified intracranial hemorrhage
433	Occlusion and stenosis of precerebral arteries
435	Transient cerebral ischemia
Renal disease	
403	Hypertensive renal disease
404	Hypertensive heart and renal disease
580	Acute glomerulonephritis
581	Nephrotic syndrome
582	Chronic glomerulonephritis
583	Nephritis and nephropathy, not specified as acute or chronic
584	Acute renal failure
585	Chronic renal failure
586	Renal failure, unspecified
	Receiving dialysis[a]
Diabetes	
250	Diabetes mellitus
	Type I or Type II[a]

ICD = International Statistical Classification of Diseases and Related Health Problems.

[a] No coding, included as additional information to disease/condition.

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