Enabling the elderly person with lower limb amputation through surgery, rehabilitation and long term care

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ENABLING the elderly person with lower limb amputation

THROUGH SURGERY, REHABILITATION AND LONG TERM CARE

Lauren Fortington

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Enabling the elderly person with lower limb amputation through surgery, rehabilitation and long term care

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Chapter 1

Introduction

AMPUTATION AND PROSTHETICS brings to mind remarkable and extreme images: the technology of The Six Million Dollar Man, rebuilt with bionic limbs to save the world; Aron Ralston, depicted in the movie 127 Hours, amputating his own arm to save his life; or the athleticism of Oscar Pistorius, the Blade Runner, competing against able-bodied athletes at the 2012 Olympic Games.* While these impressions are indeed outstanding, the reality of amputation in the Netherlands, and other developed countries, is a vastly different picture.

Most people undergoing lower limb amputation are over 65 years of age.[1,2] Chronic peripheral vascular disease or diabetes has resulted in irreversible ischemia or a life threatening infection in the lower limb. By the time an individual requires surgical intervention for the limb, there is usually serious, and systemic, disease present. It is the complications of this (cardiovascular) disease that creates one of the main difficulties in rehabilitation for the elderly person, rather than the amputation itself. For example, cardiac disease must be carefully assessed to avoid adverse events when beginning rehabilitation.[3,4] Other common conditions include renal disease requiring dialysis, cerebrovascular disease and (vascular) dementia, as well as changes of ageing which lead to functional impairment, such as reduced balance and postural control, and vision and hearing loss.

Specialist needs of the elderly person in rehabilitation are well-known. Differences in care for the elderly person with amputation are also recognised, being the subject of 'best-practice' papers and reviews.[5-7] However, very little empirical research has been carried out to identify, support or challenge what exactly these unique needs are. Despite advances in preventive care, medical treatment and peripheral revascularisation procedures, in some cases, amputation remains the best option for ending ongoing pain, hospitalisation and infection/ischaemia, and ultimately, enabling a person to live. It is the enabling of a person that the research presented in this thesis focusses on. How does an elderly person, who has recently had their limb amputated, rehabilitate and how successful are they?

* Equally striking and extreme are images of devastation and war: the Haitian earthquake in 2010 was the largest ever loss of limbs from a natural disaster; military conflict and lasting consequences of improvised explosive devices and land mines continue to result in lost (quality of) life, effecting individuals, families and their communities. The research in this dissertation is focussed on the situation of the Netherlands and similar developed economies. By no means should this be seen to exclude the importance or need for research and development of prosthetic rehabilitation services for developing nations.

Aims of this thesis

Amputation and prosthetics is a key research line of the Department of Rehabilitation Medicine, University Medical Center Groningen. Several projects have looked at different aspects of amputation rehabilitation. Beginning with "*The elderly amputee: rehabilitation and functional outcome*"[8] and "*Prosthetic prescription in lower limb amputation*"[9] the need for more research of the elderly population was evident. Mobility outcomes were investigated in "*Functional outcome after a lower limb amputation*"[10] finding the timed up-and-go test a reliable measure of prosthetic mobility and the one leg balance test a useful predictor of mobility. A conclusion of this work was that functional outcomes for elderly people with amputation are poor and rehabilitation programmes need further research. In "*Rehabilitation aspects of amputation*"[11] it was also concluded that there is a distinct lack of knowledge concerning the elderly population and the issue of bias from research in this population was raised. The problem of bias was also highlighted in "*Movement and balance control in lower limb amputees.*"[12] The majority of the population included in that research had undergone amputation due to trauma or tumor and this limited the ability to generalise results to the elderly population with a vascular related cause, despite them being the largest population who undergo the procedure.

Building on this previous work, the research presented in this thesis looks at how the elderly person is enabled from the decision to amputate, through their rehabilitation and long term care. Specifically, the following questions were considered:

1. *What is the incidence of lower limb amputation? What characteristics does the population feature?*
2. *What role does the long-term care setting play in the rehabilitation and care of the elderly person after a lower limb amputation?*
3. *What long-term outcomes can the elderly person expect after a lower limb amputation?*

Overview of chapters

Each of the following chapters addresses one or more of the questions above with the aim of understanding how, and how well, the elderly person with lower limb amputation is enabled from the time of amputation, through rehabilitation and into long term care.

A review of the medical records of all people who underwent a lower limb amputation in the Northern Provinces of the Netherlands in 2003 or 2004 forms the basis of the first chapters. The population is defined in *chapter two* where the characteristics and incidence rate are presented. Incidence rates and age groups are compared to an earlier cohort from the same region to see whether the population requiring rehabilitation and long term care has changed. *Chapter three* focusses on the high rates of mortality after amputation, comparing outcomes by different subgroups including age, sex and level of amputation. The influence of comorbidities, including diabetes, is also considered.

After amputation, patients undergo a period of rehabilitation with the aim of regaining mobility and independence. For the elderly population, traditional inpatient rehabilitation programmes can prove too demanding due to the presence of physical and cognitive comorbidity. In *chapter four,* the determinants of discharge location following the amputation are considered with a focus on the population who are discharged to long term care facilities. The provision of rehabilitation in this setting is then described in *chapter five*. Using a mixed methods approach of a facility survey and qualitative interviews, the barriers and potential of rehabilitation programmes for people with a lower limb amputation are described from the clinicians' perspectives.

Mobility is thought to be the key to independence and the basis of a higher quality of life. These outcomes are the focus of *chapters six* and *seven*. Change in health related quality of life over 18 months is analysed in a cohort of people with first lower limb amputations. The influence of age and walking ability on different HRQOL domains are investigated, along with a comparison to population norm values. A systematic review of mobility outcomes focussed on the elderly person with lower limb amputation is presented in *chapter seven* with the aim of providing a prognosis of mobility for this population.

Bias, an issue common across all research of elderly people with amputation, is explored in *chapter eight*. The implications of studying a small population, which is then further biased by the non-inclusion of elderly people, is described using the example of a prospective study of phantom pain in which an obvious selection bias had occurred.

Finally, *chapter nine* summarises the findings, presenting the current evidence and research directions for rehabilitation and long term care of the elderly person with amputation and looks back at the overriding question of *"how well is the elderly person with lower limb amputation enabled?"*

Definitions

All chapters keep the elderly person as a central focus of the research. While there is no clear biological or chronological age at which someone is 'elderly', many countries have accepted a standard use of 65 years. It is around this age that people commonly undergo a transition from working to retirement and with this there are corresponding lifestyle changes.[13] As a general rule, the age of 65 years has been used as elderly through the following chapters. An exception was made in the systematic review presented in chapter seven where the age of 60 years was used to maximise inclusion of relevant publications.

Long term care (LTC) refers to the provision of assistance, both medical and non-medical, to people with chronic illness or disability, over a prolonged time. Although different terminology has developed to suit different health settings and services, a LTC facility can be considered any institution providing rehabilitative, restorative, and/or ongoing skilled nursing care to patients or residents in need of assistance. In the Netherlands, LTC is frequently provided in a form of nursing home (Dutch: *verpleeghuis*), although the services available differ from other countries, in particular the presence of a unique specialist, the Elderly Care Physician.[14]

Lower limb amputation (LLA) is the complete surgical removal of part of the limb in the transverse plane. LLA is often termed 'minor' or 'major' in reference to the extent of limb loss although there are discrepancies on which levels these terms encompass. In this thesis, major LLA is referring to amputations at or proximal to the transtibial level.

References

(1) Moxey PW, Gogalniceanu P, Hinchliffe RJ, et al. Lower extremity amputations-a review of global variability in incidence. Diabet Med 2011;28:1144-1153.

(2) Ephraim PL, Dillingham TR, Sector M, et al. Epidemiology of limb loss and congenital limb deficiency: a review of the literature. Arch Phys Med Rehabil 2003;84:747-761.

(3) Department of Veterans Affairs and The Department of Defense. Clinical practice guideline for rehabilitation of lower limb amputation. 2007. Available from http://www.healthquality.va.gov/amputation/amp_v652.pdf.

(4) Erjavec T, Presern-Strukelj M, Burger H. The diagnostic importance of exercise testing in developing appropriate rehabilitation programmes for patients following transfemoral amputation. Eur J Phys Rehabil Med 2008;44:133-139.

(5) Frieden RA. The geriatric amputee. Phys Med Rehabil Clin N Am 2005;16:179-195.

(6) Andrews KL. Rehabilitation in limb deficiency.3.The geriatric amputee. Arch Phys Med Rehabil 1996;77:S14-7.

(7) Cutson TM, Bongiorni D, Michael JW, Kochersberger G. Early management of elderly dysvascular transtibial amputees. Journal of Prosthetics and Orthotics 1994;6:62.

(8) Rommers GM (2000) The elderly amputee: rehabilitation and functional outcome. Thesis. University of Groningen, the Netherlands.

(9) van der Linde H (2004) Prostetic prescription in lower limb amputation. Development of a clinical guideline in the Netherlands. Thesis. University of Groningen, the Netherlands.

(10) Schoppen T (2002) Functional outcomes after a lower limb amputation. Thesis. University of Groningen, the Netherlands.

(11) Bosmans J (2009) Rehabilitation aspects of amputation. Thesis. University of Groningen, the Netherlands.

(12) Vrieling A (2009) Movement and balance control in lower limb amputees. Thesis. University of Groningen, the Netherlands.

(13) World Health Organisation. [Website.] Definition of an older or elderly person. Accessed September 2012 from http://www.who.int/healthinfo/survey/ageingdefnolder/en/index.html.

(14) Ribbe MW, Ljunggren G, Steel K, et al. Nursing homes in 10 nations: a comparison between countries and settings. Age Ageing 1997;26:3-12.

Chapter 2

Lower limb amputation in Northern Netherlands: unchanged incidence from 1991-1992 to 2003-2004

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Abstract

Study design: Historical cohort study of transtibial amputation, knee disarticulation and transfemoral amputations resulting from vascular disease or infection, with or without diabetes, in 2003-2004, in the three Northern provinces of the Netherlands.

Background: Investigating population changes gives insight into effectiveness and need for prevention and rehabilitation services. Incidence rates of amputation are highly varied, making it difficult to meaningfully compare rates between studies and regions or to compare changes over time.

Objectives: To report the incidence of first transtibial amputation, knee disarticulation or transfemoral amputation in 2003-2004 and the characteristics of this population, and to compare these outcomes to an earlier reported cohort from 1991-1992.

Methods: Population based incidence rates were calculated per 100,000 person-years and compared across the two cohorts.

Results: Incidence of amputation was 8.8 (all-age) and 23.6 (≥45 years) per 100,000 person-years. This was unchanged from the earlier study of 1991-1992. The relative risk of amputation was 12 times greater for people with diabetes than people without.

Conclusions: Investigation is needed into reasons for the unchanged incidence with respect to the provision of services from a range of disciplines including vascular surgery, diabetes care and multidisciplinary foot clinics.

Introduction

Incidence rates of transtibial amputation, knee disarticulation and transfemoral amputation are highly variable. In a recent systematic review it was reported that the rate of major amputation is between 3.6 and 68.4 per 100,000 person-years.[1] Variations in incidence may occur not only because the actual rates differ but also because of differences in research methodology. These differences include: how the population is defined - minimum age cut-off; the level of amputation - (non) inclusion of partial foot amputations; and the method for identifying inclusion of cases - retrospective versus prospective collection from surgical records or national databases.[2] These differences make it difficult to meaningfully compare rates between studies and regions or to compare changes over time.

Studies which have reported long-term changes in incidence of amputation show a general trend towards a decreasing rate.[3-9] Most studies focus on amputations in people with diabetes.[1] For the Netherlands, a reduction from 550 to 363 amputations per 100,000 people with diabetes was reported.[10] Whether this decline is consistent in people without diabetes is unknown.

Investigating population changes can give insight into whether preventative, intervention and rehabilitation services are being provided effectively and to the right population. In order to look at changes in amputation for people with and without diabetes, while avoiding the limitations in comparing rates across studies, we replicated an earlier study in the Northern provinces of the Netherlands.[11] In addition, using the same methodology as that study, we reviewed the medical records directly, gaining deeper insight into individual factors than are available in the national database in which pre-amputation history is not available and side of amputation is not stated.

The aim of this study was to report the incidence of first transtibial amputation, knee disarticulation or transfemoral amputation in 2003-2004 and the characteristics of this population, and to compare these outcomes to an earlier cohort from 1991-1992.[11]

Methods

Data collection

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

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 study period of 1 January 2003 to 31 December 2004.[12]

Data collection was matched to the previous study.[11] The population included from the previous study was modified and data were re-analysed, focussing only on transtibial level and above. Each hospital compiled a list of people who had a transtibial amputation, knee disarticulation or transfemoral amputation in 2003 or 2004. People who had an amputation at any of these levels 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), cases were counted once, and the highest level of amputation is presented. 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 or infection, with or without Diabetes Mellitus. Medical records for all cases were reviewed between August 2010 and June 2011. The years 2003 and 2004 were chosen as major changes in the way that data are recorded in the Netherlands occurred from 2005 onwards. This presented concerns on the reliability of data from later years that would not have enabled the direct comparison to our earlier cohort.

Analysis

The original dataset was obtained from the authors of the 1991-1992 study for analyses.[11] Population data were obtained from the Central Bureau of Statistics (CBS),[12] including the number of people residing in each province, and their age and sex. There are no large ethnic groups in the region requiring separate analyses. The population structure in our region did not change substantially from 1991-1992 to 2003-2004, with 2% more people aged ≥ 45, and 0.7% more people aged ≥ 75 years,[12] so actual (crude) incidence rates are presented for comparison of the two time periods. Age-adjusted rates were checked and showed no differing results, and thus, they are not presented.

The population with diabetes was estimated from prevalence rates obtained from the CBS for the years 2003 and 2004 separately. These prevalence rates are only available for the population aged ≥ 45 years. The majority of the population aged < 45 years is not considered to be at high risk of amputation resulting from vascular disease or diabetes (although admittedly, there are exceptions). Therefore, it was reasonable to exclude these younger cases from the denominator in calculating incidence of those with diabetes. The population without diabetes was calculated by subtracting the estimated population with diabetes from the total population for each year. A total population incidence rate is also presented, for comparison to other studies. Population-based incidence rates were calculated per 100,000 person-years, for the different age and sex categories, with a Poisson distribution assumed for calculation of the 95% confidence interval (CI).

Age was compared using t-tests and categorical variables and incidence rates were compared with $\chi 2$ tests. Statistical significance for all analyses was set at 0.05. Analyses were performed using Microsoft Excel 2003, PASW Statistics 18 and Confidence Interval Analysis version 2.2 (Trevor Bryant, University of Southampton).

Results

Three hundred and forty two people underwent a transtibial amputation, knee disarticulation or transfemoral amputation due to vascular disease, infection or diabetes, in 2003 or 2004. Forty three people were excluded as they had undergone amputation proximal to the ankle before the study period. This resulted in 299 people, the majority of which were men (60%), with a mean age of 74.0 years (table 1).

The population characteristics from 2003-2004 showed no major differences to 1991-1992. A significant difference in age between men and women within each time period remained consistent: in 1991-1992 men were 4 years younger than women (73.1 years compared to 77.2 years, p=0.004) and in 2003-2004 men were 5 years younger than women (77.0 years compared to 72.0, p<0.001).

	1991-1992 n=285	2003-2004 n=299*
Level†		
Transtibial	48 (137)	49 (146)
Knee disarticulation	10 (27)	9 (27)
Transfemoral	36 (103)	34 (100)
Bilateral	6 (18)	9 (25)
Sex		
Men	59 (168)	60 (178)
Women	41 (117)	40 (121)
Age		
All	74.8 (11.8)	74.0 (11.2)
Men‡	73.1 (11.5)	72.0 (10.6)
Women‡	77.2 (11.8)	77.0 (11.5)
Diabetes	- -	50 (149)

*not all variables sum to total due to missing data. † % (n) presented for all variables except for age which is mean (sd); ‡Comparison of age by gender: men compared to women in 1991-1992 p=0.004; men compared to women in 2003-2004 p<0.001.

Table 1: Characteristics of people with first major lower limb amputation in 1991-1992 and 2003-2004.

The 2003-2004 incidence for the all-age population was 8.8 per 100,000 person-years and for the population aged ≥45 it was 23.6 per 100,000 person-years (table 2). Incidence was higher in the older age groups. The incidence for the total population, as well as by sex and by age, showed no significant changes from 1991-1992 to 2003-2004 (figure 1). The oldest group (≥75 years) had a reduced incidence of almost 12 per 100,000 person-years (from 80.4 to 68.8, p=0.150).

Diabetes was diagnosed in 50% of people with amputation in the period 2003-2004. The ratio of transfemoral and knee disarticulations to transtibial amputations in people without diabetes is 2:1, whereas the ratio in people with diabetes is 1:1 (p=0.017) (table 3). Women with diabetes were 3.1 years younger than women without diabetes (p=0.095). Men were significantly younger than women both in people with diabetes (71.4 years compared to 76.4 years, p=0.003) and without diabetes (73.0 years compared to 79.5 years, p<0.001).

For people aged ≥45 years with diabetes, the incidence of amputation was 150.9 per 100,000 person-years, a relative risk 12.3 (95% CI: 9.7;15.4) times higher than people without diabctes (table 4).

Table 2: Comparison of incidence rates for first major lower limb amputation in 1991-1992 and 2003-2004.

	1991-1992 Incidence (95% CI)†	2003-2004 Incidence (95% CI)†	p*
All age	8.9 (7.9 ; 9.9)	8.8 (7.8 ; 9.8)	0.467
≥ 45 years	24.8 (21.9 ; 27.8)	23.6 (20.9 ; 26.4)	0.552
≥ 65 years	52.2 (45.8 ; 59.3)	47.4 (41.6 ; 53.8)	0.292
≥ 75 years	80.4 (68.3 ; 94.0)	68.8 (58.5 ; 80.4)	0.150
Men ≥ 45	32.2 (27.5 ; 37.4)	29.9 (26.3 ; 33.7)	0.530
Men ≥ 65	72.0 (60.3 ; 85.3)	63.5 (53.2 ; 75.2)	0.303
Men ≥ 75	106.8 (84.3 ; 133.5)	88.6 (69.6 ; 111.2)	0.218
Women ≥ 45	19.5 (16.1 ; 23.3)	17.9 (15.2 ; 21.0)	0.603
Women ≥ 65	38.5 (31.4 ; 46.7)	35.7 (29.2 ; 43.2)	0.591
Women ≥ 75	65.1 (51.7 ; 80.9)	57.6 (46.0 ; 71.2)	0.432

*p is $\chi 2$ comparison of 2003-04 to 1992-92 for each sex and age group; † incidence per 100,000 people-years with Poisson rate distribution for calculation of 95% CI

Figure 1: Incidence of major lower limb amputation by age for 1991-1992 and 2003-2004

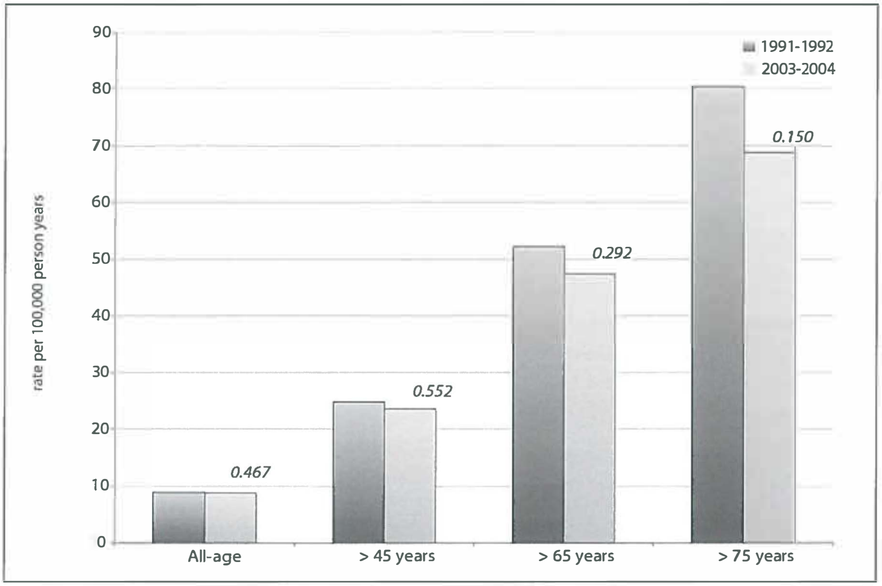

Figure shows change in incidence from 1991-1992 to 2003-2004 by age groups. P values are presented from $\chi 2$ comparison of 2003-2004 to 1992-1992 shown in table 2.

Table 3: Characteristics of people with lower limb amputation aged ≥45 years with and without diabetes.

	Diabetes	No diabetes	p
n*	50 (149)	50 (147)	
Level†			
Transtibial	55 (82)	42 (61)	0.017
Knee disart.	8 (12)	10 (15)	
Transfemoral	26 (39)	42 (62)	
Bilateral	10 (15)	6 (9)	
Sex			
Men	55 (82)	65 (95)	0.059
Women	45 (67)	35 (52)	
Age			
All	73.7 (10.3)	75.3 (10.9)	0.204
Men‡	71.4 (10.4)	73.0 (10.4)	0.361
Women‡	76.4 (9.5)	79.5 (10.5)	0.095

*% (n) presented for all variables except for age which is mean (sd)
†comparison of age by gender: men versus women with diabetes p=0.003; men versus women without diabetes p<0.001.for age which is mean (sd);
‡Comparison of age by gender: men compared to women in 1991-1992 p=0.004; men compared to women in 2003-2004 p<0.001.

Table 4: Incidence of people with first lower limb amputation aged ≥45 years, with and without diabetes.

Incidence‡	Diabetes		No diabetes		RR (95% CI)	
All						
≥ 45 years	150.9	(127.6 ; 177.2)	12.3	(10.4 ; 14.5)	12.3	(9.7 ; 15.4)
≥ 65 years	196.5	(162.4 ; 235.8)	27.6	(23.0 ; 33.0)	7.1	(5.5 ; 9.1)
≥ 75 years	287.1	(227.7 ; 357.3)	38.4	(30.3 ; 47.9)	7.5	(5.5 ; 10.2)
45 - 64 years	83.1	(57.2 ; 116.7)	3.2	(2.1 ; 4.8)	26.0	(15.1 ; 43.3)
65 - 74 years	114.6	(80.2 ; 158.6)	18.2	(13.2 ; 24.4)	6.3	(4.0 ; 9.8)
Men						
≥ 45 years	170.9	(135.9 ; 212.1)	17.1	(13.8 ; 20.9)	10.0	(7.4 ; 13.4)
≥ 65 years	242.9	(184.9 ; 313.3)	35.8	(28.2 ; 44.8)	6.8	(4.8 ; 9.5)
≥ 75 years	357.2	(250.2 ; 494.5)	51.7	(36.6 ; 71.0)	6.9	(4.4 ; 10.9)
45 - 64 years	97.1	(61.5 ; 145.6)	4.8	(2.9 ; 7.5)	20.1	(10.9 ; 36.9)
65 - 74 years	154.8	(98.1 ; 232.2)	33.3	(23.5 ; 45.7)	4.6	(2.8 ; 7.8)
Women						
≥ 45 years	130.5	(101.2 ; 165.8)	8.2	(6.1 ; 10.7)	16.0	(11.1 ; 23.0)
≥ 65 years	162.9	(123.4 ; 211.1)	16.1	(11.8 ; 21.4)	10.1	(6.9 ; 14.8)
≥ 75 years	247.4	(179.7 ; 332.1)	31.6	(22.7 ; 42.9)	7.8	(5.1 ; 11.9)
45 - 64 years	61.2	(29.4 ; 112.6)	1.3	(0.4 ; 3.0)	47.3	(16.2 ; 138.3)
65 - 74 years	78.5	(41.8 ; 134.2)	4.7	(1.7 ; 10.3)	16.7	(6.3 ; 43.8)

‡ incidence per 100,000 people-years; RR = Relative Risk

Discussion

Taken as a single time point, the amputation incidence of 23.6 per 100,000 person-years aged ≥45 years can be considered as moderate, falling in the middle of other population studies that have been presented in two systematic reviews.[1,13] Although the rate has declined slightly over time, the lack of any statistically significant reduction in the incidence of amputations in our population is of concern and supports a need to investigate the adequacy of multidisciplinary prevention programmes and interventions to save limbs. Whilst there are others who report no change in amputation rates,[14,15] most research supports an overall trend towards a significantly declining incidence.[3-9]

Reasons for unchanged amputation rates must be carefully considered in order to build effective care strategies. It was expected that there would be a shift towards an older age for people undergoing their first amputation as more interventions aim to prevent or delay the procedure. Although this has been reported in other populations,[14] there was no change to the mean age at the time of first amputation in our region. The oldest group of patients appeared to have a reduced incidence yet the overall rate remained unchanged. A possible explanation is the surgeon and patient chose not to pursue amputation as a treatment in the older population or people may have already undergone amputation at a younger age. A decision on when to amputate is made through the combined efforts of medical staff and the patients own situation and wishes. Exploration of the individual motivations behind these decisions could offer insight into some of the differences in incidence rates over time and across different regions.

In Europe throughout the 1990's, the frequency and quality of multidisciplinary foot care continued to increase[16] and there was a concerted effort made to reduce diabetes related amputations through the St Vincent's Declaration. A study conducted in a separate region of the Netherlands, showed that referral of patients at risk to multidisciplinary foot clinics, at least up until the year 2000, was very low.[17] These results, together with our findings of no change to incidence in the time period, support a need to investigate the provision of vascular services and foot clinics in more depth.

Diabetes was diagnosed in 50% of the 2003-2004 cohort. The RR of amputation was 12 times greater in people with a diagnosis of diabetes than the risk of amputation in people without diabetes. This risk is higher than reports from other Western economies including Germany, the United States, Finland and Sweden where RR is reported as approximately 7-10 times greater for people with diabetes.[6,18,19] Those studies had similar populations to ours based on the inclusion criteria. Therefore, it appears that for people with diabetes in the Northern Netherlands, the RR of amputation proximal to the ankle might be slightly higher than in comparable Western regions. Regrettably, there was no data concerning diabetes available from the 1991-1992 study and so the impact of this important diagnosis on our unchanged incidence rate cannot be determined. A nationwide study in the Netherlands demonstrated a decreased rate for diabetes-related amputation from 1991–2000.[10] If this reduction is consistent for our region specifically, then we need to look at why the changes are not being reflected in the overall incidence rate, specifically for amputations due to peripheral arterial disease.

The current study was limited to the Northern provinces of the Netherlands, enabling direct comparison to the earlier cohort. However, there are known to be considerable regional variations in incidence rates of LLA.[1,20,21] In addition, in order to match the methodology of the previous study, data presented is now somewhat outdated from 2003-2004, before a major change to the recording of this data was implemented. Both of these points – the region and timing of data collection - should be taken into account in generalizing the results. Retrospective identification of LLA poses the inevitable chance of having missed cases. The incidence rates should therefore be considered as potentially underestimated, although any additional cases would not have an effect on our main outcome of no change over time. Our findings in relation to diabetes should also be considered as an underestimation as data were recorded from medical files, some of which had limited or missing information, particularly to distinguish between diabetes type 1 and diabetes type 2. All physicians are encouraged to carefully document this diagnosis to enable differentiation between the two in future work.

Our results were suggestive that a small decrease in incidence had occurred but without statistical confirmation, which is possibly due to the small amputation population size. A repeat study with a recent cohort should be performed, with recognition that the data collection procedures in the Netherlands have changed. This study would aim to evaluate if the lack of change in incidence was due to chance, a slower implementation of changes in care and prevention, or if indeed we need to seriously consider the services being provided to people with vascular disease and diabetic foot problems.

Conclusions

Our findings of an unchanged incidence need to be investigated further with respect to the provision of services from a range of disciplines including vascular surgery, diabetes care and multidisciplinary foot clinics. The risk of LLA in people with diabetes in 2003-2004 was high but should be confirmed through a follow up study. Finding effective methods for reducing the rate of amputation is imperative with diabetes and general population ageing presenting an increased number of people at risk.

References

(1) Moxey PW, Gogalniceanu P, Hinchliffe RJ, et al. Lower extremity amputations--a review of global variability in incidence. Diabet Med 2011;28:1144-1153.

(2) van Houtum WH. Amputations and ulceration; pitfalls in assessing incidence. Diabetes Metab Res Rev 2008;24:S14-518.

(3) Witso E, Lium A, Lydersen S. Lower limb amputations in Trondheim, Norway. Acta Orthop 2010;81:737-744.

(4) Vamos EP. Bottle A, Majeed A, et al. Trends in lower extremity amputations in people with and without diabetes in England, 1996-2005. Diabetes Res Clin Pract 2010;87:275-282.

(5) Moxey PW. Hofman D, Hinchliffe RJ, et al. Epidemiological study of lower limb amputation in England between 2003 and 2008. Br J Surg 2010;97:1348-1353.

(6) Ikonen TS, Sund R, Venermo M, et al. Fewer major amputations among individuals with diabetes in Finland in 1997-2007: a population-based study. Diabetes Care 2010;33:2598-2603.

(7) McCaslin JE, Hafez HM, Stansby G. Lower-limb revascularization and major amputation rates in England. Br J Surg 2007;94:835-839.

(8) Rayman G, Krishnan STM, Baker NR, et al. Are we underestimating diabetes-related lower-extremity amputation rates? Results and benefits of the first prospective study. Diabetes Care 2004;27:1892-1896.

(9) Holstein P, Ellitsgaard N, Olsen BB, et al. Decreasing incidence of major amputations in people with diabetes. Diabetologia 2000;43:844-847.

(10) van Houtum WH, Rauwerda JA, Ruwaard D, et al. Reduction in Diabetes-Related Lower-Extremity Amputations in the Netherlands: 1991-2000. Diabetes Care 2004;27:1042-1046.

(11) Rommers GM, Vos LD, Groothoff JW, et al. Epidemiology of lower limb amputees in the north of The Netherlands: aetiology, discharge destination and prosthetic use. Prosthet Orthot Int 1997;21:92-99.

(12) Statistics Netherlands. Available at: http://www.cbs.nl. Accessed March 12, 2012.

(13) Ephraim PL, Dillingham TR, Sector M, et al. Epidemiology of limb loss and congenital limb deficiency: a review of the literature. Arch Phys Med Rehabil 2003;84:747-761.

(14) Carmona GA, Hoffmeyer P, Herrmann FR, et al. Major lower limb amputations in the elderly observed over ten years: The role of diabetes and peripheral arterial disease. Diabetes Metab 2005;31:449-454.

(15) Trautner C, Haastert B, Spraul M, et al. Unchanged incidence of lower-limb amputations in a German City, 1990-1998. Diabetes Care 2001;24:855-859.

(16) Apelqvist J, Larsson J. What is the most effective way to reduce incidence of amputation in the diabetic foot? Diabetes Metab Res Rev 2000;16:575-583.

(17) Muller IS, de Grauw WJ, van Gerwen WH, et al. Foot ulceration and lower limb amputation in type 2 diabetic patients in Dutch primary health care. Diabetes Care 2002;25:570-574.

(18) Icks A, Haastert B, Trautner C, et al. Incidence of lower-limb amputations in the diabetic compared to the non-diabetic population. findings from nationwide insurance data, Germany, 2005-2007. Exp Clin Endocrinol Diabetes 2009 Oct;117(9):500-504.

(19) Johannesson A, Larsson GU, Ramstrand N, et al. Incidence of lower-limb amputation in the diabetic and nondiabetic general population: a 10-year population-based cohort study of initial unilateral and contralateral amputations and reamputations. Diabetes Care 2009 Feb;32(2):275-280.

(20) Holman N, Young RJ, Jeffcoate WJ. Variation in the recorded incidence of amputation of the lower limb in England. Diabetologia 2012 Mar 8;55(7):1919-1925.

(21) van Houtum WH, Lavery LA. Regional variation in the incidence of diabetes-related amputations in The Netherlands. Diabetes Res Clin Pract 1996 Mar;31(1-3):125-132.

Appendix A

Supplementary table 1:
Population data for calculation of incidence rates.

	1991-1992			2003-2004		
	n	*person-years*	*crude rate*	*n*	*person-years*	*crude rate*
All age	285	3200788	8.9	299	3392903	8.8
≥ 45 years	278	1123095	24.8	296	1256654	23.6
≥ 65 years	235	450011	52.2	239	504135	47.4
≥ 75 years	158	196529	80.4	159	231060	68.8
Men ≥ 45	168	522063	32.2	178	591751	29.9
Men ≥ 65	133	184730	72.0	135	212644	63.5
Men ≥ 75	77	72083	106.8	74	83538	88.6
Women ≥ 45	117	601032	19.5	121	664903	17.9
Women ≥ 65	102	265281	38.5	104	291491	35.7
Women ≥ 75	81	124446	65.1	85	147522	57.6

Chapter 3

Short and long term mortality rates after lower limb amputation

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Abstract

Objective: to determine mortality rates after a first lower limb amputation in the Northern Netherlands and to explore the rates for different subpopulations.

Design: historical cohort study.

Methods: medical records were reviewed for people who underwent a first amputation, at or proximal to transtibial level, in 2003 or 2004, in one of 14 hospitals from an area of 1.7 million people.

Results: 299 people were included. 269 cases (90%) had a confirmed status (alive or dead) at follow-up, although the date of death was missing in 16 (5%). Median time to death was 20.3 months (95% CI: 13.1;27.5). 30-day mortality was 22%, 1-year mortality was 44% and 5-year mortality was 77%. Significant differences in median survival were seen for age groups; people aged 85+ surviving 8.8 months, younger groups were all over 20 months (p=0.028). Significant differences were also seen for age-level combined (p=0.041); of particular note, people with unilateral transfemoral amputation aged 75-84 years had significantly longer survival times (22.2 months) than younger (3.4 months) and older (2.1 months) groups. No differences in survival for people with/without diabetes were seen.

Conclusions: There was a high rate of 30-day mortality. Variation in median survival time was most apparent by age groups.

Introduction

Mortality rates after lower limb amputation (LLA) are notoriously high. This is attributed to the population consisting of old and medically frail people at the time of undergoing a major surgical procedure. Older age, proximal amputation levels and comorbidity, 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] Focussing 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 LLA 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-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 comorbidities, medical and surgical history, and admission and discharge settings.

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 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 the 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)); the 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 (ICD9 codes stated). The most frequent diagnoses were presented under combined groups of: Cardiac disease - myocardiac infarct (410, 411), congestive heart failure (398, 402, 428), or history of coronary artery bypass graft; Cerebrovascular disease (430-433, 435); Lung disease (491 – 493); Renal disease (403, 404, 580-586); and Diabetes Mellitus (250).

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 hazard ratios 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.

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

Variable (n)	Included		Diabetes		No diabetes		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 vasc. procedure	150	(50)	68	(45)	82	(55)	.093
≥ 1 minor amp pre-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 fo r the stated variable; medical and surgical history were yes or not recorded so calculations are based on whole population of 299. a p is $\chi 2$ of people with diabetes compared to people without diabetes; bcomparison 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.

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 (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 similar in the two groups (45% in diabetes compared to 55% in no diabetes, p=0.093).

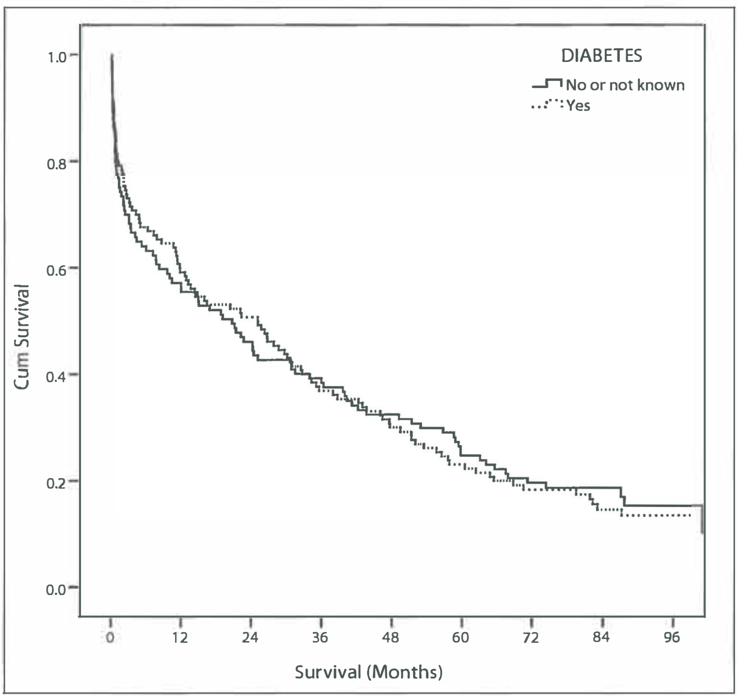

Figure 1: Kaplan–Meier survival curve split by diagnosis of diabetes

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.

Table 2: Cumulative % of people who died at key time points, and median survival estimates (months).

			% dead			Survival (months)			
	N[a]	(event)	30-day	1-year	5-year	Median	se	95% CI	P[b]
All	299	216	22	44	77	20.3	3.7	(13.1 ; 27.5)	
Level									
Unilateral Transtibial	130	100	17	35	75	27.8	3.0	(22.0 ; 33.6)	.495
Unilateral Transfemoral	83	61	27	54	77	10.6	4.8	(1.2 ; 19.9)	
Multiple Major	66	53	23	45	80	16.3	6.8	(2.9 ; 29.7)	
Sex									
Men	167	130	22	43	76	21.1	4.1	(13.0 ; 29.1)	.885
Women	116	85	21	42	76	25.0	7.3	(10.8 ; 39.2)	
Age									
< 65 years	59	38	19	38	65	26.7	9.9	(7.3 ; 46.0)	.028
65-74 years	77	61	24	45	74	21.3	7.1	(7.5 ; 35.2)	
75-84 years	103	82	15	38	81	25.0	4.1	(17.0 ; 33.1)	
85+ years	44	34	35	56	85	8.8	6.6	(0.0 ; 21.6)	
Diabetes									
No	140	102	22	45	75	20.7	5.0	(10.9 ; 30.5)	.969
Yes	143	113	20	41	77	25.0	5.8	(13.6 ; 36.4)	
Age and Level									
Unilateral Transtibial									
< 65 years	22	14	14	24	60	30.8	10.1	(11.0 ; 50.5)	.041
65-74 years	32	22	16	30	71	41.2	11.2	(19.2 ; 63.2)	
75-84 years	51	46	12	36	82	26.6	2.7	(21.4 ; 31.9)	
85+ years	25	18	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	18	14	35	70	22.2	21.7	(0.0 ; 64.7)	
85+ years	13	10	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	16	27	44	72	30.8	27.3	(0.0 ; 84.4)	
75-84 years	21	18	24	47	94	12.8	10.5	(0.0 ; 33.4)	
85+ years	6	6	17	67	100	8.6	5.8	(0.0 ; 19.9)	

a N is total number in category, (event) is number with confirmed death. Not all categories add to 281 due to missing data; b P is log rank between categories for median survival time

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

Variable (n)	total	30 days	p[a]	1 year	p[a]	5 year	p[a]
Level (266)		n %		n %		n %	
Unilateral TT	130	32 (25)	.194	55 (42)	.024	101 (78)	.758
Unilateral KD/TF	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 rehab	37	1 (3)		6 (16)		20 (54)	
Care	144	24 (17)		62 (43)		119 (83)	
Died before	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)	
Cerebrovasc. disease	42	19 (45)	.014	28 (67)	.018	36 (86)	.257
No	241	64 (27)		113 (47)		188 (78)	
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. proc	141	35 (25)	.097	63 (45)	.085	110 (78)	.639
None	142	48 (34)		78 (55)		114 (80)	
≥ 1 minor amp.	61	13 (21)	.120	24 (39)	.065	49 (80)	.799

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 $\chi 2$ with survivors and non-survivors; b t-test for age with survivors and non-survivors; not all variables add to 299 (population total) due to missing data.

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

	ß (se)	P	OR	95% CI
30-day death	-1.20 (0.17)			
Cerebrovascular disease	0.85 (0.35)	.016	2.34	1.17 ; 4.68
Age (centred 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 (centred 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 (pre-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 (centred 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. OR = odds ratio
Nagelkerke R square 30-day=.050; 1-year=.143; 5 year =.159

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), with no significant differences in sex (P=.095) or level of amputation (P=.088). 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 (figure 1).

Twenty-two percent of the population died within 30-days. Factor 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 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 programmes 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 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 comorbidities and items that were listed in the medical files 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. As reported in results, unknown cases were older than confirmed cases with no significant differences in sex or level of amputation seen. Mortality rates were presented as a proportion of known cases, and we expect that these estimates would not be largely affected by the unknown cases, if anything we may have underestimated mortality rates.

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References

(1) Kristensen MT, Holm G, Kirketerp-Moller K, et al. Very low survival rates after non-traumatic lower limb amputation in a consecutive series: what to do? Interact Cardiovasc Thorac Surg 2012; 14 (5): 543-547.

(2) Icks A, Scheer M, Morbach S, et al. Time-dependent impact of diabetes on mortality in patients after major lower extremity amputation: survival in a population-based 5-year cohort in Germany. Diabetes Care 2011;34(6):1350-1354.

(3) Subramaniam B, Pomposelli F, Talmor D, et al. Perioperative and long-term morbidity and mortality after above-knee and below-knee amputations in diabetics and nondiabetics. Anesth Analg 2005;100(5):1241-1247

(4) Mayfield JA, Reiber GE, Maynard C, et al. Survival following lower-limb amputation in a veteran population. J Rehabil Res Dev 2001;38(3):341-345.

(5) Lavery LA, Hunt NA, Ndip A, et al. Impact of chronic kidney disease on survival after amputation in individuals with diabetes. Diabetes Care 2010;33(11):2365-2369.

(6) Remes L, Isoaho R, Vahlberg T, et al. Major lower extremity amputation in elderly patients with peripheral arterial disease: Incidence and survival rates. Aging Clin Exp Res 2008;20(5):385-393.

(7) Eskelinen E, Lepantalo M, Hietala EM, et al. Lower limb amputations in Southern Finland in 2000 and trends up to 2001. Eur J Vasc Endovasc Surg 2004;27(2):193-200.

(8) Norgren L, Hiatt WR, Dormandy JA, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg. 2007; 33 Suppl 1:S1-75.

(9) Statistics Netherlands. Available at: http://www.cbs.nl. Accessed March 12, 2012.

(10) Fortington LV, Rommers GM, Postema K, et al. Lower limb amputation in Northern Netherlands: Unchanged incidence from 1991-1992 to 2003-2004. Prosthet Orthot Int 2013. Epub ahead of print, doi: 10.1177/0309364612469385

(11) Davenport DL, Ritchie JD, Xenos ES. Incidence and risk factors for 30-day postdischarge mortality in patients with vascular disease undergoing major lower extremity amputation. Ann Vasc Surg 2012;26(2):219-224.

(12) Vamos EP.. Trends in lower extremity amputations in people with and without diabetes in England, 1996-2005. Diabetes Res Clin Pract 2010;87:275-282.

(13) Aulivola B. Major lower extremity amputation: outcome of a modern series. Arch Surg 2004;139:395-399.

(14) Cruz CP, Eidt JF, Capps C, et al. Major lower extremity amputations at a Veterans Affairs hospital. Am J Surg 2003;186(5):449-454.

(15) Moxey PW, Hofman D, Hinchliffe RJ, et al. Delay influences outcome after lower limb major amputation. Eur J Vasc Endovasc Surg. 2012 Nov;44(5):485-90.

(16) Schofield CJ, Libby G, Brennan GM,et al. Mortality and hospitalization in patients after amputation: a comparison between patients with and without diabetes. Diabetes Care 2006;29(10):2252-2256.

(17) Moxey PW, Gogalniceanu P, Hinchliffe RJ, et al. Lower extremity amputations--a review of global variability in incidence. Diabet Med 2011;28(10):1144-1153.

(18) Papazafiropoulou A, Tentolouris N, Soldatos RP, et al. Mortality in diabetic and nondiabetic patients after amputations performed from 1996 to 2005 in a tertiary hospital population: a 3-year follow-up study. J Diabetes Complications 2009;23(1):7-11.

(19) Abola MT, Bhatt DL, Duval S, et al. Fate of individuals with ischemic amputations in the REACH Registry: three-year cardiovascular and limb-related outcomes. Atherosclerosis. 2012;221:527-35.

(20) Game F. Choosing life or limb. Improving survival in the multi-complex diabetic foot patient. Diabetes Metab Res Rev 2012;28 Suppl 1:97-100.

(21) Rommers GM, Vos LD, Groothoff JW, et al. Epidemiology of lower limb amputees in the North of The Netherlands: aetiology, discharge destination and prosthetic use. Prosthet Orthot Int 1997;21:92-99.

Chapter 4

Determinants of discharge to long term care after lower limb amputation

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Introduction

Rehabilitation after lower limb amputation (LLA) in long term care (LTC) has many positive outcomes, with up to 57% of the population successfully discharged within 12 months.[1] After LLA, it is important that rehabilitation begins without delay, particularly for older adults, who experience a rapid decline in physical conditioning.[2] Knowing who will be discharged to a LTC setting enables planning to begin immediately, even before surgery. Research from the United States and Finland has shown that being older, being female, living alone and having transfemoral amputation increases the chance of discharge to LTC.[3-5] The aim of this study was to investigate determinants of discharge to LTC after LLA in a Dutch setting.

Methods

Medical records of all people who underwent a first transtibial (TTA), knee disarticulation (KD) or transfemoral amputation (TFA) due to vascular disease, infection or diabetes mellitus between 1 January 2003 and 31 December 2004, were reviewed as part of a study on incidence of amputation. The primary dependent variable was discharge destination, recorded as LTC or other (home, inpatient rehabilitation, supported residential home, other hospital). Independent variables included were age, sex, level (unilateral TTA, unilateral proximal (KD or TFA), or multiple major amputations), living alone (includes single, widowed, divorced) or with a partner, living situation before amputation (care or home) and comorbidities (yes, no: diabetes mellitus, cardiac (myocardial infarct, cerebrovascular disease, or coronary artery bypass graft), lung disease, or renal disease). Variables with $p<0.1$ in bivariate analyses, were included in a logistic regression analysis (backward stepwise logistic regression).

Results

Two hundred ninety-nine people with a first amputation were initially included. Fifty-six (19%) died before discharge from hospital and were excluded from further analyses. The mean age of the population discharged (n=243) was 74.0± 11.4 years, 146 (60%) were men, 114 (47%) underwent unilateral TTA and 70 (29%) unilateral TFA or KD. 5 cases had missing data for discharge location. Bivariate analyses according to discharge location showed that sex, age and living with a partner were all significantly associated with discharge location (table 1). Logistic regression analyses showed that older people were more likely to be discharged to LTC (β (standard error) 0.053 (0.014); odds ratio = 1.05, 95% confidence interval = 1.03 –1.08) $P < .001$; constant (standard error) -0.078 (0.157)).

Table 1: Determinants of discharge to long term care after lower limb amputation

	Long term care		Other		p
% (n)*	55	(130)	45	(108)	
Sex					
Women	25	(60)	15	(35)	0.031
Men	29	(70)	31	(73)	
Age					
Mean (sd)	76.5	(9.4)	70.8	(12.6)	<0.001
Before amputation					
Lived with partner	25	(48)	30	(58)	0.038
Lived alone	27	(53)	18	(35)	
Level of amputation					
Unilateral TT	24	(57)	23	(54)	0.139
Unilateral TF or KD	19	(44)	10	(24)	
Multiple major	12	(27)	12	(28)	
Admitted from					
Home	31	(70)	31	(71)	0.243
Care	22	(49)	16	(36)	
Comorbidities					
Diabetes	31	(73)	22	(52)	0.218
Cardiac disease	23	(55)	15	(35)	0.117
Lung disease	14	(34)	10	(23)	0.382
Kidney disease	11	(27)	7	(17)	0.320

Characteristics were compared by discharge location (LTC or other) using $\chi 2$ for categorical variables and t-test for age (normal distribution). Variables with p < 0.1 were included in a logistic regression model (stepwise backward LR) with discharge location as the dependent variable. Statistical significance was set at $p<0.05$ and analyses were performed in SPSS Statistics 20. TT = transtibial, KD = knee disarticulation, TF = transfemoral. *not all categories sum to their respective totals due to missing data.

Discussion

Older age was the sole factor associated with discharge to LTC. Rehabilitation after LLA can take place in a number of settings, but most previous research has focussed on inpatient rehabilitation programmes. This setting yields the best outcomes in terms of longer survival, a greater chance of receiving a prosthesis, greater mobility, being more likely to return to independent living, greater medical stability, fewer subsequent amputations and better quality of life.[4,6-8] However, inpatient rehabilitation programmes operate at an intensive level of training, which a large proportion of the LLA population is unable to manage because of older age and comorbidity. Research of rehabilitation in LTC is gaining increasing interest,[1] because it may offer a suitable option for the older LLA population.

It is likely that differences in the model of care provided accounted for the different findings in this study from those in the literature. Studies on discharge destination are mainly limited to U.S. settings, where a much smaller percentage of people were discharged to LTC (18.5–21%,[5,9] vs 55% in the Netherlands). No association between amputation level and discharge to LTC[4,5] was found in the current study. In addition to differences in care models, inclusion of people with partial foot amputations in those studies might have contributed to the importance of amputation level on discharge, partial foot amputation being a less-aggressive procedure performed more frequently in a younger and somewhat healthier population.

This study covered a large regional population of all people undergoing LLA over a 2-year period, and findings can be generalised to the Dutch setting, but given that the design was a retrospective cross-sectional review, prospective, longitudinal studies should be undertaken to confirm the results. In the Netherlands, older adults can expect to be discharged to LTC after amputation.

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References

(1) Buijck BI, van Eijk MS, Zuidema SU, et al. Determinants of quality of life in older adults after lower limb amputation and rehabilitation in skilled nursing facilities. J Am Geriatr Soc 2012;60:796-798.

(2) Cutson TM, Bongiorni D, Michael JW, et al. Early management of elderly dysvascular below-knee amputees. JPO 1994;6:62-66.

(3) Remes L, Isoaho R, Vahlberg T, et al. Predictors for institutionalization and prosthetic ambulation after major lower extremity amputation during an eight-year follow-up. Aging Clin Exp Res 2009;21:129-135.

(4) Dillingham TR, Pezzin LE. Rehabilitation setting and associated mortality and medical stability among persons with amputations. Arch Phys Med Rehabil 2008;89:1038-1045.

(5) Lavery LA, Van Houtum WH, Armstrong DG. Institutionalization following diabetes-related lower extremity amputation. Am J Med 1997;103:383-388.

(6) Czerniecki JM, Turner AP, Williams RM, et al. The effect of rehabilitation in a comprehensive inpatient rehabilitation unit on mobility outcome after dysvascular lower extremity amputation. Arch Phys Med Rehabil 2012;93:1384-1391.

(7) Kurichi JE, Small DS, Bates BE, et al. Possible incremental benefits of specialized rehabilitation bed units among veterans after lower extremity amputation. Med Care 2009;47:457-465.

(8) Stineman MG, Kwong PL, Kurichi JE, et al. The effectiveness of inpatient rehabilitation in the acute postoperative phase of care after transtibial or transfemoral amputation: study of an integrated health care delivery system. Arch Phys Med Rehabil 2008 10;89:1863-1872.

(9) Dillingham TR, Yacub JN, Pezzin LE. Determinants of postacute care discharge destination after dysvascular lower limb amputation. PMR 2011;3:336-344.

Chapter 5

Rehabilitation in long term care for the elderly person with lower limb amputation; a mixed methods, descriptive study

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Submitted

Abstract

Objectives: To describe the current set up, barriers and potential for providing rehabilitation to people with lower limb amputation in a long term care setting.

Design: Survey and interviews

Subjects/Participants: Elderly care physicians, physiotherapists

Methods: In 2011, clinicians from 34 long term care facilities participated in a semi-structured interview covering rehabilitation and daily care, personal skills and training, team work and communication, discharge processes.

Results: Each facility sees only a small proportion of people with amputation (maximum of 3.6% of all admissions). This limited number of patients appeared the main barrier in providing care, as it is difficult for clinicians to maintain knowledge and resources are spread widely. Two main areas of improvement were suggested by participants: [a] use of guidelines in care and [b] collaboration with specialised team members.

Conclusion: The spread of patients across many centres makes it difficult for professionals working in long term care to obtain skills and knowledge for care of people with amputation. A designated facility for amputation rehabilitation is presented as a solution but also smaller clinical changes are suggested, including improvements in communication and training.

Introduction

After a lower limb amputation (LLA), many people enter a rehabilitation programme with the aim of learning how to manage changes in physical, psychological and social functioning. Rehabilitation can take place in a number of settings. People who are enrolled for specialised inpatient rehabilitation programmes tend to have better outcomes than those who receive rehabilitation in other settings such as home or nursing care. These outcomes include longer survival, a higher chance of receiving a prosthesis, improved mobility, being more likely to return to independent living, greater medical stability, a lower number of subsequent amputations or a higher quality of life.[1-5] Inpatient rehabilitation programmes are generally targeted toward a population who are able to manage an intensive level of training. However, LLA frequently has an underlying cause of peripheral vascular disease or diabetes mellitus with most people over the age of 65 years.[6,7] Additional comorbidities and changes from ageing often result in cognitive and cardiovascular problems that impact a person's ability to meet the demands required for participation in high intensity rehabilitation. A lower intensity programme, undertaken in a long term care (LTC) setting, might offer a reasonable alternative from traditional inpatient programmes for elderly people with LLA.

Admission to a LTC facility after LLA is common in the Netherlands with 55% of all people who survive the acute hospital phase discharged to this setting.[8] As many as 65% return home within one year of admittance for amputation rehabilitation.[9] The average length of rehabilitation is 81.5 days, which is longer than patients with other pathology including stroke (69.1 days) and elective orthopedic surgery (40.6 days).[10] Around 150 people undergo vascular related amputations per year in the Northern Netherlands.[11] However, with more than 34 LTC facilities in the region, very few patients with LLA are seen at any one facility. This leads to questions concerning the clinicians' ability to maintain adequate skills and knowledge in treatment of this population.[12]

Given the large proportion of patients with LLA discharged to this setting, the relatively long length of stay and the high costs associated with providing their care, it is surprising that so little is known about the actual rehabilitation treatment provided. For example, what are the rehabilitation aims and expectations on admission? What type of training is provided and with what frequency? Do clinicians have the relevant expertise for treating someone with LLA? With an increasing expectation to provide evidence based care, this lack of information is insupportable. As a starting point, the rehabilitation programme that is currently provided to people with LLA in the LTC setting needs exploration. The aim of this study was to describe the current set up, barriers and potential for providing care to people with LLA in a LTC setting.

Methods

The Medical Ethics Committee of the University Medical Center Groningen determined that formal approval was not required for this study conducted with health professionals and LTC administrative data.

Setting

There are 34 LTC facilities ((specialist) nursing homes) with a geriatric rehabilitation unit in the 3 northern provinces of the Netherlands. The area has a population of around 1.7 million people of which 17% are over the age of 65 years.[13] Elderly Care Physicians (ECP) are a specialisation in the Netherlands responsible for the treatment and support of elderly and chronically ill in LTC. The project was introduced through presentations at the ECP regional professional meetings and in their association newsletter, as well as meetings with the ECP and physiotherapists (PT) in their workplace.

Design

A mixed methods design was used. Part one of the study involved a questionnaire sent to all LTC facilities in December 2009. The questionnaire asked how many admissions the facility had in total, how many people were admitted with LLA, and the characteristics of this population (sex, date of birth, reason for and level of amputation). The period surveyed was from 1 January 2008 to 31 December 2009. A reminder letter to return the survey was sent in early 2010 to all non respondents. Descriptive data are presented.

Part two involved interviews with the ECPs and PTs in 2011. A series of open questions was developed based around 5 key themes: rehabilitation and daily care procedures; personal skills and training; communication; the multidisciplinary team; and care after discharge. Themes were developed in discussion with rehabilitation physicians and ECP over the most common issues encountered in clinical practice. Participants were encouraged to respond with their own line of thinking on each theme, with prompts given where needed (see Appendix A). The interviewer (AW) was a qualified ECP who was undergoing training to become a rehabilitation physician. The interview procedure was piloted with rehabilitation physicians from our centre, to ensure there was clear understanding of the questions and continuity of the interview. Participants were chosen using research-based recruitment,[14] from the survey responses concerning LTC admission numbers and location. This strategy was designed to include nursing homes with relatively frequent admissions with amputation and others with infrequent admissions, as well as an even geographical representation across the three provinces. The interviewer contacted each professional, explained the project in full and asked if they were able and willing to participate. All those approached gave consent. After 3 facilities per region (9 interviews with ECPs, 9 interviews with PTs), no new information or topics were being discussed and data saturation was deemed complete. As such, no further interviews took place. Interviews were completed throughout 2011, with an ECP and PT from the same facility, separately. The interviews lasted approximately 60 minutes and were conducted in the participant's workplace during their regular work hours.

Analysis

The interviews were recorded on tape and transcribed verbatim. Identifying information was replaced with descriptors to ensure anonymity for participants. Interview transcripts were read by two investigators (LF and GR), to familiarise themselves with the data. A coding book was developed by one investigator (LF) (using a constant comparison approach) and tested by a second (GR) on a full transcript. Discrepancies were discussed; these mainly concerned overlap between the codes. Three interviews were then coded in full, independently, and inter-coder agreement was reviewed for consistency.[14] No substantial differences were apparent and the remaining transcripts were coded in full by LF and reviewed by GR. Data were then arranged in a matrix according to their codes and linked to the different themes. Two investigators (JG and PD), who did not participate in the initial coding, reviewed these themes and the data, adding their interpretations. A native English speaker (LF) translated all quotes presented in results together with a native Dutch speaker (PD) to ensure context and nuances were maintained.

Results

Survey of facilities

Seventeen (52%) LTC facilities responded to the survey, reporting on 90 people admitted after LLA in a two-year period. Fifty-nine (66%) of the admissions were men and 82 (91%) amputations resulted from a vascular cause. The median age at admission was 77 years (IQR: 14 years; range 46-100 years). Individual facilities admitted between 0 and 19 people in the 2 year period surveyed, which represented a maximum of 3.6% of all admissions to a facility.

Interviews

19 people participated, 9 ECPs and 10 PTs (one facility had two PTs participate together). Participants had a mean age of 44 years (sd=8), worked 30 hours per week (sd=7), and had 12 years of experience (sd=8). Seven participants had undergone postgraduate training in LLA rehabilitation and prosthetics. The main findings from the interviews are presented below, under the subtitles of the key themes investigated. 'Teamwork' and 'communication' were combined due to overlap in the results and an additional theme 'elderly person with amputation' is presented. The results are presented using the words and perspective of the participants.

Elderly person with amputation

Independent return to home is the main goal of admission to rehabilitation in LTC. Patients would otherwise be directed immediately to a long-stay ward. Clinicians are aware that rehabilitation outcomes are dependent on many factors including the availability of family and home care. People also need a high level of intrinsic motivation. If a patient can return home independent in transfers and household walking, rehabilitation is considered successful. However, most independent people still need substantial help with, for example, putting on their prosthesis.

The expectations of rehabilitation from patients and their families often exceed their likely potential. People have little understanding of the physical capacity that is required to walk with a prosthesis or the cognitive capacity for understanding how to use it safely. However, realising the difficulties they face may be part of accepting their LLA.

"People often have very high expectations. They have their operation and think they can just get a prosthesis and walk again. And sometimes it is not going to succeed or it is not what they hoped for. So that is difficult. It is a difficult conversation." [PHYSIOTHERAPIST]

In contrast to younger patients, older patients with LLA tend to present with a more complex range of comorbidities. Clinicians acknowledge that an older patient's life experience can bring value to their rehabilitation. Treatment is approached from an open perspective, giving attention to what the patient wants to happen. Essentially, you have to look at the person, not their missing limb.

> *"The main difference is that in this population there are more things at play. The high biological age often has consequences, such as deconditioning, older people move less and then even more so after the amputation. You often see people are immobile for a long period beforehand. So their whole fitness level is much lower. Then there are still other diseases and disorders, and a poor psychosocial network. If people live alone and need a prosthesis to go home, that's somewhat complex."* [PHYSIOTHERAPIST]

Rehabilitation and daily care

Although some clinicians describe the older person with LLA as being no different from other patients in LTC, differences in treatment were evident. The intensity of care, both in time and energy, was a major discussion point. Facilities are funded to provide 4 hours of treatment to each patient per week. This time is for all treatment: medical, physiotherapy and also other para-medical treatment. There is no strict adherence to the time allocations, nor is there pressure from management staff to adhere; some patient groups simply need more time, some less. It was felt that the person with LLA requires more time, particularly in the beginning phases of care. The PT alone takes up most or all of the 4 hours, in stump management, strengthening exercises and so forth.

The application of standard protocols or care plans is hampered by both the amputation population and by frequently changing clinicians (table 1). The population differs too greatly in their presentation, particularly the range of comorbidities and cognitive abilities, to apply protocols. However, a basic set of guidelines from which to work would be useful. It should be flexible, enabling independent choices for individual patients. One example where protocols are not used is clinimetric measures. They are used for other conditions, particularly stroke. The reliability of performing the tests with a prosthesis was questioned, but also the overall value for a patient's treatment or care was not seen.

Personal skills and training

The ECPS/PTS described knowledge as being more important than any specific skill. Attendance at a training course in prosthetics and amputation was a stand out factor for gaining this knowledge. The people who had participated in a course for amputation rehabilitation have confidence in what they are doing, and are more informed and interested in amputation-specific factors (volume

Table 1: Barriers in provision of amputation rehabilitation described by participants.

Difficulty implementing and using guidelines	*"(Amputation rehabilitation) is based a lot on clinical intuition. We have to wait a bit and just see what happens."* [PHYSIOTHERAPIST] *"We need a much stricter protocol. Then we could take admission and discharge measurements, yes, I think that would actually be very good. But again it takes time and I think the current quality of rehabilitation depends on the fact we only see three or four (amputation) patients per year. That's not many; perhaps if we saw more patients, we would be more inclined to change."* [ELDERLY CARE PHYSICIAN]
Lack of involvement and specialisation from multidisciplinary team members	*"Better training of clinicians in the department is needed. This is actually very important; it's what I really miss. Things are often missed simply because people don't know, for example how the liner should be fitted or how the prosthesis should sit. Yes, these things mostly, these are things that quite often go wrong."* [PHYSIOTHERAPIST] *"Well, for us, what is very clear in the nursing home is that the rehabilitation physician and physiotherapist take care of someone with an amputation. We (elderly care physicians) take care of the wound."* [ELDERLY CARE PHYSICIAN] *"I would like better cooperation with occupational therapy. I don't mean to say that it is their fault, but working together as a team we could better assess what is necessary for someone to go home, use of a wheelchair and also the prosthesis, and we could better streamline their care."* [PHYSIOTHERAPIST]
Case mix – lack of patients with amputation seen in each facility	*"I'd like to see more patients with amputation. I would really like to encourage more to come here. With experience, we get more experienced."* [ELDERLY CARE PHYSICIAN] *"I'd like to see better training of the nurses, but then you run into the problem of seeing so few patients (with amputation), simply because there is only 5 or 6 per year, and with the varying nursing staff, it's just a question of which patients they happen to see."* [PHYSIOTHERAPIST] *"Well the best thing really would be if you could have a little section where the care is very specialised, because every time (there is an amputation admission) we spend quite a lot of time teaching others how to care for those (patients) in the right way. It costs a lot of energy, but there are just too few people with amputation admitted here."* [PHYSIOTHERAPIST]

control, technical aspects of prostheses, etc), frequently helping colleagues with problems. Patients may even be referred to a particular centre because of this knowledge and experience.

General skills that are important in treatment of people with amputation included geriatric assessment skills and specifically, assessment of patients from a 'geriatric' viewpoint. Assessment should include questions about the patient's wishes, the home situation and function prior to amputation. Thinking from a functional perspective was emphasised, so not always focussing on what might be technically correct but rather what is important or needed for the patient. For example, the ability to perform independent transfers and walking to get from A to B is more important than how well they do it. Patience is a vital skill, as this population need intensive care for their rehabilitation training, which can continue for a long time. Skills in working as a team are needed, with colleagues frequently discussing situations and problem solving together.

To maintain knowledge and skills it is important that people with amputation are seen on a regular basis. Participants found it difficult to answer the question "what is the minimum number of patients needed per year to maintain skills and knowledge?" and responses ranged from unknown, 2, 5 and up to 20 per year or even weekly. Seeing more patients with amputation might help to maintain the working partnerships with other (external) professionals. The problem of too few patients was consistent throughout all facilities with no major differences seen in the responses given throughout the interviews by clinicians working where relatively more or less people are admitted with LLA.

Teamwork and communication

The PTs have a key role in the care of people with amputation. They take charge of decisions concerning amputation rehabilitation. In particular, they act to refer patients in a timely manner to an appropriate professional, such as the surgeon or wound care specialist. This 'signalling role' occurs naturally as they spend the most time with the patients. The ECP is responsible for medical care, directing family meetings and external communication, including discussion with other medical specialists, the general practitioner (at admission and discharge) or the surgeon (rarely, as needed e.g. wound healing problems). Some ECPs describe wound care as the limit of their 'amputation role' and beyond that they are responsible only for medical management. They were quick to refer any and all amputation issues to the rehabilitation physician or PT. This was also apparent in the interviews, with amputation questions answered with 'you can better ask the PT'. Other ECPs tried to ensure they have a wider range of amputation knowledge, such as basics of prostheses and biomechanics.

The role of the rehabilitation physician varies from having all decisions and issues concerning the LLA referred directly to them and the LTC facility wanting more direct face time, to the feeling that the ECP can manage most issues themselves and questioning how much value for money having a more intense presence from the rehabilitation physician would give. Other allied health professionals are available onsite in the LTC. Occupational therapists have only a small role in the care of people with amputation, covering wheelchair prescriptions and a home visit before discharge. Social workers, psychologists, dieticians, and other therapists are consulted if needed but the general feeling is that there is a lack of knowledge about amputation and most care falls back on to the PT.

There is a weekly multidisciplinary team meeting in all facilities with patients discussed regularly. The rehabilitation physician and prosthetist attend fortnightly or monthly clinics. Most discussion occurs between these structured meetings. A feature of communication was the informal nature of relationships and flexibility from team members. The PTs and ECPs freely approach each other at any time enabling prompt resolutions to problems. The whole team goes out of their way to assist others, with training, advice or flexibility in care such as the prosthetist dropping by the nursing home before or after work.

Many of the nursing professionals work part-time or shift work. Knowledge may be passed on, e.g. a nurse is instructed by the PT in bandaging or safe-transfers, but that person may not encounter the patient again. This is one of the main differences from inpatient rehabilitation, where an entire unit may be dedicated to LLA with all nursing, medical and paramedical professionals 'specialised' in the condition.

Care after discharge

The general practitioner, rehabilitation physician and prosthetist are the key contacts for patients after discharge. Some patients continue in the LTC in outpatient care. Others are referred to community PT. The relationship with external clinicians is good with referrals and handover back and forth. External health providers are generally chosen by locality. Some people had concerns over not knowing about the community PT's skills or interest areas and that once a patient is discharged they would not hear anything more. Having the option to bring patients back 2-3 months after discharge would be good to 'top-up' their rehabilitation. In other disciplines, particularly stroke, there is more coordination in the community setting, but there are too few people with LLA for this to work.

Discussion

This study aimed to provide an overview of the current treatment for people with LLA admitted to LTC in the Northern Netherlands to identify the barriers and potential for providing evidence based care in this setting. Internationally, there is an increasing need to find cost-effective rehabilitation options for people with amputation with different approaches of current interest and importance. Dutch LTC differs from other systems, in particular the medical specialisation of ECPS and presence of onsite multidisciplinary rehabilitation teams offering geriatric-tailored treatment. The influence of rehabilitation setting on outcomes has been investigated in reference to other conditions in older people, mostly orthopaedic disorders and stroke. The clinicians interviewed recognised that treatment for these other conditions, particularly stroke, is stronger with better planning and coordination of care. Outcomes of amputation rehabilitation have mainly been looked at from the perspective of traditional inpatient care. Two recent studies showed that good outcomes from LTC can be achieved, particularly in terms of independent discharge to home, with rates of 57-65% within one year, greater pre-amputation function being a key factor for success.[12,15] Despite these positive outcomes, it appears that the current rehabilitation process in LTC is largely unsustainable, certainly within the Dutch setting, with the burden of care falling largely to PTS.

Two key areas to improve stood out: [a] the need for use of guidelines in care and [b] a wider collaboration with specialised team members. There were no protocols or guidelines in use for people with amputation in LTC, which was attributed to the highly variable nature of the patients presentation. However, the idea of having some guidance was very much supported. Guidelines for management of people with amputation are available[16] and these guidelines should be reviewed for their applicability to the LTC setting. Rehabilitation after LLA benefits from a multidisciplinary team.[16] The set up of Dutch LTC with an onsite multidisciplinary team enables comprehensive provision of a range of services specific for the geriatric population. Despite this team available, PTS work largely in isolation concerning issues related to patients with amputation, with referral to rehabilitation physician and prosthetist when necessary. The PTS find it quicker and easier to do something themselves, for example, they take charge of bandaging the limb rather than re-training nursing staff with each new amputation admission. Other potentially valuable professions, in particular nursing and occupational therapy, lacked knowledge of rehabilitation for people with amputation. Nurses can provide essential support between PT sessions and occupational therapists play an important role in functional training.[17]

The tendency for the PT to take on a substantial amount of the responsibility is perhaps one of the reasons why the 'intensity' of care was described so strongly for this condition.

The issues raised make it difficult to provide efficient care to people with amputation in the LTC setting. One solution would be to designate an amputation rehabilitation facility in each province. This would offer advantages such as an increased number of patients with amputation, more specialisation by professionals, and stronger relationships with external colleagues. However, the aversion of people to travel away from their local area may prevent this success, particularly if applied to a larger geographical setting. Other small changes can be readily implemented, for example annual training for the PTS and the set up of a partnership with a larger rehabilitation centre. This training and formalised access to support from a specialist can address weaknesses in the PT's skills and knowledge. It will not reduce the burden in care provision but provide the tools for them to better manage. Finding methods to capitalise on other multidisciplinary team members available in LTC should be a priority.

The high expectations of the patient and family were one of the only negative aspects described. Early involvement of the rehabilitation physician is recommended, including pre-operative consultation where appropriate.[16] Although a successful outcome cannot be reliably predicted, the rehabilitation physician has the experience to provide education and advice to the patient about likely outcomes and what to expect from the rehabilitation process.

We investigated centres with many and few amputation admissions expecting to see differences in the issues raised. Surprisingly, this was not the case, with all more or less in agreement. We suspect this is because even those centres with relatively more amputation admissions still only see one patient every few weeks or months, so the problem of having too few patients remains. The issues described by participants were remarkably similar across the different facilities with data saturation reached after 18 interviews. We hope this will provide some positive and interesting discussion points for the clinicians involved in enabling changes in the near future.

Some limitations of the study need consideration. The response to the survey was low at only 50%. Nevertheless, it provided the insight we needed to ensure that facilities which admitted a larger and smaller number of people with LLA were included for interviews. The study was conducted in Dutch LTC settings, which offers onsite multidisciplinary rehabilitation. This approach differs from other developed countries limiting generalisation to other settings. Finally, there was a potential for bias introduced by the interviewer who was a rehabilitation specialist in training but also a former ECP. Given the descriptive nature of the questions we do not believe this connection provided any substantial influence over the participant's responses.

Conclusions

This study shows that although current care of people with amputation is associated with good outcomes it is, to a large extent, dependent on the problem solving abilities, energy and empathy of the individual clinicians involved. With funding agents requiring greater evidence and accountability in decision making, the current care appears unsustainable. Each LTC facility sees a relatively small proportion of people with amputation. This spread of patients across many centres makes it difficult for professionals to obtain and maintain skills and knowledge for care. A designated LTC facility for amputation rehabilitation is presented as a solution but also smaller clinical changes are suggested, including improvements in communication and training.

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References

(1) Czerniecki JM, Turner AP, Williams RM, et al. The effect of rehabilitation in a comprehensive inpatient rehabilitation unit on mobility outcome after dysvascular lower extremity amputation. Arch Phys Med Rehabil 2012;93:1384-1391.

(2) Kurichi JE, Small DS, Bates BE, et al. Possible incremental benefits of specialized rehabilitation bed units among veterans after lower extremity amputation. Med Care 2009;47:457-465.

(3) Stineman MG, Kwong PL, Kurichi JE, et al. The effectiveness of inpatient rehabilitation in the acute postoperative phase of care after transtibial or transfemoral amputation: study of an integrated health care delivery system. Arch Phys Med Rehabil 2008;89:1863-1872.

(4) Dillingham TR, Pezzin LE. Rehabilitation Setting and Associated Mortality and Medical Stability Among Persons With Amputations. Arch Phys Med Rehabil 2008;89:1038-1045.

(5) Pezzin LE, Dillingham TR, MacKenzie EJ. Rehabilitation and the long-term outcomes of persons with trauma-related amputations. Arch Phys Med Rehabil 2000;81:292-300.

(6) Moxey PW, Gogalniceanu P, Hinchliffe RJ, et al. Lower extremity amputations--a review of global variability in incidence. Diabet Med 2011;28:1144-1153.

(7) Ephraim PL, Dillingham TR, Sector M, et al. Epidemiology of limb loss and congenital limb deficiency: a review of the literature. Arch Phys Med Rehabil 2003;84:747-761.

(8) Fortington LV, Dijkstra PU, Geertzen JHB. Determinants of discharge to long term care after lower limb amputation. J Am Ger Soc 2013;61:298-299.

(9) Spruit- van Eijk M, van der Linde H, Buijck B, et al. Geriatric Rehabilitation of lower limb amputees: a multicenter study. Disabil Rehabil 2012;34:145-150.

(10) Peerenboom PBG. Rehabilitation in the AWBZ (general act on exceptional medical expenses) (Dutch: Revalidatie in de AWBZ: Omvang, aard en intensiteit). 2008. Available online at: http://www.vumc.nl/, accessed March 2012.

(11) Fortington LV, Rommers GM, van Netten SJJ, et al. Lower limb amputation in Northern Netherlands; unchanged incidence from 1991-1992 to 2003-2004. Prosthet Orthot Int. Early online DOI: 10.1177/0309364612469385

(12) Spruit- van Eijk M, van der Linde H, Buijck B, et al. Predicting prosthetic use in elderly patients after major lower limb amputation. Prosthet Orthot Int 2012;36:45-52.

(13) Central Bureau of Statistics, Netherlands. [database on the Internet] Accessed March, 2012. Available at: http://www.cbs.nl.

(14) Hennick M, Hutter I, Bailey A. Qualitative research methods. London: SAGE Publications; 2011.

(15) Hershkovitz A, Dudkiewicz I, Brill S. Rehabilitation outcome of post-acute lower limb geriatric amputees. Disabil Rehabil 2012 June [Epub ahead of print]

(16) Netherlands Society of Physical and Rehabilitation Medicine. Draft guidelines in amputation and lower extremity prosthetics (Dutch: Conceptrichtlijn amputatie en prothesiologie onderste extremiteit). VRA - Dutch Association of Rehabilitation Physicians; 2011. Available online at www.cbo.nl, accessed August 2011.

(17) Spiliotopoulou G, Atwal A. Is occupational therapy practice for older adults with lower limb amputations evidence-based? A systematic review. Prosthet Orthot Int 2012;36:7-14.

Appendix A: Interview guide

Describe the aims of the interview and ask if there are questions
Remind participants that their responses are given in confidence and will be anonymous.
Ask permission to record interview.

Demographic data
Personal details – age, sex, etc
Working details – years in present position, hours worked, etc
Specialisation - training and additional relevant information

TOPIC 1: Personal skills and training
Are there any special skills needed for treatment of elderly people with amputation? Descriptions.
Have you and where did you learn these skills?
Do you feel that you have sufficiently mastered these skills? Have you followed any extra training?
How many patients do you think you need to treat to maintain these skills?

TOPIC 2: Rehabilitation and daily care
Who is involved in rehab? What are their tasks? Who is responsibile for the patient's treatment?
Do you think there are arguments for special treatment of the elderly with LLA? Or not?
Do you use treatment protocols / guidelines?
What is the frequency of therapy? Who determines the frequency?
Are patients encouraged to use a prosthesis? Who decides whether the patient will be fitted with a prosthesis? Who prescribes?
How involved are the nursing / care staff in the rehab? Examples - wound care, bandaging, compression, stump inspection, donning and doffing prosthesis, transfer training.
What do you see as the main goals of rehab for people with LLA in this setting?
Do you use outcome measurements? Berg balance scale, sit-up-and-go, Barthel index.
What resources are available for rehab of people with LLA? What is missing? Do you have a wish list?

TOPIC 3: Communication
How does the team communicate over patient's rehab? Consults, writing, phone, email, in person?
How is the relationship with physio and ECP? Other team members? Professional or personal?
Are there any problems in communication? With patient, nursing, family...
What happens if there are problems? Would you like to see anything different?

TOPIC 4: Team work / collaboration (external to LTC team)
Who else is involved in the rehab of the person with LLA?
What is the role of the general practitioner when their patient is admitted for rehab? Are they involved?
How is the cooperation/communication between yourself and other team members?

TOPIC 5: Discharge / and follow up
What / who determines when the patient can be discharged?
Where is discharge paperwork/ letter distributed?
Are there any problems / difficulties with discharge process?
Who is responsible for follow-up care if problems arise after discharge? Does the patient know who to contact with questions or problems?

Concluding
Do you have other issues /suggestions related to the care of the elderly patient with amputation, which you think should have been discussed?

Chapter 6

Change in health related quality of life in the first 18 months after lower limb amputation; a prospective, longitudinal study

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Abstract

Objective: To describe changes in health related quality of life in people with lower limb amputation from time of amputation to 18 months, with consideration of the influence of age and walking distance. A comparison of quality of life in people with amputation to Dutch population norm values is also made.

Design: Multicentre, longitudinal study

Subjects: All people undergoing first amputation: 106 were referred, 82 were included (mean (sd) age 67.8 years (13.0), 67% men). 35 remained in the study at 18 months.

Methods: Dutch language RAND-36 questionnaire was completed at time of amputation, 6 and 18 months after amputation.

Results: A significant improvement with time was seen in physical function, social function, pain, vitality, perceived change in health (all $p<0.001$). People over 65 years had a poorer outcome compared to people <65 years only for physical function ($p<0.001$). Walking distance was associated with improved scores in social function ($p=0.047$).

Conclusions: Quality of life improved significantly in 5 of 7 domains investigated; most change occurred in the first 6 months. Physical function remained well below population norm values. Different domains may be affected in different ways for older and younger age groups; the source and reasoning needs investigation.

Introduction

Lower limb amputation (LLA) results in not only a permanent physical change to an individual, but also has an impact on psychological and social well being. The changes can affect a range of aspects that contribute to a persons health related quality of life (HRQOL).[1,2] HRQOL is an important indicator of overall health. Research of people with LLA reflects the growing attention toward HRQOL with increasing use as an outcome measure.[3]

HRQOL in people with LLA is generally lower than population norm values or control subjects[4,5] particularly in physical components.[6-9] HRQOL after LLA may improve over time; higher scores being reported by individuals with a longer duration of time since amputation.[10,11] However, most studies of HRQOL after LLA have been cross sectional in design and include a majority of subjects who have lived with their amputation for at least 2 years.[4-7,11-13] There remains a gap concerning the post-operative response and adjustment early after amputation.[3,14,15] Longitudinal studies, extending beyond the post-acute period, are needed to substantiate or refute previous cross-sectional findings.

Walking distance is thought to play a key role in independence and HRQOL for people with LLA.[13] An ability to walk 500m was previously proposed as a minimum walking distance needed for independent living.[16] It is assumed that this independence is associated with having a positive effect on psychosocial aspects of HRQOL. However, how the influence of walking distance might change over time, and which specific aspects of HRQOL are affected, remain unknown.

Learning to walk with a prosthesis is a laborious task, requiring cognitive ability, conditioning and balance. LLA is most frequently performed in elderly people due to chronic peripheral vascular disease or diabetes mellitus.[17] The co-morbidities prevalent in this population make regaining walking an even more difficult task. There are additional physical, psychological and social co-morbidities associated with both the underlying cause of the amputation, such as cardiovascular disease, contractures and infection, and with ageing, including arthritis, social isolation, and a reduced capacity for learning. Walking ability in the elderly population is highly varied.[18] The elderly person with vascular LLA faces a different set of challenges on HRQOL compared to younger people or people with other causes of amputation but it is not clear if there is an association between age and HRQOL.

The aim of this study was to describe changes in HRQOL in people with LLA from time of amputation to 18 months, with consideration to the influence of age and walking distance. Finally, a comparison of HRQOL in people with LLA to Dutch population norm values is made.

Methods

Vascular surgeons from all hospitals of the 3 Northern provinces of the Netherlands were requested to refer people undergoing amputation to this multicentre, longitudinal study from 1 November 2003 to 30 April 2008. Included were people: aged ≥18years; undergoing primary lower limb amputation (transtibial, knee-disarticulation, transfemoral); underwent amputation due to vascular disease, infection, or diabetes. Excluded were people who: had a previous major amputation on ipsilateral limb; were unable to read/write Dutch, were unwell or showed signs of clinical dementia which prevented completion of questionnaires; or were recruited >5days after the amputation due to the risk of recall bias.

The study protocol was approved by the medical ethics committees of participating hospitals. All participants gave informed consent.

Data collection

Questionnaires were completed 1-2 days before amputation. In acute cases, this was not possible, and patients were included up to 5 days after the operation. Questionnaires were sent to participants again at 6 and 18 months post-amputation. Patients were included up to 1 May 2007; some patients had a maximum follow up time of 1 year due to the study end date.

Outcome measures

Baseline assessment included characteristics (sex, date of birth) and amputation details (date, level, side, cause). Baseline and post-operatively, the primary outcome measure was the Dutch-language RAND-36.[19] This is a self-reported questionnaire, similar to the SF-36, taking approximately 10 minutes to complete. Nine domains contributing to HRQOL are addressed: physical function, role limitation physical, social function, role limitation emotional, mental health, pain, vitality, general health, and perceived change in health. Scores range from 0 (worst reported health) to 100 (best reported health). The RAND-36 is valid for the Dutch population.[20] Participants also answered a (non-validated) question on walking distance, choosing between: 'unable to walk', '<100m walking', '100m to 500m walking', '500m to 1km walking' or '>1km walking'. These categories were recoded for analysis as non-walker, <500m or ≥500m walking distance.

A study of the Northern Dutch population provided norm values for the RAND-36.[19] The authors were contacted for their original dataset, enabling different age groups to be compared. A minimum age cut off of 30 years in the norm data was used to correspond with our youngest included patient of 30.9 years.

Data analysis

Descriptive results are presented with mean and standard deviation (sd) for continuous variables and number and percentage for categorical variables. Differences between characteristics of groups were compared using independent sample t-test for age (2 groups), one way ANOVA for age and baseline domain scores (3 groups) and χ^2 for categorical variables.

Changes over time for each domain of the HRQOL were evaluated using multilevel models. These models have not been widely used in amputation outcome research so far. Multilevel analyses are frequently used for longitudinal data, since they also take the correlation between repeated measures within individuals into account. In this type of analyses, a linear regression model is estimated for each individual, together with the variability between all individuals.[21]

A random effects model with unstructured covariance was used, with individuals as the highest level and different time points as the lowest level. Age was centred at 65 years. In case of significant time effect, predictors (age and walking distance) were added stepwise in the model. Interaction effects for time with age were explored. Walking distance was not analysed in respect to the domain physical function due to substantial overlap of the constructs; the level of amputation was instead considered.

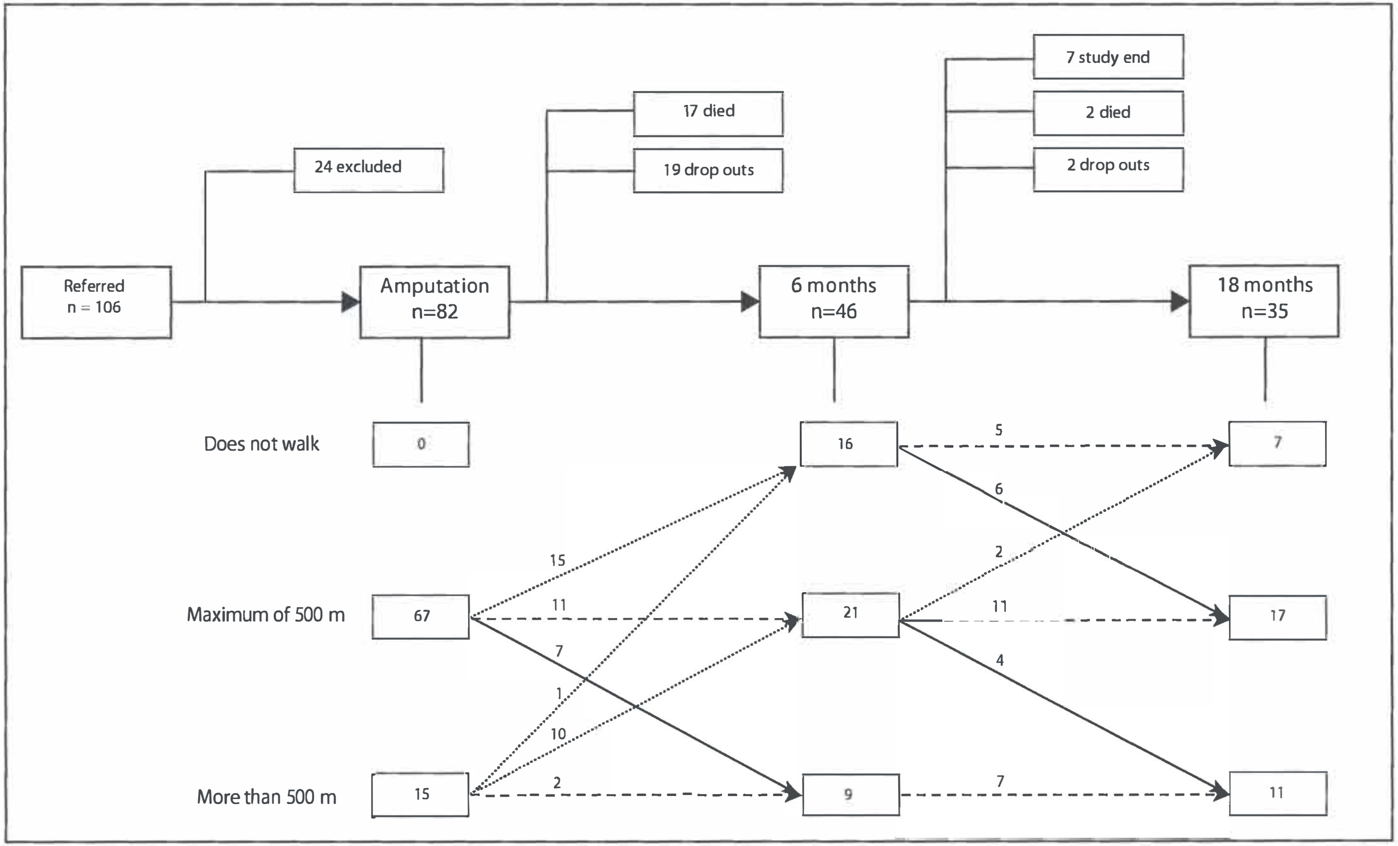
To test for differences in HRQOL scores at 18-months, the means of the norm values were compared to the 95% confidence interval of LLA population. For each domain, if the mean norm score fell outside this range, the LLA population was considered as significantly different.

Significance for all analyses was set at 0.05 (two-sided) and were performed with PASW Statistics 18, mixed models.

Results

From 106 referred patients, 82 (77%) were included (figure 1). Ten patients were excluded because they were referred too late (>5 days) and 14 patients because they had a previous ipsilateral LLA. Excluded patients were slightly younger than included patients (not significant) and more likely to have had a transfemoral amputation (p=0.001, table I). For 7 patients, the study period ended before their 18-month follow up.

Figure 1: Inclusion, drop out, death and walking ability of participants at each time point.



By 18 months, 21 patients had dropped out of the study. They had a median age 10.3 years older than those who stayed in (not significant) (table 1). Reported reasons for drop out were worsening of co-morbidities or patients were no longer interested in participating because they experienced few or no problems. Nineteen patients died before their 18-month follow up, 17 (90%) of which were men (p=0.038). There were no significant differences in age (p=0.076) or level (p=0.744) between patients who stayed in the study, died or dropped out.

The domains, role-limitation emotional and role-limitation physical, were not included for analysis. The responses in these domains were frequently missing, dichotomised and were not interpretable.

There were no statistically significant differences in HRQOL domain scores at time of amputation between patients who stayed in the study, died or dropped out (table 1). In addition, there were no significant differences in domain scores at amputation when comparing by sex or level of amputation or comparing between people who completed the questionnaire pre-operatively (n=59) with those who completed the questionnaire post-operatively (n=23) (data not presented).

Walking distance across each time point is shown in figure 1. All patients reported that they were able to walk at least 500m before their amputation. In the first 6 months, 26 (32% of all participants; 57% of remaining participants)

Table 1: Characteristics of patients by category at time of amputation: included versus excluded patients; and patients who stayed in study, died or dropped out.

	Included	Excluded	p*	Stayed in	Died	Dropped out	p*
n (%)	82	24		42 (51)	19 (23)	21 (26)	
Age, mean (sd)	67.8 (13.0)	64.7 (10.1)	0.292	64.6 (14.2)	71.4 (8.2)	70.8 (13.0)	0.076
Men, n (%)	55 (67)	16 (67)	0.577	27 (64)	17 (90)	11 (52)	0.038
Level, n (%)							
Proximal	30 (37)	18 (75)	0.001	16 (38)	8 (29)	6 (42)	0.744
Distal	52 (63)	6 (25)		26 (62)	11 (71)	15 (58)	
RAND-36, mean (sd)							
Physical function	8.9 (12.8)	-		10.6 (14.3)	5.6 (8.7)	7.9 (11.9)	0.398
Social functioning	34.7 (31.7)	-		29.6 (26.9)	50.0 (37.5)	32.1 (34.6)	0.101
Mental health	70.7 (20.0)	-		68.2 (18.8)	72.0 (26.2)	75.7 (13.7)	0.505
Pain	26.2 (26.8)	-		26.4 (29.5)	25.5 (25.5)	26.5 (21.5)	0.928
Vitality	47.1 (23.7)	-		47.1 (23.2)	48.8 (25.1)	45.4 (24.7)	0.992
General health	60.5 (20.8)	-		63.0 (21.8)	60.0 (14.9)	54.3 (23.8)	0.410
Change in health	24.3 (25.3)	-		26.8 (27.6)	18.8 (21.4)	23.2 (22.9)	0.555

*$\chi 2$ for level and sex; age compared using t-test (for included versus excluded); one way ANOVA for age and domain scores by end status.

declined in walking distance. From 6 to 18 months, walking distance was stable or improved for the majority of participants, with two people declining to a non-walking status.

A statistically significant improvement in mean score from amputation to 6 months and from amputation to 18 months is seen in 5 of the 7 domains evaluated (physical function, social function, vitality, pain and perceived change in health, all p<0.001) (table 2). Mental health and general health were consistent across all time points.

Table 2: Change in HRQOL over time, according to walking ability and age

	Independent	ß	se	95% CI	p
Physical function*	Constant	12.0	1.7	8.5 ; 15.5	
	Proximal level	-7.7	2.7	-13.1 ; -2.2	0.007
	6 months	21.4	3.8	13.8 ; 29.0	<0.001
	18 months	22.6	4.2	14.2 ; 31.1	<0.001
	Age	-0.4	0.1	-0.6 ; -0.2	<0.001
Social function†	Constant	12.5	8.6	-5.3 ; 30.3	
	6 months	37.7	6.0	19.0 ; 56.3	0.007
	18 months	38.6	5.9	26.2 ; 51.0	<0.001
	< 500 m	20.7	8.4	3.5 ; 38.0	0.020
	≥ 500 m	29.6	9.3	9.3 ; 49.8	0.008
Mental health‡	Constant	70.7	2.3	66.2 ; 75.2	
	6 months	2.2	3.7	-5.1 ; 9.5	0.553
	18 months	5.8	4.0	-2.1 ; 13.6	0.148
Pain‡	Constant	26.2	3.2	19.8 ; 32.6	
	6 months	47.8	5.2	37.4 ; 58.2	<0.001
	18 months	42.8	5.3	32.2 ; 53.4	<0.001
Vitality‡	Constant	47.4	2.8	41.8 ; 53.0	
	6 months	18.8	3.6	11.5 ; 26.1	<0.001
	18 months	17.7	3.8	9.5 ; 25.9	<0.001
General health‡	Constant	60.6	2.5	55.3 ; 65.5	
	6 months	3.9	3.5	-3.2 ; 11.0	0.273
	18 months	-1.4	3.5	-8.5 ; 5.7	0.689
Change in health‡	Constant	24.3	3.0	18.3 ; 30.3	
	6 months	50.0	5.2	39.5 ; 60.5	<0.001
	18 months	42.2	5.6	30.9 ; 53.5	<0.001

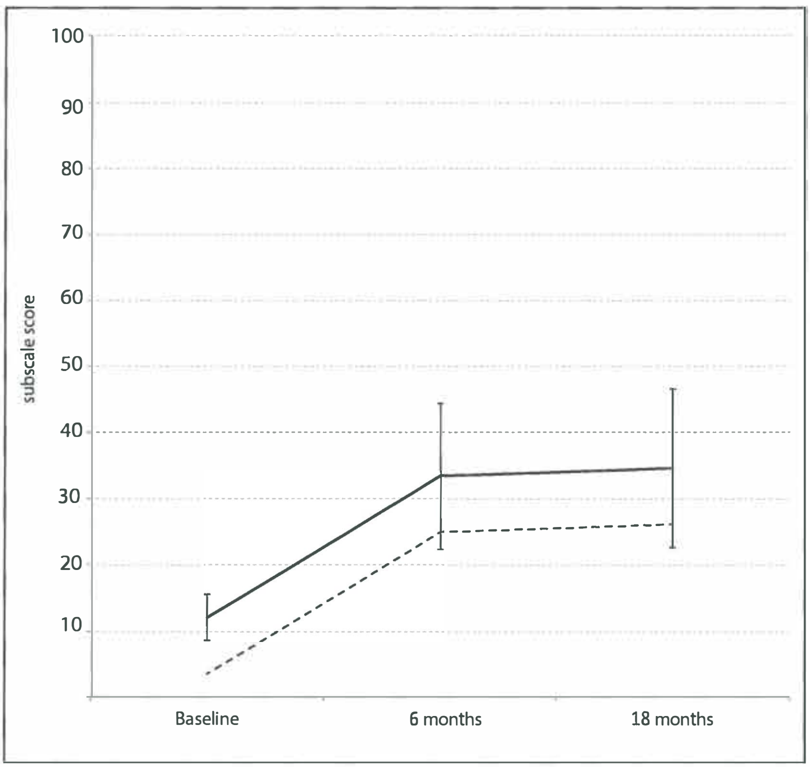
*Constant is people aged 65, time of amputation, transtibial level. Walking ability was not analysed in respect to physical function due to substantial overlap of the constructs, instead the level of amputation was included. Proximal level refers to people with knee disarticulation or transfemoral level amputation; se: standard error; CI: confidence interval. †Constant is people who did not walk, time of amputation; ‡Constant is time of amputation

An ability to walk gave significantly improved scores in social function (p=0.047). Age was significant factor on HRQOL for physical function (p=0.001) (figure 2 and figure 3). Physical function was also influenced by level of amputation, people with a knee disarticulation or transfemoral amputation reporting significantly lower scores (-7.7, p=0.007).

Eighteen months after their amputation, people with LLA had significantly poorer HRQOL scores compared to norm values in three domains and better scores in perceived change in health (table 3). Mental health, vitality and general health showed no significant differences between people with LLA and norm values. Physical function had the largest difference between mean scores, 43.7 less for people with LLA than norm values.

The difference in mean scores seen for the all-age population was not statistically significant for social function and pain when considering the age-specific values for people 65 years and over.

Figure 2: Change in physical function over time

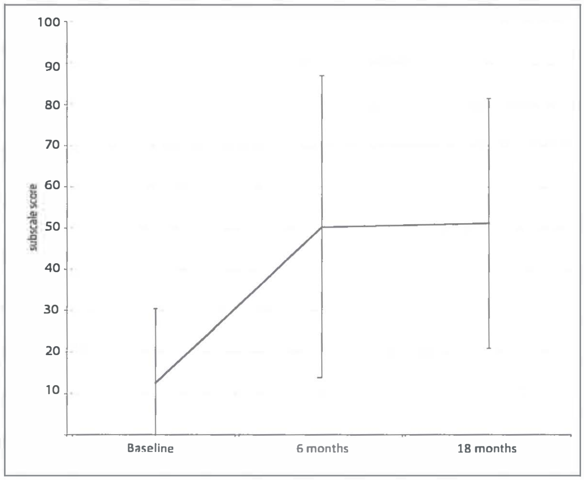


Solid line shows change in physical function over time for a 65 year old with transtibial amputation. Error bars represent 95% confidence interval of the mean. For each year over 65 years of age scores are: -0.4; For each year under 65 years, scores are: + 0.4 (p < 0.001); For a knee disarticulation or transfemoral amputation scores are: -7.7 (p=0.007); As example: dashed line represents a 70 year old, with transfemoral amputation.

Figure 3: change in HRQOL domain scores over time

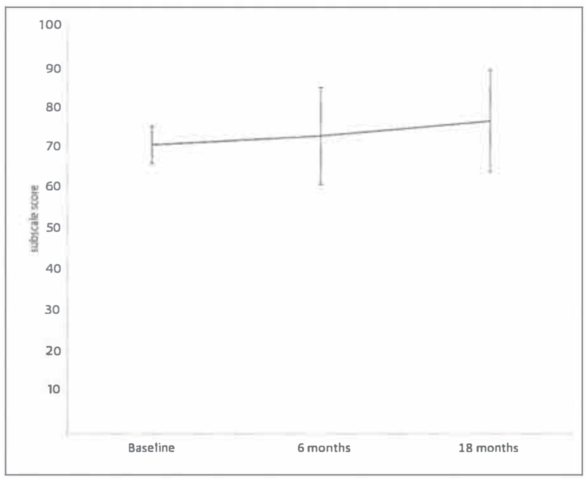
Social function

Change in social function score over time for non-walker with transtibial amputation; error bars represent 95% confidence interval of mean; For cases with walk ability < 500m scores are: + 20.7 (p = 0.020); For cases with walk ability >500m scores are: + 29.6 (p = 0.008)

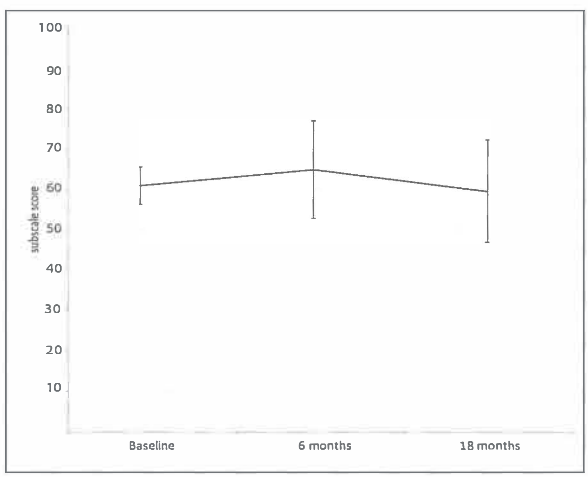


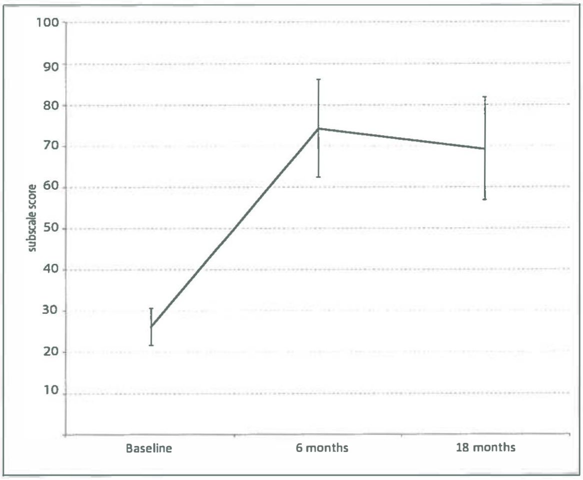
Mental health*

*Change in domain score over time, error bars represent 95% confidence interval of mean.

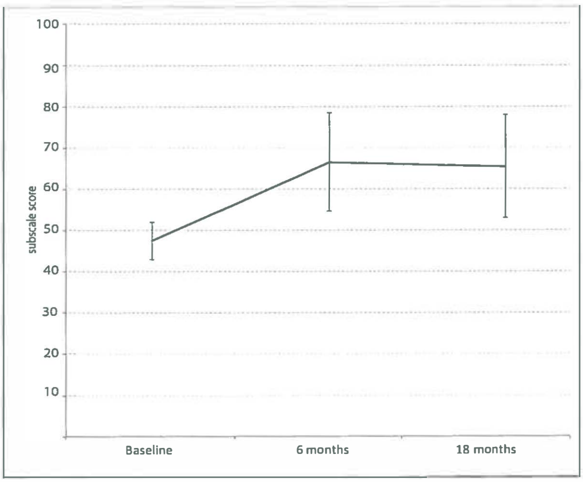


General health*

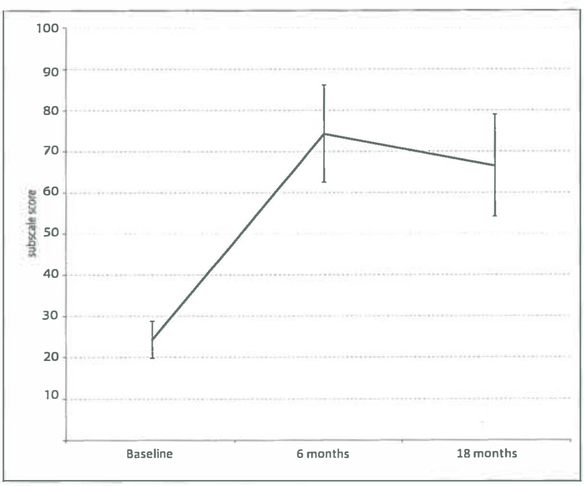




Pain*



Vitality*



Perceived change in health*

Table 3: Mean (sd) RAND-36 domain scores at 18 months for people with lower limb amputation compared with population norm values.

	All age groups			≥ 65 years			< 65 years		
	LLA (n=35)	95% CI of LLA	Population (n=804)	LLA (n=15)	95% CI of LLA	Population (n=170)	LLA (n=20)	95% CI of LLA	Population (n=634)
Physical function	34.7 (25.8)	25.5; 43.9	78.4 (25.2) *	30.0 (24.1)	23.1 ; 51.6	62.5 (28.1)*	37.4 (26.9)	17.9 ; 42.1	82.6 (22.6) *
Social function	73.2 (26.3)	64.4; 82.0	85.2 (22.4) *	75.9 (23.2)	59.1 ; 83.4	80.8 (25.7)	71.3 (28.7)	63.3 ; 88.5	86.4 (21.3)
Mental health	76.5 (15.3)	71.1; 81.9	76.7 (18.5)	76.4 (15.2)	67.6 ; 85.6	75.5 (17.3)	76.6 (15.7)	69.5 ; 83.3	77.0 (18.8)
Pain	69.3 (24.6)	60.8; 77.8	78.8 (25.9) *	68.9 (25.9)	54.9 ; 84.2	73.3 (28.7)	69.6 (24.5)	58.2 ; 79.7	80.3 (25.0) *
Vitality	64.5 (17.1)	58.5; 70.5	66.8 (20.3)	66.8 (17.8)	52.7 ; 73.8	63.9 (21.8)	63.3 (17.0)	59.4 ; 74.3	67.5 (19.8)
General health	64.7 (16.0)	59.1; 70.3	69.4 (23.1)	68.2 (14.7)	54.1 ; 71.4	59.7 (23.7)	62.8 (16.7)	60.8 ; 75.5	71.9 (22.2)
Change in health	66.4 (28.1)	56.7; 76.1	51.2 (18.5) *	68.8 (24.1)	51.3 ; 78.7	46.9 (19.2) *	65.0 (30.8)	55.3 ; 82.2	52.4 (18.1) *

*population mean falls outside 95% confidence interval of lower limb amputation (LLA) population at 18 months;
The sample from which the norm values were derived consisted of:
Minimum age of 30 used to correspond with our youngest included patient at 30.9 years:
All ages: n = 804, 35% men, median (IQR) = 50 years (38 to 63).
≥ 65 years: n = 170, 37% men, median (IQR) = 71 years (68 to 76).
< 65 years: n = 634, 34% men, median (IQR)= 45 years (36 to 53).

Discussion

The results of this study showed that substantial improvements in HRQOL can be achieved after LLA. HRQOL scores were reflective of the difficult situation faced at the time of amputation; only mental health and general health scoring over 50 (out of 100). However, for people who survive, significant improvements are gained across the differing domains, with most change evident in the first 6 months. While realising that it is not always clear who will survive the post-operative period, for those who do their situation can improve substantially within a relatively short time frame. With the exception of physical function, domain scores differed little from the population norm values after 6-18 months.

Previously, this positive change could only be inferred from cross-sectional studies that show people with longer time since amputation report higher HRQOL than those with more recent amputation.[10,11] The impact of time has been considered in relation to depression, anxiety, problems with sex and relationships, and body image, with findings suggestive that these aspects become evident only after 6 to 24 months.[1,22,23] However, those studies were all conducted in relatively young populations with LLA, with a mean age less than 60 years. The population investigated can have an important impact on the outcomes. In general, older people with LLA have different coping strategies, resilience and goals.[24] During the first year after amputation, people with vascular-related LLA may undergo less change than people with traumatic LLA.[25] Although HRQOL shows changes over time, the contrasting findings from this and other studies, specifically in reference to which aspects are changing and when, needs further investigation.

The increase in HRQOL over time for this population may occur as the amputation signals the end of a long period of pain, infection, immobility and hospitalisation. After surgery and a period of rehabilitation, many patients are able to return home, possibly with greater mobility than prior to the amputation. Events leading up to the amputation may have had an important influence on the baseline scores, such as the number of previous procedures or the duration of hospitalisation. These events were unable to be evaluated in the current study. The improvement in scores may also occur from a response shift, reported in LLA populations previously.[1,11,26] After experiencing an event such as amputation, expectations and importance of different aspects of HRQOL are altered.[27] Any given score at the time of amputation may not have the same meaning for an individual 6 or 18 months later. The importance given to a specific domain may also change; for example, social function may be considered less important compared to physical function at the time of amputation, increasing or decreasing in its relative importance over time. The influence that a response shift may have on longitudinal patient reported HRQOL scores, particularly in elderly patients, is unclear[28] and it may result in an over- or under-estimation of HRQOL.

Physical function for all participants remained very poor, especially in comparison to norm values. The low scores observed at the time of amputation were in accordance with those previously reported using the RAND-36 for 16 patients with vascular LLA.[29] Unfortunately, important details from that study are missing (time since amputation, level of amputation) so further comparison is not possible. Physical function scores 18 months after LLA were lower than observed in other studies using the RAND-36. However, those studies had highly selected populations of people who walk with a prosthesis,[13] a high proportion of people with LLA due to trauma and who were of working age.[7] Those populations are generally healthier than a population with vascular-related LLA so it was not surprising that participants in the current study had poorer physical scores.

Despite the low physical function, other domains were comparable to population norm values. The idea that mobility enables independence and this in turn translates to a higher HRQOL[11,13,16,30] was not seen in this population, with only social function improving with walking ability. A walking distance of more or less than 500m was the most important determinant of HRQOL in a study investigating phantom pain and other determinants of HRQOL.[13] The majority of that population were prosthetic users and only half had amputation due to a vascular-related cause. Our population consisted only of people with vascular-related LLA, not all of whom walked. One explanation might be that HRQOL is linked to walking distance only when focussing on a population who actually walk, the inclusion of non-walking participants negating this link. We did not have enough non-walking participants to look at this idea with more certainty.

With the exception of physical function, there were no significant differences between age groups over time seen in the regression equations. However, comparing age-specific domain scores to norm values suggests there are indeed differences in how older and younger people perceive HRQOL after LLA. For example, social function for the all-age group differed significantly from norm values, but when these results are broken into age-specific groups the differences were no longer apparent. The importance of a social network has been reported for people with LLA previously[12] but it also might be linked to age-appropriate comparisons. Age is thought to be an important determinant of many outcomes after LLA, for example walking ability, yet few studies have looked specifically at different age groups, particularly elderly people.[18] It seems there may be important age-specific variation in HRQOL after LLA that warrant further attention. Looking at the influence of time on HRQOL, age should be explored further as it may translate to different time-dependent HRQOL outcomes that can be targeted during rehabilitation and long-term care.

The lack of differences by age and walking ability seen in the regression model may also be accounted for by the small sample size (although for a longitudinal study of LLA, the sample size can be considered relatively large).

The elderly person with vascular LLA is often excluded from research due to limitations from study designs such as selection bias and recruitment settings.[3,5,6,13] Investigations of HRQOL, which include the elderly person with vascular LLA, could not only increase sample size, but enable results to be more widely generalised.

The influence of time, age and walking ability on HRQOL were considered. Previously investigated determinants of HRQOL in patients with amputation have included sex, amputation level and cause, phantom pain, stump pain, phantom sensations, sexual satisfaction, depression and social setting.[3] Our findings concerning time, walking ability and age should be considered knowing that a range of other factors might also play a role with research of HRQOL in people with LLA still very much in its infancy.

To incorporate a representative sample of all people undergoing vascular related amputations, there were minimal exclusion criteria. However, a substantial number of patients were still missed from the study and selection bias was evident; the expected population for the region being 6 years older with a mean (sd) age of 74.0 (11.2) years[31] (current study with 67.8 (13.0) years), with 46% of amputations being transfemoral/knee disarticulations (compared to 37% in current study). Participants were referred from hospitals across three provinces, and potential differences in pre- and post-amputation care may also have had an impact on HRQOL.

For longitudinal data, a multilevel model gives unbiased results if there is missing at random.[32] In our data, the baseline characteristics did not differ significantly by status (stayed in study, dropped out or died), indicating that in the beginning all patients had similar risk of drop-out (due to death or other reasons). However, quality of life is likely to be related to the probability of dropping out due to morbidity or death. We are aware that the assumption of missing at random might be not true in our data. The sample size of our study, however, is too small to do more sophisticated analyses. In a post-hoc analysis of data of the 35 participants who remained in the study at 18 months, a similar pattern of improvement in HRQOL results was seen. This indicates that the improvement in HRQOL was not attributable to patients with a poorer health status dropping out or dying.

The RAND-36 is a generic health status questionnaire. Therefore, results can be compared across different populations, both healthy and with pathology. However, use of a generic measure does not identify issues that are of specific importance for the LLA population. Use of the RAND-36 along with an amputation specific measure, for example, the Trinity Amputation and Prosthesis Experience Scales[10] is encouraged. This combination will allow comparison to other populations whilst still highlighting problems that are specific for people with LLA.

The population of elderly patients with vascular-related LLA may have found some of the questions of the RAND-36 limiting as the questionnaire is considered as potentially burdensome for the elderly population.[20] In particular, the domains role-limitation emotional and role-limitation physical were unable to be evaluated due to substantial number of missing responses and floor/ceiling effects, which made the results non-interpretable. A Veteran's version of the RAND-36 has been developed[33] and might be a better alternative for future investigations.

Conclusions

In this longitudinal study, we report a significant improvement in many aspects of HRQOL after LLA, with most change evident in the first 6 months. Use of multilevel analysis incorporated results from all patients, including those who later dropped out of the study or died. For elderly patients, physical function was rated very poorly but the remaining domains of HRQOL did not differ or were better than norm values. Younger patients differed from the norm values in physical function and pain. The ability to walk was linked only to social function, the distance walked did not matter. Time, age and walking distance are just three of many factors to be considered when evaluating HRQOL after LLA.

References

(1) Zidarov D, Swaine B, Gauthier-Gagnon C. Quality of life of persons with lower-limb amputation during rehabilitation and at 3-month follow-up. Arch Phys Med Rehabil 2009;90:634-645.

(2) Hanley MA, Jensen MP., Ehde DM, et al. Psychosocial predictors of long-term adjustment to lower-limb amputation and phantom limb pain. Disabil & Rehabil 2004;26:882-893.

(3) Sinha R, Van Den Heuvel WJ. A systematic literature review of quality of life in lower limb amputees. Disabil Rehabil 2011;33:883-899.

(4) Davidson JH, Khor KE, Jones LE. A cross-sectional study of post-amputation pain in upper and lower limb amputees, experience of a tertiary referral amputee clinic. Disabil Rehabil 2010;32:1855-1862.

(5) Pezzin LE, Dillingham TR, MacKenzie EJ. Rehabilitation and the long-term outcomes of persons with trauma-related amputations. Arch Phys Med Rehabil 2000;81:292-300.

(6) Hammarlund CS, Carlstrom M, Melchior R, et al. Prevalence of back pain, its effect on functional ability and health-related quality of life in lower limb amputees secondary to trauma or tumour: a comparison across three levels of amputation. Prosthet Orthot Int 2011;35:97-105.

(7) Schoppen T, Boonstra A, Groothoff JW, et al. Job satisfaction and health experience of people with a lower-limb amputation in comparison with healthy colleagues. Arch Phys Med Rehabil 2002;83:628-634.

(8) Harness N, Pinzur MS. Health related quality of life in patients with dysvascular transtibial amputation. Clin Orthop Relat Res 2001;(383):204-207.

(9) Smith DG, Horn P., Malchow D, et al. Prosthetic history, prosthetic charges, and functional outcome of the isolated, traumatic below-knee amputee. J Trauma 1995;38:44-47.

(10) Gallagher P, MacLachlan M. The Trinity amputation and prosthesis experience scales and quality of life in people with lower-limb amputation. Arch Phys Med Rehabil 2004;85:730-736.

(11) Asano M, Rushton P, Miller WC, et al. Predictors of quality of life among individuals who have a lower limb amputation. Prosthet Orthot Int 2008;32:231-243.

(12) Deans SA, McFadyen AK, Rowe PJ. Physical activity and quality of life: A study of a lower-limb amputee population. Prosthet Orthot Int 2008;32:186-200.

(13) van der Schans CP., Geertzen JHB, Schoppen T, et al. Phantom pain and health-related quality of life in lower limb amputees. J Pain Symptom Manage 2002;24:429-436.

(14) Horgan O, MacLachlan M. Psychosocial adjustment to lower-limb amputation: a review. Disabil Rehabil 2004;26:837-850.

(15) Bak P., Muller WD, Bocker B, et al. [Changes in Health-Related Quality of and Functional Independence in Patients after Lower Limb Amputation and In-Patient Rehabilitation Program] [German]. Physikalische Medizin Rehabilitationsmedizin Kurortmedizin 2003;13: 345-353.

(16) Geertzen JHB, Bosmans JC, van der Schans CP., et al. Claimed walking distance of lower limb amputees. Disabil Rehabil 2005;27:101-104.

(17) Ephraim PL, Dillingham TR, Sector M, et al. Epidemiology of limb loss and congenital limb deficiency: a review of the literature. Arch Phys Med Rehabil 2003;84:747-761.

(18) Fortington LV, Rommers GM, Geertzen JH, et al. Mobility in elderly people with a lower limb amputation: a systematic review. J Am Med Dir Assoc 2012;13:319-325.

(19) Van der Zee KI, Sanderman R. Het meten van de algemene gezondheidstoestand met de RAND-36.Een handleiding. [Measuring general health status with the RAND-36. Users manual]. Groningen: Northern Center of Health Care Research; 1994.

(20) Van der Zee KI, Sanderman R, Heyink JW, et al. Psychometric qualities of the RAND 36-Item Health Survey 1.0: a multidimensional measure of general health status. Int J Behav Med 1996;3:104-122.

(21) Singer JD, Willett JB. Applied Longitudinal Data Analysis: Modeling Change and Event Occurrence. New York: Oxford University Press; 2003.

(22) Price ME, Fisher K. How does Counseling Help People with Amputation? J Prosthet Orthot 2002;14:102-106.

(23) de Godoy JMP, Braile DM, Buzatto SHG, et al. Quality of life after amputation. Psychol, Health Med 2002;7:397-400.

(24) Briggs W. The mental health problems and needs of older people following lower-limb amputation. Rev Clin Gerontol 2006;16:155-163.

(25) Kratz AL, Williams RM, Turner AP, et al. To lump or to split? Comparing individuals with traumatic and nontraumatic limb loss in the first year after amputation. Rehabil Psychol 2010;55:126-138.

(26) Epstein RA, Heinemann AW, McFarland LV. Quality of life for veterans and servicemembers with major traumatic limb loss from Vietnam and OIF/OEF conflicts. J Rehabil Res Dev 2010;47:373-385.

(27) Sprangers MA, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. Soc Sci Med 1999;48:1507-1515.

(28) McPhail S, Comans T, Haines T. Evidence of disagreement between patient-perceived change and conventional longitudinal evaluation of change in health-related quality of life among older adults. Clin Rehabil 2010;24:1036-1044.

(29) McCutcheon T, Knepp T, Richards N, et al. Comparison of quality of life of persons who have experienced amputations and persons who have had bowel resections. Gastroenterol Nurs 2005;28:221-226.

(30) Pell JP, Donnan PT, Fowkes FGR, et al. Quality of life following lower limb amputation for peripheral arterial disease. Eur J Vasc Surg 1993;7:448-451.

(31) Fortington LV, Rommers GM, JJ van Netten, et al. Lower limb amputation in Northern Netherlands; unchanged incidence from 1991-1992 to 2003-2004. Prosthet Orthot Int. Early online DOI: 10.1177/0309364612469385.

(32) Rubin DB. Inference and missing data. Biometrika 1976:63;581–592.

(33) Kazis LE, Miller DR, Clark JA, et al. Improving the response choices on the veterans SF-36 health survey role functioning scales: results from the Veterans Health Study. J Ambul Care Manage 2004;27:263-280.

Chapter 7

Mobility in elderly people with a lower limb amputation: a systematic review

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Abstract

Background: Elderly people with a lower limb amputation impose a heavy burden on health resources, requiring extensive rehabilitation and long term care. Mobility is key to regaining independence. However, the impact of multiple comorbidities in this patient group can make regaining mobility a particularly challenging task. An evidence based prognosis for mobility is needed for rehabilitation and long term care planning. This systematic review summarises the prosthetic and non-prosthetic mobility outcomes achieved by elderly people with a lower limb amputation, to determine whether an accurate prognosis for mobility can be made.

Methods: MEDLINE, EMBASE and CINAHL were searched for studies published prior to May 2010 in English, German, Dutch or French, using keywords and synonyms for elderly, mobility, rehabilitation and amputation. Mobility focussed on actual movement (moving from one place to another) and was limited to long term measurements, 6 months after amputation or 3 months after discharge from rehabilitation.

Results: The fifteen included studies featured a diversity of objective outcome measures and mobility grades which proved difficult to compare meaningfully. In general, studies which included selected populations of prosthetic walkers showed that advanced prosthetic mobility skills can be achieved by the elderly person with a lower limb amputation, including outdoor/community walking. Studies which included all subjects undergoing a lower limb amputation reported that less than half of the elderly population achieved a household level of prosthetic mobility.

Results: The predominant findings from the included studies were incomplete reporting of study populations and poor reporting of the reliability of the mobility measures used. Therefore, the strength of conclusions from this review was limited and the prognosis for mobility in elderly people after lower limb amputation remains unclear. Further research into mobility outcomes of this population is needed to provide evidence that enables more informed choices in rehabilitation and long term care needs.

Introduction

Major lower limb amputation (LLA) is a frequently performed procedure in elderly people requiring extensive rehabilitation and long term care. Most LLA are in people older than 60 years with vascular disease and/or diabetes[1] and many people are discharged to nursing homes for their post-acute or long term care.[2,3] Population ageing and increasing rates of diabetes suggest that elderly people with LLA will remain an important subgroup and will continue to place a significant burden on health resources and long term care facilities.

The specific presentation of elderly persons with LLA, with multiple physical, psychological, cognitive, and social comorbidities, imposes unique challenges to ongoing care. Patients are often systemically unwell with their related comorbidities, for example, cardiovascular disease or end-stage renal disease.[4-6] In addition, there are comorbidities experienced by the wider elderly population, physiological changes from ageing, and complications from immobilisation through attempts to save the limb, such as deconditioning and contractures.[4-6] Post amputation, there is a relatively short life expectancy with 50% survival after 2 years.[7,8] Together, the combination of comorbidity and mortality imposes some pressure on determining a prognosis and choosing the right course of action for rehabilitation and/or long term care.[4,6]

Mobility is a key component of independent living, enabling the performance of activities of daily living. For people with LLA, mobility provides independence and a higher quality of life,[9,10] and can mean the difference between returning to home or remaining in a long term care facility. Rehabilitation of mobility after LLA focusses primarily on prosthetic walking. Although an older age alone does not prevent prosthetic walking,[11-14] the comorbidities described previously can impede against the higher energy, strength, and cognitive demands required for prosthetic walking.[4,6] Older age is associated with less use of a prosthesis and with lower rates of prosthetic prescription.[9,10,14-18] After discharge from rehabilitation, it is reported that elderly people use their prosthesis infrequently or not at all,[9,19,20] and there may be times when problems with the residual limb or prosthesis will prevent prosthetic walking. Therefore, rehabilitation programmes also include training in nonprosthetic mobility skills, for example, use of a wheelchair and training in transfers. These mobility skills can enable continued independence in personal and household care, or provide greater opportunities to be active in the community.

Despite the assumed importance of both prosthetic and nonprosthetic means of mobility, particularly for elderly amputees, previous systematic reviews have focussed only on prosthetic walking outcomes or predictors of walking.[15,17,18] The prognosis for mobility in elderly persons with LLA is unclear. Options and goals for rehabilitation are subsequently based largely on empirical knowledge. Stronger evidence is needed to facilitate discussion, enable informed rehabilitation choices, and help in formulating case-specific goals for long term care.[12] The aim of this systematic review was to summarise publications reporting an established (long term) prosthetic or nonprosthetic mobility outcomes in elderly people with LLA, and to determine whether a prognosis for mobility can be made.

Methods

Search Strategy

A systematic literature search of MEDLINE (Ovid), EMBASE, and CINAHL was performed using database specific keywords, medical subject headings, and free text synonyms for (lower limb) amputation, aged, rehabilitation and mobility . All publications were included; no restrictions to date were applied, and initially no restrictions to language were applied.

Two investigators independently assessed all publications at each stage of the review according to predefined inclusion and exclusion criteria. Only titles that were excluded by both investigators were removed; where one or both investigators included a title, the publication was reviewed further. Where results differed on the exclusion of an abstract or full-text publication, the investigators reached agreement through discussion or, if disagreement remained, a third person was consulted for a final decision. A measure of agreement between the 2 investigators (Cohen's κ) was calculated at each stage of the review for those publications dated before November 2008.

The search was first performed in November 2008, and updated in May 2010; in the updated search, the investigators were no longer considered as independent assessors and a measure of agreement could not be calculated. The reference lists of all fulltext publications were examined for additional studies with the same inclusion and exclusion criteria applied to the titles, abstracts, and full text of relevant publications accordingly.

Inclusion and Exclusion Criteria

Publications were first screened by title to include those with a focus on rehabilitation outcomes after LLA. Excluded were studies with a surgical, pathology or technical focus, expert reviews, case reports, letters and opinions, and studies that were clearly not undertaken in a population of elderly persons with LLA, for example, where the title stated upper limb or pediatric subjects. Abstracts and full-text publications were assessed to include those reporting a long term mobility outcome, in an elderly population consisting of 10 or more subjects with major LLA. Major LLA was considered as being at or proximal to the transtibial level and included unilateral and bilateral amputations.

Elderly persons were defined as being 60 years and older. Abstracts were included where the mean age was older than 60 years and the full text was reviewed for detailed information on the age range of included subjects. Where a mobility outcome was reported in a clearly defined (sub)group older than 60 years, the publication was included. Mobility was defined as independent movement from point A to point B, with or without a prosthesis, gait aids, or wheelchair. Mobility included transfers from one point to another (for example, wheelchair to car) and standing up from sitting or lying, but did not include small changes in position, such as shifting position within a bed or chair. Global measures that include many outcomes, such as functional tasks or activities of daily living, were included only if a score for a mobility subscale was reported separately. Prosthetic prescription, prosthetic use versus nonuse, and reporting of time spent wearing a prosthesis, were not considered as measures of mobility. Mobility was to have been measured at a minimum of 6 months after amputation or 3 months after discharge from a rehabilitation programme. If the timing of the measurement was not clearly stated, the publication was excluded.

Publication Assessment

Two investigators independently assessed all included studies. No existing quality assessment checklist was applicable to the included study designs and our aim. Taking into account items from the Downs and Black criteria[21] and items that the authors agreed were important for the description of mobility in elderly people with LLA, an assessment strategy was developed (Table 1). The items were assessed as yes, no, or unclear for the entire reported study population, irrespective of whether separate data were given for an elderly subgroup. A score with a maximum of 8 was given.

Table 1: Publication assessment criteria

Description of assessment criteria
1. The aim, research question and/or hypotheses was clearly reported
2. Eligibility criteria (inclusion and/or exclusion of subjects) were reported
3. The population and/or setting from which subjects were drawn was reported
4. Descriptive data* for sex were reported
5. Descriptive data* for cause of amputation were reported
6. Descriptive data* for level of amputation were reported
7. Descriptive data* for unilateral/bilateral amputations were reported
8. A statement concerning reliability of the mobility measure was reported

* number, percentage or ratio.

Summary Data Extraction

Summary data were extracted for subject characteristics, study design, and mobility outcomes for the older subgroups only. If separate data were not available, the table result was left blank.

The studies were grouped by the type of outcome measure: (1) objectively measured, for example, the time taken to perform a test or an actual distance walked; or (2) assigned by a researcher, for example allocating a patient to a mobility grade. All results were presented as a total of the original included population who were older than 60 years.

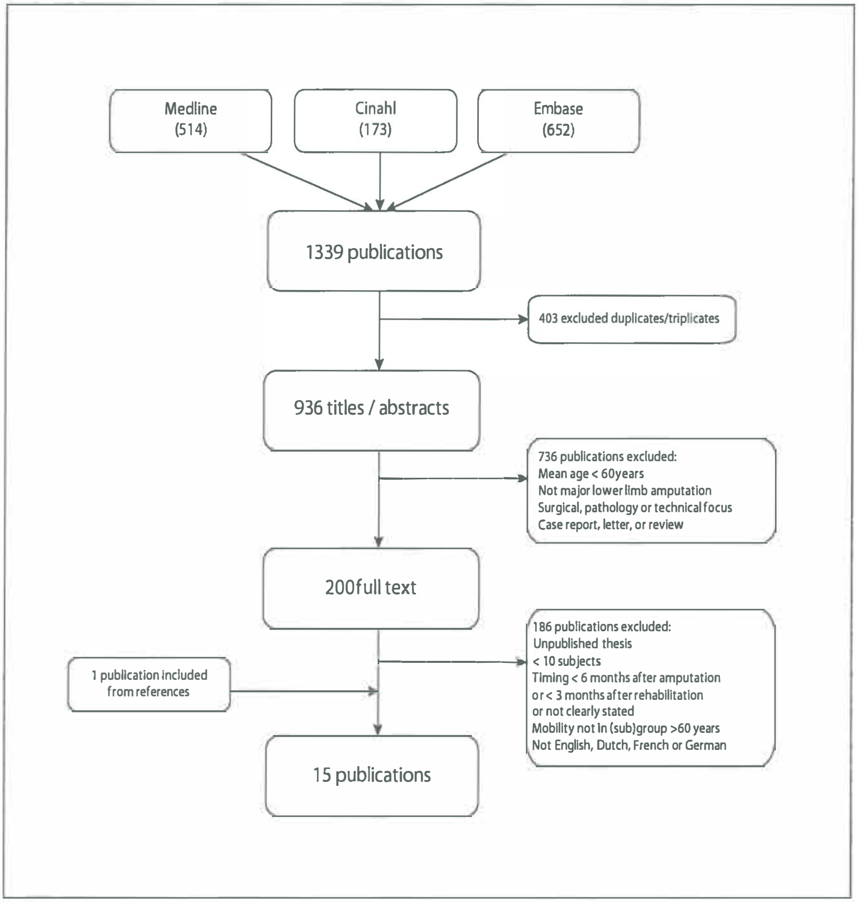
For the mobility grades, a level was selected that most closely represented: (1) household prosthetic walking, with or without a gait aid; and (2) independent mobility through any means, for example, by using a wheelchair or gait aids. Results for elderly subjects scoring at or above the corresponding level were summed; the result presented is the number achieving at least that level of mobility. The mobility grade descriptions were summarised from each authors own wording.

Results

A total of 936 unique publications were identified after removal of duplicates and triplicates (Figure 1). Screening by title and abstract excluded 736 publications and a further 186 were excluded after full-text revision. Cohen's kappa was 0.58 (title), 0.36 (abstract), and 0.53 (full text). One publication was included after thoroughly searching the reference lists of all 200 included full-text publications. Fifteen studies, dating from 1967 to 2005, met all inclusion criteria. Data relating to the population characteristics and mobility outcomes for the elderly (sub) groups were summarised (Table 2). Two studies reported 2 different mobility measures; these studies are presented twice in Table 2 accordingly.[22,23] One study referred to previously published data; this was combined and presented together.[24,25]

Assessment of prosthetic mobility was the primary aim in 5 publications.[24,26–29] In others, mobility was reported alongside a range of different outcomes including survival, wound healing, and activities of daily living[23,30–33] or a mobility outcome ensued from assessment of the clinimetric properties of a measurement tool.[22,34,35] From the setting and population, patients could be divided into (1) those who were "selected," referring to people admitted to a rehabilitation or prosthetic centre, who were prosthetic walkers and/or had a prosthesis prescribed and (2) those who were "unselected," referring to the

Figure 1: Publication selection



inclusion of all patients who underwent a lower limb amputation. Table 2 shows that most studies performed a cross-sectional mobility measure, with 4 studies reporting a longitudinal mobility measure for the older population.[27,28,34,35] Five studies scored a maximum of 8 for reporting of all assessment criteria.[22,23,26,27,34]

Objective measures were used to record the time taken to walk a distance, the actual distance walked, or the number of steps taken in a day. All objective measures were applicable only for prosthetic walkers with a sample size between 14 and 53. One study included all patients undergoing amputation, with 18 (39%) of 46 able to perform the objective test.[23] Timed walk tests, incorporating a chair stand, short walk, and 180° turn, were used in 2 studies, with a walking distance of 3m[23] or 5m[22] covered. Poorer performance by people with a transfemoral amputation versus a transtibial level was apparent where compared. This included

Table 2: Summary data for long term mobility outcomes for elderly people with lower limb amputation

									MOBILITY GRADES	
Author, Year	Aim	Criteria met ‡	Pop	N (%)	Age	Men n (%)	Vasc n (%)	Level n (%)	Mobility measure (no.of grades) [Reliability] [Type of	Results
Davies, 2003	Prosthetic mobility	8	S	127 (281)	- (65-95)	-	-	BK=97 (49) AK=100 (51) [B=4 (2)]	Harold-Wood-Stanmore scale (1-6) [Y] [C]	H: 107 (54%): gait aids indoors, minimal outdoor walking M: 114 (58%): transfers, walks with therapist or carer
Schoppen, 2003*	General outcomes	8	U	46 (46)	74 ±8 (≥60)	32 (70)	46 (100)	BK=33 (72) AK=13 (28)	Adapted Narang/ Pohjolainen scale (1-8) [N] [C]	H: 18 (39%): indoor prosthetic walking with gait aids M: 26 (57%): non-ambulatory mobility, w/c users
Hermodsson, 1998	Mobility tool assessment	8	U	50 (50)	79 +7 (61-92)	26 (52)	50 (100)	BK=52 (100)	Functional rating scale for amputees (1-8) [Y] [L]	H: 8 (16%) discharge; 11 (22%) 6 mo: with gait aids M:19 (38%) discharge;18 (36%) 6 mo: w/c, ind. transfers
Datta, 1996*	Mobility tool assessment	8	S	53 (53)	70 (60-80)	36 (68)	43 (81)	BK=26 (49) AK=27 (51)	Volpicelli scale (0-6) [N] [C]	H: 50% (median): walking < 30m, w/c used outdoors
Valentine, 1996	General outcomes	7	U	75 (125)	67 ±0.6 (60-80)	66 (88)	75 (100)	BK=46 (61) AK=29 (39) [B=21 (28)]	Modified Volpicelli scale (1-4) [N] [C]	H: 21 (28%): indoors, negotiates carpets, stairs with rails M: 61 (81%): w/c ambulators, independent transfers
McWhinnie, 1994	General outcomes	7	U	31 (96)	- (80-95)	-	31 (100)	BK=20 (65) AK=11 (35)	Self developed scale (1-3) [N] [C]	H: 7 (23%): walking in the home M: 19 (61%): prosthetic walking or use of w/c
Campbell, 1994	General outcomes	7	U	- (210)	- (80-96)	-	-	-	Self developed scale (1-6) [N] [C]	-
Wong, 2005	General outcomes	6	U	- (184)	- (80-93)	-	-	-	Volpicelli scale (0-6) [N] [C]	H: of 53 successful community ambulators 18.9% were > 80 years
Steinberg, 1985	Prosthetic mobility	6	S	116 (116)	73 (65-86)	71 (61)	-	BK=66 (57) AK=30 (26) ?=2(2),B=18(16)‖	Self developed scale (1-3) [N] [C]	H: 81 (70%): prosthetic walking, w/c for trips
Lam, 1981	-	6	S	58 (115)	- (61-85)	-	-	-	Self developed scale (1-3) [N] [C]	H: 33 (57%): walking with gait aids, w/c used outdoors
Nehler, 2003	-	5	U	11 (154)	- (≥75)	-	11 (100)	-	Self developed scale (1-3) [N] [C]	H: 2 (18%): ambulatory indoors
Siriwardena, 1991	Mobility tool assessment	5	S	- (598)	- (≥60)	-	- (100)	BK=196 (49) AK=220(51) B= -	Self developed, Walking Ability Index (1-6) [N] [L]	-
Anderson, 1967†	Prosthetic mobility	5	S	81 (92)	70 (60-87)	46 (57)	81 (100)	BK=44 (54) AK=23 (28) B=14 (17)‖	Russek scale (1-6) [N] [C]	H: 46 (57%): enabling complete self care

OBJECTIVE MEASURES

Author, Year	Aim	Criteria met ‡	Pop	N (%)	Age	Men n (%)	Vasc n (%)	Level n (%)	Mobility measure [Reliability] [Type of measure]	Results
Schoppen, 2003*	General outcomes	8	U	46 (46)	74 ±8 (≥60)	32 (70)	46 (100)	BK=33 (72) AK=13 (28)	3m Timed up & go [Y] [C]	18 (39%) performed test. Mean (SD) = 23.9s (13.2) median = 21.3s Age not associated with up & go score
Datta, 1996*	Mobility tool assessment	8	S	53 (53)	70 (60-80)	36 (68)	43 (81)	BK=26 (49) AK=27 (51)	5m Timed walking test [Y] [C]	Mean (SD, range) = 36.9s (25.0, 13-140)
Devlin, 2002	Prosthetic mobility	8	S	14 (14)	70 ±6 (61-80)	11 (79)	14 (100)	AK = 14 (100)	2min walk test [Y] [L]	Mean (SD) distance with articulating knee=44.9 +28.9m with locked knee=54.4+35 (p=0.001)
Holden, 1987	Prosthetic mobility	7	S	36 (-)	- (65-90)	-	-	BK=22 (61) AK=14 (39)	Electronic step count (steps/day) [-] [L]	Mean (SD): discharge=570 (337); 1st year=1314 (1135) 2nd year=1356 (1309) TF 1st year = 686 (-)

Pop, population described as U (unselected) or S (selected); N, number of elderly amputees (total number of subjects in study). Age, Mean age + SD and (range for elderly subgroup); Men, number of men in population; Vasc, amputations due to peripheral vascular disease or related causes; BK, below-knee amputation (includes transtibial); AK, above-knee amputation (includes knee disarticulation, transfemoral and hip disarticulation); B=n, bilateral amputees contributing independently to the total of all amputation levels; [B=n], bilateral amputees are counted within the total of all other amputations; ?, data reported as unknown in study; Reliability, there is a statement concerning reliability of the mobility measure Y (yes) or N (no); Type of measure, the mobility outcome was a C: cross-sectional measurement or L: Longitudinal measurement; m, meters; min, minutes; H, n(%) with household mobility or higher level; M, n(%) mobilizes independently or higher level; mo, months; w/c, wheelchair; s, seconds; IQR, interquartile range; TT, transtibial; TF, transfemoral.

* Publication appears twice in table, as it reports more than one type of mobility measure.

† Data extracted from Table 1 Anderson et al 1967 and Table 2 Cummings et al 1963.

‡ Criteria based on Table 1, for all included patients, maximum score of 8.

‖ Percentages do not add to 100 due to rounding.

15.8 seconds slower in the 5m walk test[22] and fewer steps taken per day 1 year after amputation, transfemoral taking 686 steps compared with 1314 steps for transfemoral and transtibial levels combined.[28] One year after discharge, people with transfemoral or transtibial amputations increased the number of steps taken per day from 570 steps at discharge to 1314 steps. They maintained this in the second year with 1356 steps.[28] Finally, people with transfemoral amputation who used a locked knee compared with when they used an articulating knee were able to walk 9.5m further in 2 minutes.[27]

Thirteen studies assigned patients to a mobility grade with data ascertained from clinical records or by clinical assessment. The mobility scales defined 3 to 8 levels of mobility according to skill, environment, independence, and/or use of gait aids. Six scales were self-developed.[29–31,35–37] Three studies used a scale originally described by Volpicelli.[38] However, results were summarised and presented differently.[22,32,33] A mobility level equivalent to independent household prosthetic walking with or without gait aids, or higher, was achieved by 18%[37] to 39%[23] of unselected patients and by 50%[24] to 70%[29] of selected patients. A minimum mobility level equivalent to being independent through prosthetic or nonprosthetic means, was achieved by 36%[34] to 81%[32] of unselected patients. One study of selected patients reported 58% of people achieving at least a level of independent mobility, using a prosthesis for transfers and walking only with a therapist or carer.[26]

Discussion

In this systematic review, we aimed to summarise the prosthetic and nonprosthetic mobility outcomes achieved by elderly people with LLA. Evidence of mobility outcomes is needed to assist planning of rehabilitation and long term care needs. Elderly people with LLA have long been the subject of expert reviews and “current best practice” articles. They are recognised as a unique population owing to the combination of physical, psychological, and social comorbidity they often present with. The potential bias from the inclusion of younger patients into a study with an elderly population with LLA supports the need for independent investigation.[12] Despite this, there were relatively few high-quality scientific studies of mobility that looked at the population independently of younger patients. Considered together with a Cochrane Review into patients older than 60 years with transfemoral amputation, which found only 1 trial concerning the preferred weight of a prosthesis,[16] it is clear that there is a need for more research focussed on this population.

Elderly patients and mobility outcomes were not the primary focus of all included studies; instead, a mobility outcome was reported in a subgroup of elderly patients, alongside amputation healing, mortality, and other general functional outcomes. Most studies were descriptive, cross-sectional studies of a case series. The application of existing quality assessment tools proved too extensive with a substantial number of items inapplicable. Therefore, assessment of methodological quality was based on items addressing internal and external validity, which the authors agreed were important in describing mobility in people with LLA. The bias inherent in selected populations of prosthetic walkers, compared with unselected populations inclusive of all patients, must be taken into account when describing mobility after LLA.[12] Few studies met all assessment criteria, which limits generalisation of the results.

A mobility outcome should be reliable and valid for patients with LLA and responsive to change.[39] The assessment of these aspects in this review was minimal, simply "*Is there a statement anywhere in the article concerning reliability of the mobility outcome measure*?" Only 5 studies included this information.[22,23,26,27,34] Limitations in comparing results between studies have also been described in previous systematic reviews of prosthetic walking and mobility scales.[17,18,40] Improvements, such as standardisation in reporting of outcome measures (with the inclusion of a statement about reliability of the measure), as well as population characteristics (including the level of amputation, cause of amputation, and so forth), is essential for improving the overall methodological quality of future studies.

Fifteen different measurement tools were used to assess mobility in elderly people with LLA. These were presented in 2 categories: objective measures and assigned measures of mobility. The objective measures included 3 walk tests. The 2-minute walk test measures the distance walked in 2 minutes and the up-and-go test measures how quickly a person can stand from a chair, walk a short distance, turn 180°, and return to a seated position; 2 variations of this test were conducted over different distances (3m and 5m), so unfortunately could not be compared.[22,23] For prosthetic walkers, including the elderly population specifically, the timed up-and-go test is recommended for use in assessing mobility. It has demonstrated reliability, validity, responsiveness, ease of use in a clinical setting, and it replicates the type of mobility needed for a household situation.[22,41–43] Use of the detailed procedure described by Schoppen et al[43] is recommended to allow the results of future studies to be compared.

A second objective measure identified was the electronic step-count device.[28] Ambulation monitoring devices, including specific devices for use with prostheses, have been more extensively developed in recent years, but not as yet studied in an elderly population.[44,45] Accuracy with use of the devices may be limited in people who walk at a slow velocity or with a nonsymmetrical gait.[46] An important first step is selection and testing of reliability and validity of these devices in the elderly population.

The second group of outcome measures were those that saw subjects assigned to a mobility grade, either by direct observation or by review of clinical records. In general, scales are simple for routine clinical use, giving descriptive information not only on achievement of prosthetic walking, but also on use of gait aids, use of a wheelchair, and ability to transfer. From the included studies, explicit and identifiable differences in mobility were lost owing to the great diversity of scales and definitions used; some described just 3 levels of mobility and others provided detail of up to 8 levels. Many scales were self-developed by the authors of each study. Only 2 of the studies gave consideration to reliability of the scale: the Functional Rating Scale for Amputees and the Harold- Wood-Stanmore scale.[26, 34] The latter was previously found as the most frequently used scale in literature[40] and was later developed into the Special Interest Group in Amputee Medicine (SIGAM) scale.[47] The SIGAM scale is recommended for use to describe basic, clinically useful functional levels, with demonstrated reliability.[11,42,47] However, the SIGAM scale was not identified in this review as having been used in an elderly population; it is limited to prosthetic mobility only and whereas the Harold-Wood- Stanmore scale is a therapist-assigned measure, the SIGAM scale is based on results from a questionnaire.[47] The Functional Rating Scale for Amputees incorporates prosthetic and nonprosthetic mobility including (in)dependence with a wheelchair and use of assistive devices but has not been used extensively. Three studies[22,32,33] used a scale originally described by Volpicelli but the clinimetric properties of this scale have not been reported.[42] Consensus on the use and application of mobility scales that include prosthetic and nonprosthetic mobility, as well as a preferred option for the elderly population, is required to enable more accurate comparison of results between studies.

Results from the included studies confirmed that when looking at selected populations of elderly patients, mobility can be achieved by a high proportion of patients. From the mobility grading scales, up to 70% of people from a selected population maintained a household level of prosthetic walking for at least 6 months post amputation or 3 months post rehabilitation.[29] Studies inclusive of all patients undergoing amputation reported up to 39% maintained prosthetic walking.[23] Taking into account that a proportion of the population will not survive the acute post amputation phase, the potential for surviving patients to achieve prosthetic walking appears quite high. In contrast, however, 3 studies reported that only about 20% of people maintained household prosthetic walking long term.[31,34,37] From a broader view, incorporating measures of both prosthetic and nonprosthetic mobility, between 36% to 81% of people were reported as being independently mobile.[32,34] With such great discrepancy in the results, a clinically useful prognosis for mobility in the elderly person with LLA cannot be made.

Amputation, patient characteristics and population selection are presented in Table 2. Additional variables addressed in the included studies were physical abilities (1-leg standing balance, pre-amputation mobility, physical comorbidity (cardiovascular disease, diabetes, stroke, chronic obstructive pulmonary disease), psychological comorbidity (depression, cognitive decline), cognitive traits (motivation, confidence), and social situation (marital status). Further investigation of these variables was prevented from the limitations imposed by the included studies, which were described earlier. Within the limitations of this review, the 1-leg balance test seems an important factor with potential for predicting prosthetic mobility. Missing from the included literature is the influence of rehabilitation setting, which may also affect mobility outcomes of elderly people with LLA. The variables described should be further investigated for their influence on mobility in this population. Provision of a prosthesis and gait training is a costly and time-consuming process. Being able to better select patients by their mobility potential, for example, those who will achieve and maintain prosthetic walking or those who could better focus on regaining nonprosthetic mobility, is an important goal for future research to aim toward.

Limitations of the review

A cautious approach was taken for the exclusion of articles, with 2 investigators independently reviewing all publications at each stage of the search and exclusions made only where both reviewers had agreed. Nevertheless, titles are inherently limited in the information that they can convey and we cannot rule out having excluded relevant studies if the focus appeared otherwise. A thorough reference check of all 200 full-text articles found only 1 additional publication, published in 1967, that lends support to the comprehensiveness of the original search strategy. Although agreement between reviewers during each stage of the original search was only moderate, as measured through Cohen's κ, no publication was excluded before discussion and agreement from at least 2 reviewers. A further limitation was that no measure of agreement could be calculated for the updated search, as the reviewers were no longer independent, having discussed publications in consensus meetings of the original search.

Isolating studies concerning elderly patients with LLA was problematic because of varied definitions. There were publications that, although they described "older" or "elderly" patients in the title, included patients younger than 50 years,[48–51] reported only a mean age,[52] or did not report the age at all.[53] There were also studies where nothing was immediately indicative that an elderly population had been studied.[23,30,34] To minimise the risk of missing a relevant publication, all abstracts were included where the mean or median age was older than 60 years, and then the full text was reviewed for detailed data concerning mobility in a subgroup older than 60 years. Age is frequently used in statistical models to predict mobility outcomes, with an increased age associated with a poorer mobility outcome. In general, these studies did not meet our inclusion criteria, as they presented no detail on the outcome for the elderly patient other than having a poorer outcome compared with their younger counterparts, and the publications were therefore excluded. Analysis within elderly-only groups would be of value to determine the effects of ageing within the elderly population.

There are many varied and important aspects to be addressed in rehabilitation of the elderly person with LLA, including psychological health, social support, care of the residual limb, and other physical functioning skills, such as activities of daily living. This article considered only mobility outcomes. Presently, there is no consensus on what constitutes a successful mobility outcome. Our criteria provided a strict time frame for measurement of mobility that would inform on established outcomes; that is, mobility was to be assessed 6 months after the amputation or 3 months after rehabilitation. Many publications were excluded because they gave no specific detail on timing or gave only the mean follow-up, with no standard deviation or range. Our criteria excluded reports of prosthetic use versus nonuse, prescription of a prosthesis, or duration of wearing a prosthesis, such as hours per day, although these measures may provide information on a preference for prosthetic walking. Studies considering balance only were also excluded, as the patient was not moving from one point to another, although balance may be a prerequisite for mobility.[17,18,23] Possibly, outcomes related to nonprosthetic mobility are studied through secondary measures such as general daily functioning or activities; for example, mobility may be implicit in a functional measure of performing a task such as independent meal preparation. The relationship between nonprosthetic mobility and functional independence could be investigated in future studies.

Many mobility grades have similarities with more general scales of daily function and independence. Publications were included where there was a focus on mobility but this was difficult to judge in some cases. Results from the mobility grades were summarised into (1) household prosthetic walking with or without a gait aid and (2) independent mobility through any means, for example, by using a wheelchair or gait aids. Given the variation in the number of mobility grades and scope of definitions within each grade, this categorisation was somewhat subjective. However, it did provide clarity and consistency in presentation of the studies, which would otherwise have not been evident. Summarising also allowed consistency in reporting of the results, with all reported as a proportion of the study's total included population.

Conclusions

The lack of strong findings drawn from this systematic review does not reflect the importance that mobility can afford in enabling independence for the elderly person with LLA. Evidence to support a prognosis for prosthetic and nonprosthetic mobility is not available in current literature. The unique requirements that elderly people face in their rehabilitation, arising from multiple comorbid conditions and a short life expectancy, support a need for further investigation of mobility in this population.

References

(1) Ephraim PL, Dillingham TR, Sector M et al. Epidemiology of limb loss and congenital limb deficiency: A review of the literature. Arch Phys Med Rehabil 2003;84:747-61.

(2) Rommers GM, Vos LD, Groothoff JW et al. Epidemiology of lower limb amputees in the north of The Netherlands: aetiology, discharge destination and prosthetic use. Prosthet Orthot Int 1997 August;21(2):92-9.

(3) Adunsky A, Wershawski M, Arad M et al. Non-traumatic lower limb older amputees: A database survey from a geriatric centre. Disabil Rehabil 2001;23(2):80-4.

(4) Andrews KL. Rehabilitation in Limb Deficiency. 3. The Geriatric Amputee. Arch Phys Med Rehabil 1996;77:S14-S17.

(5) Hakimi KN. Pre-operative Rehabilitation Evaluation of the Dysvascular Patient Prior to Amputation. Phys Med Rehabil Clin N Am 2009;20:677-88.

(6) Uustal H. Prosthetic rehabilitation issues in the diabetic and dysvacular amputee. Phys Med Rehabil Clin N Am 2009;20:689-703.

(7) Carmona GA, Hoffmeyer P, Herrmann FR et al. Major lower limb amputations in the elderly observed over ten years: The role of diabetes and peripheral arterial disease. Diabetes Metab 2005;31(5):449-54.

(8) Pohjolainen T, Alaranta H. Ten-year survival of Finnish lower limb amputees. Prosthet Orthot Int 1998;22:10-6.

(9) Bilodeau S, Hebert R, Desrosiers J. Lower limb prosthesis utilisation by elderly amputees. Prosthet Orthot Int 2000;24:126-32.

(10) Geertzen JHB, Bosmans JC, Van Der Schans CP et al. Claimed walking distance of lower limb amputees. Disabil Rehabil 2005;27:101-4.

(11) Graham LA, Fyfe NCM. Prosthetic rehabilitation of amputees aged over 90 is usually successful. Disabil Rehabil 2002;24:700-1.

(12) Fletcher DD, Andrews KL, Butters MA et al. Rehabilitation of the geriatric vascular amputee patient: A population-based study. Arch Phys Med Rehabil 2001;82:776-9.

(13)Hamamura S, Chin T, Kuroda R et al. Factors affecting prosthetic rehabilitation outcomes in amputees of age 60 years and over. J Int Med Res 2009;37:1921-7.

(14) Kurichi JE, Kwong PL, Reker DM et al. Clinical factors associated with prescription of a prosthetic limb in elderly veterans. J Am Geriatr Soc 2007;55(6):900-6.

(15) Adams E, Flynn K, Alligood E. A systematic review of clinical predictors of outcome in adults with lower limb amputation. http://www4 va gov/VATAP/docs/ClinicalPredictorsAdultsOutcomesLowerLimbAmputation2005tm pdf 2005. AccessedJune 10, 2009.

(16) Cumming JCO, Barr S, Howe TE. Prosthetic rehabilitation for older dysvascular people following a unilateral transfemoral amputation. Cochrane Database of Systematic Reviews 2006 December;(4).

(17) Sansam K, Neumann V, O'Connor R et al. Predicting walking ability following lower limb ampuation: a systematic review of the literature. J Rehabil Med 2009;41:593-603.

(18) van Velzen JM, van Bennekom CAM, Polomski W et al. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006 November;20:999-1016.

(19) Beekman CE, Axtell LA. Prosthetic use in elderly patients with dysvascular above-knee and through-knee amputations. Phys Ther 1987;67:1510-6.

(20) Collin C, Collin J. Mobility after lower-limb amputation. Br J Surg 1995;82:1010-1.

(21) Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;52:377-84.

(22) Datta D, Ariyaratnam R, Hilton S. Timed walking test - an all-embracing outcome measure for lower-limb amputees? Clin Rehabil 1996;10:227-32.

(23) Schoppen T, Boonstra A, Groothoff JW et al. Physical, mental, and social predictors of functional outcome in unilateral lower-limb amputees. Arch Phys Med Rehabil 2003;84:803-11.

(24) Anderson AD, Cummings V, Levine SL et al. The use of lower extremity prosthetic limbs by elderly patients. Arch Phys Med Rehabil 1967;48:533-8.

(25) Cummings V, Anderson AD, Levine SA et al. The Elderly Medically Ill Amputee. Arch Phys Med Rehabil 1963;44:549-54.

(26) Davies B, Datta D. Mobility outcome following unilateral lower limb amputation. Prosthet Orthot Int 2003;27:186-90.

(27) Devlin M, Sinclair LB, Colman D et al. Patient preference and gait efficiency in a geriatric population with transfemoral amputation using a free-swinging versus a locked prosthetic knee joint. Arch Phys Med Rehabil 2002;83(2):246-9.

(28) Holden JM, Fernie GR. Extent of artificial limb use following rehabilitation. J Orthop Res 1987;5:562-8.

(29) Steinberg FU, Sunwoo I, Roettger RF. Prosthetic rehabilitation of geriatric amputee patients: A follow-up study. Arch Phys Med Rehabil 1985;66:742-5.

(30) Campbell WB, St Johnston JA, Kernick VFM et al. Lower limb amputation: Striking the balance. Ann R Coll Surg Engl 1994;76:205-9.

(31) McWhinnie DL, Gordon AC, Collin J et al. Rehabilitation outcome 5 years after 100 lower-limb amputations. Br J Surg 1994;81:1596-9.

(32) Valentine RJ, Myers SI, Inman MH et al. Late outcome of amputees with premature atherosclerosis. Surgery 1996;119:487-93.

(33) Wong MWN. Changing dynamics in lower-extremity amputation in China. Arch Phys Med Rehabil 2005;86:1778-81.

(34) Hermodsson Y, Ekdahl C. Assessing functional ability in patients with unilateral trans-tibial amputation for vascular disease. Scand J Occup Ther 1998 December;5:167-72.

(35) Siriwardena GJA, Bertrand PV. Factors influencing rehabilitation of arteriosclerotic lower limb amputees. J Rehabil Res Dev 1991;28:35-44.

(36) Lam VT, Nieto J. Rehabilitation of unilateral femoral amputees, over 55 years of age and of vascular origin. Union Med Can 1981 September;110:774-9.

(37) Nehler MR, Coll JR, Hiatt WR et al. Functional outcome in a contemporary series of major lower extremity amputations. J Vasc Surg 2003;38:7-14.

(38) Streiner DL, Norman GR. Health measurement scales. A practical guide to their development and use. 4th ed. Oxford: Oxford University Press; 2008.

(39) Rommers GM, Vos LDW, Groothoff JW et al. Mobility of people with lower limb amputations: Scales and questionnaires: A review. Clin Rehabil 2001;15:92-102.

(40) Condie E, Scott H, Treweek S. Lower Limb Prosthetic Outcome Measures: A Review of the Literature 1995 to 2005. J Prosthet Orthot 2006;18:13-45.

(41) Deathe AB, Wolfe DL, Devlin M et al. Selection of outcome measures in lower extremity amputation rehabilitation: ICF activities. Disabil Rehabil 2009;31:1455-73.

(42) Schoppen T, Boonstra A, Groothoff JW et al. The timed 'up and go' test: Reliability and validity in persons with unilateral lower limb amputation. Arch Phys Med Rehabil 1999;80:825-8.

(43) Stepien JM, Cavenett S, Taylor L et al. Activity Levels Among Lower-Limb Amputees: Self-Report Versus Step Activity Monitor. Arch Phys Med Rehab 2007;88(7):896-900.

(44) Parker K, Kirby RL, Adderson J et al. Ambulation of people with lower-limb amputations: relationship between capacity and performance measures. Arch Phys Med Rehabil 2010 April;91(4):543-9.

(45) Ramstrand N, Nilsson KA. Validation of a patient activity monitor to quantify ambulatory activity in an amputee population. Prosthet Orthot Int 2007 June;31(2):157-66.

(46) Ryall NH, Eyres SB, Neumann VC et al. The SIGAM mobility grades: a new population-specific measure for lower limb amputees. Disabil Rehabil 2003 August 5;25(15):833-44.

(47) Harris KA, van SL, Carroll SE et al. Rehabilitation potential of elderly patients with major amputations. J Cardiovasc Surg 1991 July;32:463-7.

(48) Hutton IM, Rothnie NG. The early mobilization of the elderly amputee. Br J Surg 1977;64:267-70.

(49) Klein B, Gilad M, Gabbai N et al. Prosthetic rehabilitation following below-knee amputation in elderly persons. Int J Rehabil Res 2001;24:161-4.

(50) Sakuma J, Hinterbuchner C, Green RF et al. Rehabilitation of geriatric patients having bilateral lower extremity amputations. Arch Phys Med Rehabil 1974;55:101-11.

(51) Reyes RL, Leahey EB, Leahey J. Elderly patients with lower extremity amputations: Three year study in a rehabilitation setting. Arch Phys Med Rehabil 1977;58:116-23.

(52) Hubbard WA, McElroy GK. Benchmark data for elderly, vascular trans-tibial amputees after rehabilitation. Prosthet Orthot Int 1994;18:142-9.

Chapter 8

Bias in amputation research; impact of subjects missed from a prospective study

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Abstract

Background: For research findings to be generalised, a sample must be representative of the actual population of interest. Lower limb amputation is most frequently performed in older patients with vascular disease, a population that is often under-represented in research.

Aim/methods: The aim of this study was to explore the impact of selection bias by comparing characteristics from a sample included in a prospective study of phantom pain with the actual population who underwent amputation.

Results: Only 27% of all potential patients were referred during the first year of the prospective study. The referred patients were 8 years younger ($p<0.001$) and less likely to have had amputation because of a vascular condition, diabetes or infection ($p=0.003$) than those not referred. There was also a significant difference in one year survival between the groups; 67% of referred patients survived compared with just 40% of non-referred patients ($p=0.004$).

Conclusions: The biased population in the phantom pain study may have resulted in an underestimation of phantom pain in the original study and subsequent protective factors should be considered within the context of the younger population reported. Selection bias is common in amputation research, and research methods to minimise its impact must be given greater attention.

Introduction

After a lower limb amputation (LLA), people face a number of challenges including loss of mobility, altered body image and phantom pain. Research to better understand these consequences allows planning for rehabilitation and long term care and builds an evidence base from which we can more accurately inform patients on their expected outcomes. However, difficulties with population sampling are frequent in amputation research and this impacts our ability to draw accurate conclusions.

LLA is most frequently performed in older patients with vascular disease, a population that is, for the most part, under-represented in research.[1] Multiple comorbidities and cognitive decline can prevent this sub-population from meeting required inclusion criteria. The issue of bias in studies of elderly people is well recognised.[1-4] The same is true of amputation research, with authors' invariably describing selection bias within their sample as a limitation of their study.[5-11] However, the impact of this bias is rarely described.[12] It is important to understand this research limitation in applying results to clinical practice and to better design future studies.

In a prospective study of phantom limb pain, it was noted that the population characteristics of the included sample were considerably different from what would be expected in the LLA population.[5] The aim of the current study is to explore the impact of this bias on the primary outcomes (factors associated with phantom pain) by comparing the study sample with the actual population who underwent amputation.

Methods

Ethics statement

The study protocol was approved by the medical ethics committees of the University Medical Center Groningen. Patients participating in the phantom pain study provided their written informed consent.

Setting

Both studies were conducted in the 3 northern provinces of the Netherlands: Groningen, Friesland and Drenthe. Fourteen hospitals in the region performed lower limb amputations, generally under the care of a vascular surgeon. This study looks at patients who had a first ever unilateral transtibial amputation, knee disarticulation or transfemoral amputation between 1 January 2004 and 31 December 2004.

Phantom pain (PP) study

A prospective study ran from 1 November 2003 to 30 April 2008. At a face-to-face meeting, and confirmed afterwards in writing, surgeons were informed about the study including the aims, inclusion and exclusion criteria, and recruitment procedures.

The surgeons were requested to include all patients: [1] aged ≥18 years; [2] undergoing primary major amputation (at or proximal to metatarsophalangeal level); and [3] able to read and write in Dutch. The primary investigator discussed the study aims with the patient and they were asked to participate and give their written consent.

Exclusion criteria were: [1] had a previous ipsilateral amputation; [2] were too unwell or showed signs of clinical dementia which prevented completion of the questionnaires; or [3] were recruited more than 5 days after the amputation. If the surgeons themselves decided to exclude a patient, they agreed to send the characteristics of the patient (age, sex) and amputation details (level, cause) to the primary investigator to ensure a complete census of patients was recorded. The primary investigator maintained regular contact with the study coordinator at each hospital.

Population study

In 2010, surgeons from each hospital were contacted about a new study on the incidence of LLA. Surgeons from all hospitals agreed to participate. They were requested to compile a list of patients who underwent major amputation in 2004. The medical records of these patients were reviewed between August 2010 and July 2011 for patient data (age, sex), amputation details (level, cause), marital status, comorbidities and medical history including previous minor amputations or peripheral vascular procedures (angioplasty, embolectomy or peripheral bypass) and survival or date of death. To ensure a complete survival dataset, general practitioners were contacted for patients whose status was not up to date in hospital records.

Statistical analysis

Characteristics of referred patients (irrespective of whether they were included or excluded from analyses in the original study) were compared with the non-referred patients using $\chi 2$ tests for categorical variables, Mann-Whitney U test for age distribution and log rank tests for survival. Significance was set at 0.05 and analyses were performed using PASW Statistics version 18.0.

Results

Surgeons representing 12 of 14 hospitals attended the information meeting of the PP-study. Two hospitals were unable to participate because of restrictions from their local administration and medical ethics procedures. Surgeons from ten hospitals agreed to participate in recruitment of patients. From the current study, one hospital was unable to identify the relevant files because of changes in their database. This hospital was excluded and subsequently, one patient from this hospital who had been referred to the PP study was excluded.

Thirty nine (27%) of a possible 146 patients were referred during the first full year of the study (table 1). The referred population had a median age 8 years younger ($p< 0.001$) and were less likely to have had amputation because of a vascular condition, diabetes or infection ($p=0.003$) than those who were not referred. More non-referred patients had bilateral amputation while more referred patients had a knee disarticulation ($p=0.049$). No differences in the number or type of major comorbidities were seen, although referred patients were more likely to have had undergone a previous vascular intervention ($p=0.042$) such as a peripheral bypass procedure or angioplasty. Referred patients were more frequently discharged home or to a rehabilitation centre with non-referred patients more often discharged to a care centre ($p=0.020$).

There was a significant difference in one year survival between the groups; 67% of referred patients survived compared with 40% of non-referred patients ($p=0.004$). Overall survival time after amputation also differed significantly (figure 1): median (standard error) survival for referred group = 41.1 (7.9) months, non-referred = 13.6 (6.6) months, $\chi 2(1df) = 5.6$; $p=0.018$.

To verify whether or not the differences in the groups were linked to the significantly poorer survival of the non-referred population, characteristics of patients who survived to 12 months are presented in table 2. There remained a significantly younger median ($p=0.016$) and mean ($p=0.007$) age difference between the referred and non-referred group. Again, the referred group were more likely to have had a knee disarticulation, less likely to have had a transtibial amputation ($p=0.041$), and more frequently had amputation because of non-vascular causes (0.012). There were no other significant differences between the referred and non-referred groups in 12 month survivors. Overall survival differed by 9 months (median (standard error) survival for referred group = 64.1 (14.7) months, non-referred = 55.6 (11.5) months, $\chi 2(1df) = 1.8$; $p=0.177$) and non-referred patients were more frequently discharged to a care centre while referred patients were more often discharged to a rehabilitation centre ($p=0.130$).

Table 1: Characteristics of referred and non-referred patients and actual population.

n (%)	Referred (PP study)		Not referred		p	Actual population
Total included	39	(27)	107	(73)		146
Age, median (IQR) *	67.6	(50.8 ; 72.9)	75.5	(68.1 ; 83.3)	<0.001†	73.0 (65.2 ; 80.9)
Age, mean (sd)	63.0	(13.9)	74.4	(12.0)	<0.001‡	71.4 (13.5)
Men	24	(62)	63	(59)	0.463	87 (60)
Cause of amputation						
vascular	31	(80)	101	(96)	0.003	132 (92)
other	8	(21)	4	(4)		12 (8)
Level of amputation						
bilateral	2	(5)	11	(10)	0.049§	13 (9)
transfemoral	12	(32)	32	(30)		44 (30)
knee disarticulation	7	(18)	5	(5)		12 (8)
transtibial	17	(45)	59	(55)		76 (52)
Admitted from						
home	24	(75)	58	(62)	0.125	82 (65)
care	8	(25)	36	(38)		44 (35)
Marital status						
married/partnership	21	(64)	42	(49)	0.118	63 (53)
single/widow/ divorced	12	(36)	43	(51)		55 (47)
Number of comorbidities						
0	7	(23)	9	(10)	0.171	16 (13)
1-2	15	(48)	56	(63)		73 (59)
≥ 3	9	(29)	24	(27)		33 (28)
Comorbidities						
peripheral vasc disease	21	(57)	54	(51)	0.320	75 (52)
hypertension	16	(42)	39	(36)	0.334	55 (38)
diabetes	14	(37)	45	(42)	0.358	59 (41)
congestive heart failure	6	(16)	26	(24)	0.217	32 (22)
myocardial infarct	5	(13)	14	(13)	0.593	19 (13)
cerebrovascular disease	3	(8)	17	(16)	0.185	20 (14)
chronic lung disease	8	(22)	18	(17)	0.335	26 (18)
kidney disease	9	(24)	21	(20)	0.376	30 (21)
Peripheral vasc. procedure	23	(59)	44	(41)	0.042	67 (46)
Discharged to						
home	10	(26)	16	(16)	0.020	26 (18)
rehabilitation centre	9	(23)	8	(8)		17 (12)
care	15	(39)	53	(52)		68 (48)
died before discharge	5	(13)	25	(25)		30 (21)
12 month survival	26	(67)	43	(40)	0.004	69 (47)
Hospital						
> 10 amputations	29	(27)	80	(73)	0.960	109 (75)
≤ 10 amputations	10	(27)	27	(73)		37 (25)

p is difference between referred and non-referred groups; *Median age presented because data were not normally distributed, and mean age also presented to enable comparison to original PP-study; † Mann Whitney U Test; ‡ Independent sample t-test; all others are χ-square test; §Exact method used as cell count assumptions not met;**Comparison of hospitals with >10 (n=6) amputations to ≤10 amputations (n=7); Actual population is presented to enable comparison of characteristics, no statistical analysis was performed; not all percentages add up to 100 because of rounding.

Table 2: Characteristics of referred and non-referred patients who survived ≥ 12 months after amputation.

n (%)	Referred (PP study)		Not referred		p	Actual population	
Total included	26	(38)	43	(62)		69	
Age, median (IQR) *	65.4	(50.1 ; 75.3)	72.1	(65.2 ; 81.2)	0.016†	70.2	(61.8 ; 77.9)
Age, mean (sd)	62.2	(15.1)	71.3	(12.0)	0.007‡	67.9	(13.9)
Men	14	(54)	28	(65)	0.249	42	(61)
Cause of amputation							
vascular	19	(73)	41	(95)	0.012	60	(87)
other	7	(27)	2	(5)		9	(13)
Level of amputation							
bilateral	0	(0)	3	(7)	0.041§	3	(4)
transfemoral	8	(31)	8	(10)		18	(26)
knee disarticulation	6	(23)	2	(5)		8	(12)
transtibial	12	(46)	28	(65)		40	(58)
Peripheral vasc. procedure	15	(58)	20	(47)	0.258	35	(51)
Discharged to							
home	8	(31)	10	(24)	0.130	18	(27)
rehabilitation centre	8	(31)	6	(14)		14	(21)
care	10	(39)	26	(62)		36	(53)

p is difference between referred and non-referred groups; *Median age presented because data were not normally distributed, and mean age also presented to enable comparison to original PP-Study; † Mann Whitney U Test; ‡ Independent sample t-test; all others are χ-square test; §Exact method used as cell count assumptions not met; Actual population is presented to enable comparison of characteristics, no statistical analysis was performed; not all percentages add up to 100 because of rounding.

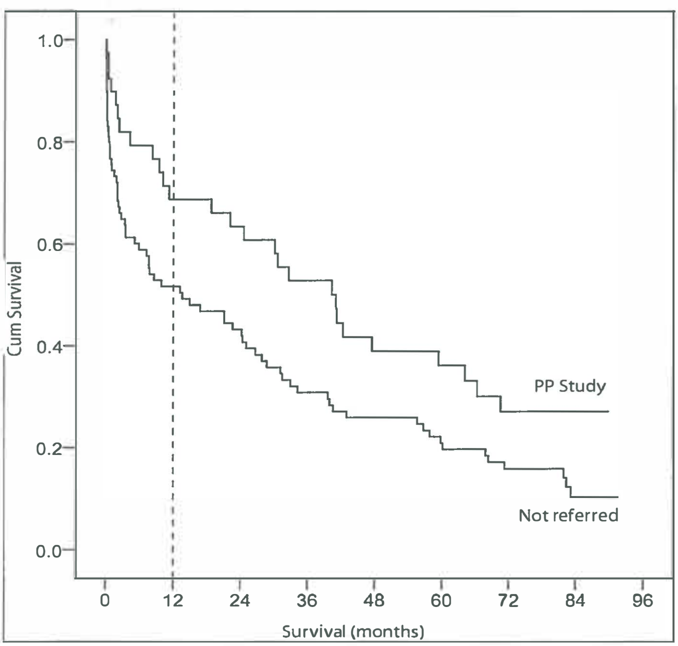

Figure 1:
Survival of patients referred and not referred to study after lower limb amputation.

Discussion

A prospective study of phantom pain aimed to report all patients undergoing primary major lower limb amputation yet more than 70% of potential participants were not referred in the first year. This resulted in a sample that was younger, less likely to have had vascular related amputation and differed in both pre and post care setting than the actual population who underwent LLA.[5]

The PP-study described a prevalence rate for phantom pain of 32% measured 6 months after amputation.[5] Other literature measuring occurrence at 6 months has reported more than double this amount, with 65-79% of people having phantom pain.[13,14] Occurrence rates at 6 months in trials to treat phantom pain range from 0-38% (0/10 in intervention; 5/13 in control group)[15] to 9-73% (1/11 in intervention; 8/11 in control).[16] The PP-study has a lower rate of phantom pain than expected which raises some uncertainty in generalisation and clinical application of the protective factors identified. These protective factors should be considered within the context of the biased population.

Three protective factors against the development of phantom pain were described: being male, having a lower limb amputation (versus an upper limb amputation) and time since amputation.[5] In the current study, there were no differences in sex between referred and non-referred patients (upper limb amputations were not included and only one year of the PP-study was analysed). Other factors in the PP-study were also investigated but not found to be significant, including level of amputation, cause of amputation and age at time of amputation. None of these factors were accurately represented by the sample referred to the PP-study and it is not possible to draw a valid conclusion over their influence based only on this data.

The factors identified in the PP-study were largely in disagreement to other literature. In addition to prevalence rates being much higher than the PP-study, sex is reported as being unrelated to occurrence of phantom pain[13,17] although males and females may deal with the pain differently.[18] Increasing age is shown as having a higher risk of phantom pain[19] while others have reported no relation[17] or not included age in their analysis.[13] More proximal amputation levels and having bilateral amputation, may increase a person's risk of phantom pain[19] although again, others have found no association between the two.[13,20]

The contradictory findings surrounding phantom pain in these different populations are, at least in part, also partly attributable to differences in definitions and study design. Cut off points for what constitutes phantom pain can include people with almost constant pain or people who experience only occasional pain.[5] Most previous studies of phantom pain are cross sectional and direct cause and effect cannot be stated. Studies include people with differing lengths of time since amputation, from a few months to many years,[18,19,21] yet time since amputation is another factor potentially linked to phantom pain. Poor physical condition from comorbidities and cognitive deficit leads to difficulties in patient inclusion and sample sizes are generally small. As amputation research is also characterised by a high mortality rate, follow up rates are often low. In this study almost 50% of the total population had died within 12 months of their first major amputation, including 33% of the referred group. The PP-study is the largest longitudinal study of phantom pain performed (total included at first follow up was 85 from 120 included) and followed patients for up to 3.5 years.[5] Unfortunately, the substantial bias seen in the population presents a major limitation and there remains limited evidence around risk factors associated with phantom pain. Reviews looking at mechanisms and treatment of phantom limb pain reveal similar shortcomings in methodology.[22-26]

A major difficulty with amputation outcome research is obtaining large and representative samples. The reasons for having an amputation make it difficult for many cases to be included in research as elderly people with systemic disease tend not to be considered for participation and have a higher rate of drop out or death.[1] This appeared to be a key element of (non)recruitment to the PP-study, with patients who were older and with amputation due to vascular disease least likely to be referred. Data, or at least their estimates, on non-participants (including people who did not give consent, patients who are excluded, deaths and drop outs) should be communicated by authors. In the PP-study, all referral sources were requested to provide this information, but unfortunately it did not occur. Minimal data presented in amputation research should include the number of participants and non-participants, age, sex, level of amputation and cause of amputation.

Our data were split to look at 12 month non-survivors compared to survivors. With outcomes of interest for the frailer group likely differing from the survivors, it is reasonable that they are not included in longitudinal outcome research. Unfortunately, our results showed that a substantial number of this healthier group, the 12-month survivors, also failed to be included in the PP-study. In designing any study, gaining strong interest and support from relevant stakeholders and referral sources is vital. In the case of the PP-study, referral sources (surgeons and staff) were informed of the aims and methodology at a regional meeting, with verbal agreements given for participation (referral of patients). The high referral rate (>85% of all within hospital, contributing >69% of all referred) from the study's operating/base hospital, suggests either the physical presence of the investigator and/or simply being the study's main location are the most effective strategies for recruitment. Across the entire regional network of hospitals, a physical presence was not possible. Attempts to counter this limitation through regular phone and newsletter contact were unsuccessful, with 6 hospitals not referring patients in the first year despite their agreement. Improving recruitment via clinicians is a difficult task; even large randomised controlled trials have great difficulty identifying successful strategies.[27] Adding to this are strict timeframes of the inclusion criteria of the PP-study with referral set for within 5 days. This meant that surgeons (and their staff) were primarily responsible for identifying cases, at a time when other factors, such as pre-operative assessment, can naturally be of a greater priority. It is not routine practice for the rehabilitation physician to be involved pre-surgically so this additional referral source was not utilised. Other alternatives were not considered as clinically relevant options, such as extending the inclusion period to > 5 days, as this would have introduced problems with recall.

Limitations

The population study used data from a retrospective review of medical files and as such, information was limited to what is included in these. The data were collected for a concurrent study on incidence and as such, they are considered to be complete. However, we acknowledge that cases may have been missed. If anything, the sample is an underestimation, although we do not expect that this would have any large affect on our main findings. Another limitation from the study design (review of medical records) is not having access to information on disease severity or duration of disease. Further, unless it is of a very severe nature, cognitive status is infrequently noted in the medical files. However, this is likely to be a major source of selection bias in LLA research given that vascular disease affects the body systemically. Finally, there was no information on survival status available for 27 patients and our results are likely to be an underestimate of survival time.

In the current study, all patients referred to the PP-study were considered as one group. However, 16 (41%) of these patients were not part of the analyses as they did not meet the criteria for inclusion. These excluded patients were older and more likely to have had amputation because of vascular disease than included patients.[5] The findings of this current study should therefore be considered as a conservative estimate of the impact of selection bias as these excluded older patients with vascular disease remained within the 'referred' group.

Conclusion

Selection bias is common, and perhaps inherent, in amputation research. Over 70% of patients were missed in a study of phantom pain, resulting in a younger population who were less likely to have had vascular related amputation and differed in respect to their pre- and post-care setting. As a result, phantom pain was possibly underestimated and the resultant protective factors identified should be considered only within the context of the biased population. Two important elements for improving research into amputation outcomes were identified: [1] failure to refer relevant cases (recruitment bias); and [2] failure to communicate 'reasonable' non-inclusions. Potential bias should be more clearly presented by authors and subsequent conclusions and clinical decisions made with greater caution. In addition, maximum efforts should be directed to research methodology which minimises the influence of bias.

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References

1. Hardy SE, Allore H, Studenski SA. Missing data: A special challenge in aging research. J Am Geriatr Soc. 2009;57(4):722-9.

2. Chatfield MD, Brayne CE, Matthews FE. A systematic literature review of attrition between waves in longitudinal studies in the elderly shows a consistent pattern of dropout between differing studies. J Clin Epidemiol. 2005;58(1):13-9.

3. Euser SM, Schram MT, Hofman A, et al. Measuring cognitive function with age: The influence of selection by health and survival. Epidemiology. 2008;19(3):440-7.

4. Hernan MA, Alonso A, Logroscino G. Cigarette smoking and dementia: Potential selection bias in the elderly. Epidemiology. 2008;19(3):448-50.

5. Bosmans JC, Geertzen JH, Post WJ, et al. Factors associated with phantom limb pain: A 31/2-year prospective study. Clin Rehabil. 2010;24(5):444-53.

6. O'Neill BF, Evans JJ. Memory and executive function predict mobility rehabilitation outcome after lower-limb amputation. Disabil Rehabil. 2009;31(13):1083-91.

7. Unwin J, Kacperek L, Clarke C. A prospective study of positive adjustment to lower limb amputation. Clin Rehabil. 2009;23(11):1044-50.

8. Geertzen JHB, Bosmans JC, van der 5chans CP, et al. Claimed walking distance of lower limb amputees. Disabil Rehabil. 2005;27(3):101-4.

9. van der Schans CP, Geertzen JHB, Schoppen T, et al. Phantom pain and health-related quality of life in lower limb amputees. J Pain Symptom Manage. 2002;24(4):429-36.

10. Miller WC, Speechley M, Deathe AB. Balance confidence among people with lower-limb amputations. Phys Ther. 2002;82(9):856-65.

11. Ehde DM, Czerniecki JM, Smith DG, et al. Chronic phantom sensations, phantom pain, residual limb pain, and other regional pain after lower limb amputation. Arch Phys Med Rehabil. 2000;81(8):1039-44.

12. Bosmans JC, Geertzen JH, Hoekstra HJ, et al. Survival of participating and nonparticipating limb amputees in prospective study: Consequences for research. J Rehabil Res Dev. 2010;47(5):457-64.

13. Jensen TS, Krebs B, Nielsen J, et al. Immediate and long-term phantom limb pain in amputees: Incidence, clinical characteristics and relationship to pre-amputation limb pain. Pain. 1985;21(3):267-78.

14. Richardson C, Glenn S, Nurmikko T, et al. Incidence of phantom phenomena including phantom limb pain 6 months after major lower limb amputation in patients with peripheral vascular disease. Clin J Pain. 2006;22(4):353-8.

15. Bach S, Noreng MF, Tjellden NU. Phantom limb pain in amputees during the first 12 months following limb amputation, after preoperative lumbar epidural blockade. Pain. 1988;33(3):297-301.

16. Jahangiri M, Jayatunga AP, Bradley JW, Dark CH. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. Ann R Coll Surg Engl. 1994 Sep;76(5):324-6.

17. Nikolajsen L, Jensen TS. Phantom limb pain. Br J Anaesth. 2001;87(1):107-16.

18. Hirsh AT, Dillworth TM, Ehde DM, et al. Sex differences in pain and psychological functioning in persons with limb loss. J Pain. 2010;11:79-86.

19. Dijkstra PU, Geertzen JHB, Stewart R, et al. Phantom pain and risk factors: A multivariate analysis. J Pain Symptom Manage. 2002;24(6):578-85.

20. Rayegani SM, Aryanmehr A, Soroosh MR, et al. Phantom pain, phantom sensation, and spine pain in bilateral lower limb amputees: Results of a national survey of Iraq-Iran war victims' health status. JPO. 2010;22(3):162-5.

21. Byrne KP. Survey of phantom limb pain, phantom sensation and stump pain in Cambodian and New Zealand amputees. Pain Med. 2011;12(5):794-8.

22. Wolff A, Vanduynhoven E, van Kleef M, et al. 21. phantom pain. Pain Pract. 2011 Jul-Aug;11(4):403-13.

23. Halbert J, Crotty M, Cameron ID. Evidence for the optimal management of acute and chronic phantom pain: A systematic review. Clin J Pain. 2002;18(2):84-92.

24. Flor H. Phantom-limb pain: Characteristics, causes, and treatment. Lancet Neurol. 2002;1(3):182-9.

25. Subedi B, Grossberg GT. Phantom limb pain: Mechanisms and treatment approaches. Pain Res Treat. 2011;2011:864605.

26. Casale R, Ceccherelli F, Labeeb AA. Phantom limb pain relief by contralateral myofascial injection with local anaesthetic in a placebo-controlled study: Preliminary results. J Rehabil Med. 2009;41(6):418-22.

27. Fletcher B, Gheorghe A, Moore D. Improving the recruitment activity of clinicians in randomised controlled trials: A systematic review. BMJ Open. 2012;2(1):e000496.

Chapter 9

General discussion

IN THIS THESIS, research on how, and how well, the elderly person with lower limb amputation (LLA) is enabled through rehabilitation and long term care (LTC) was presented. In *chapters two* and *three*, we saw the vulnerability of the population, arising from a combination of older age and comorbidities. This population presents unique challenges in amputation rehabilitation and research, some of which were described in *chapters four* to *eight*. The discussion following summarises the key findings and current literature. The clinical implications of amputation in this population are considered under three areas: determining when to amputate and at which level; rehabilitation setting; and mobility. Research suggestions are presented within each of these discussion points. Finally, the strengths and limitations of this research, as well as amputation research more broadly, are presented.

Summary of main results

The incidence of LLA resulting from vascular disease, infection and/or diabetes in 2003-2004 was 24 per 100,000 person-years (*chapter two*). This was unchanged from an earlier cohort from 1991-1992, confirming that around 150 people each year have a first amputation in the northern provinces of the Netherlands. There was no change in the mean age (74.0 years) and there remained slightly more men than women (60% versus 40%) in both cohorts. In 2003-2004, 50% of the population undergoing LLA had a diagnosis of diabetes. The relative risk of amputation in people with diabetes was 12 times higher than that of people without diabetes.

From this population, 22% of people died within 30 days of their surgery (*chapter three*). A history of cerebrovascular disease doubled the risk of death within 30 days. After one year, 44% of the population had died and after 5 years, this was 76%. Renal disease was associated with higher mortality risk at these time points. No significant differences in survival time were seen by any of the subgroups analysed, including different age groups and sex, the level of amputation, or by diagnosis of diabetes.

Of those patients who survived the acute admission period, 55% were discharged to long term care for their rehabilitation (*chapter four*). The only factor associated with this outcome was older age. Although the overall number of people with LLA admitted to LTC is substantial, patients are spread across a number of facilities. In 2008-2009, there were between 0-19 admissions with LLA, representing a maximum of 3.6% of all patients. Due to the relatively small numbers seen in each centre, the ability of clinicians working in LTC to obtain and maintain knowledge and skills for treating older people with LLA was questioned.

Results of the qualitative study (*chapter five*) confirmed the difficulty that professionals working in LTC face in obtaining skills and knowledge for treating people with LLA. From interviews with 9 elderly care physicians (ECPS) and 9 physiotherapists (PTS), three main issues were presented: difficulty implementing and using guidelines; a lack of involvement and specialisation of the multidiscplinary team; and a lack of people admitted with amputation to each center. There was a lot of overlap with these weak points, summarised by a PT:

"The best thing really would be if you could have a little section where the care is very specialised, because every time (there is an amputation admission) we spend quite a lot of time teaching others how to care for those (patients) in the right way. It costs a lot of energy, but there are just too few people with amputation admitted here."

In *chapters six* and *seven*, two important outcomes after LLA, HRQOL and mobility, were considered in respect to the elderly population. Eighteen months after amputation, significant improvements were seen in 5 of 7 domains investigated – physical function, social function, pain, vitality and perceived change in health. Most change occurred in the first 6 months. The pattern of change over time differed only for physical function for people aged over 65 years compared to those younger. As this may have been related to the very small sample size, we also compared older and younger groups to population normal values of their respective age categories. These results also supported the idea of age-specific differences in the domains affected by LLA.

In a systematic review of mobility outcomes, we found advanced skills are achieved in selected populations of elderly people with LLA, including outdoor and community walking. However, when mobility is considered in unselected populations, inclusive of all people undergoing LLA, including those who die post-operatively, less than 50% of the elderly population were able to achieve a household level of prosthetic mobility. A range of different tools were used to assess mobility, and combined with poor reporting of included populations, it was difficult to compare the outcomes from the included studies. Measures of non-prosthetic mobility were limited to non-validated mobility scales that categorise people as being bed-bound or wheelchair dependent.

Issues of population inclusion and selection bias were noted throughout the research presented in this thesis. In *chapter eight*, the extent of this problem was described in reference to a previously published prospective study on phantom pain. By comparing to the actual population who had LLA (derived from *chapter two*), we identified that more than 70% of potential inclusions had not been referred to the study. The missing population was 8 years older, more likely to have had LLA because of a vascular-related cause and there was a significant difference in one year survival between the groups (40% not referred versus 67% referred). When comparing the included and missing populations without 'reasonable non-inclusions' (i.e. we excluded all of the population who did not survive 12 months, who were most likely not referred to the study because of the severity of their condition), important differences in the age and amputation level remained.

Determining when to amputate and at which level

Looking from the focus of how we can best enable the elderly person with LLA, the idea of being more aggressive needs due focus, by operating sooner and/or at a more proximal level or by choosing not to amputate at all. Two findings from this thesis lend additional support to this idea: [1] a very high rate of post-operative mortality and [2] the improvement seen in HRQOL and mobility for those who survive. Although at first the idea of amputation is highly confronting, it might in fact be a disservice to some patients to continue attempts at limb salvage, through (endo-) vascular procedures, medications or prolonged hospitalisation and immobility.

This line of thought has been termed "choosing life or limb"[1] to describe the reasoning that a person at risk needs to make an informed decision, ideally before the limb has reached a critical stage.

> *"Just as the functional status of the patients is often a contra-indication to other disease treatments, chemotherapy for some cancers, for example, then we should be considering carefully whether we should be removing limbs from patients whose functional and medical status will not improve significantly as a result. Equally, there may be patients who may benefit from an early amputation and ambulation with a prosthesis."* [1: Game, 2012, p 97]

Put simply, 'choose life' and the patient will undergo amputation, enabling them to get out of hospital and get moving again. Also referred to as "positive, early amputation," the amputation can be performed before the limb reaches a critical level, in which the patient's life is at risk. So far, this early intervention approach has mainly been reported in respect to younger patients with diabetes,[2] or in the population with trauma who are considering limb salvage versus amputation.[3-5] For the elderly population, early intervention might reduce an otherwise lengthy period of immobility and hospitalisation while attempts to heal the limb are pursued. This is an important consideration as it is during this time that a substantial decrease in physical condition and function can occur, leading to poorer potential for good rehabilitation outcomes;[6] pre-operative function being an important element for achieving a better outcome from rehabilitation in LTC.[7] Alternatively, a patient and their team may choose a more palliative pathway for care. This choice will effectively reduce their life expectancy. The decision on 'life or limb' is, of course, never straightforward and it is often complicated by the urgency with which people must be treated, when patients' do not seek timely care.[8] A case description highlights the myriad issues involved (see text box "Late in life, an agonizing choice over surgery").

A high incidence of LLA and poor mortality are often considered a failure of care. However, these rates must be viewed in the context of many additional influences, such as the population at risk, access to foot clinics, skills and knowledge of the surgical team, systems of recording hospital episodes. In short, incidence and mortality rates should not be considered as representative of the quality of care provided.[9] Instead these rates must be placed into context of individual and institutional preferences in determining a medical or surgical pathway. It is now more accepted that LLA should not always be viewed as a negative outcome as it can represent healing and the end of pain. Previously maximising limb length was the overriding aim, whereas now, choosing to amputate at a proximal level, in some cases, is preferable if it provides the patient or carer a more functional outcome.[10] Following a similar approach, and keeping focus on what the patient sees as important, high incidence and poor mortality rates should also not always be viewed as a negative outcome.

Research suggestions

Continued surveillance of incidence of LLA and population characteristics can give insight into the need for preventative, rehabilitation and LTC services. Our results were suggestive that a small decrease in incidence was apparent, but without statistical confirmation. To gain a more confident answer to the question, a repeat study with a recent cohort is suggested. This would aim to evaluate if the lack of change in incidence in the northern provinces was due to chance or if we need to seriously consider the preventative services currently being provided. A repeat of the study presented in *chapter two*, would also enable the evaluation of changes in LLA performed as a complication of diabetes, data that was unfortunately not available in the 1991-1992 cohort studied.

The reasons for high and varied rates of mortality also need to be explored. In chapter three over 20% of the population died within 30 days of their amputation. A similar rate has been reported,[11-14] while others have found it to be substantially less at around 8-10%.[15-20] The population included in a study has a direct effect on

Late in Life, an Agonizing Choice Over Surgery

FORGOING A POTENTIALLY LIFE-SAVING medical procedure may be easier at age 94 than age 54, but for my patient George Pollack it was a wrenching decision anyway. Suffering from a severe foot ulcer that would not heal, he was told his only chance of a cure was a partial amputation of his leg. Even then, there were no guarantees.

George was a savvy medical customer. He had been a lawyer in New York for more than 60 years — among other things, serving as executor for the estate of Lou Gehrig's widow, Eleanor, and making sure that any payments from the use of Gehrig's image went toward A.L.S. research at Columbia University Medical Center. I originally met George when I was doing research on Lou Gehrig's illness.

George was suffering from peripheral vascular disease, or obstruction of the arteries that feed the limbs. Early on, it is possible to reopen clogged blood vessels with a balloon. But when the disease worsens, blood-starved areas, usually the feet, may develop life-threatening ulcers. By the time I met George, in 2002, he was already prone to ulcers — a result of flat feet and decades of poor circulation — and he required a complex combination of antibiotics, ointments and dressings. I gave what advice I could, referring him to an infectious-disease specialist who helped cure one of the largest ulcers.

By April 2009, things were worse. George had a large ulcer that would not heal on his left foot and was requiring hospitalizations and intravenous antibiotics. One surgeon strongly advised a below-the-knee amputation of the left leg.

George got a second opinion from Dr. Alan I. Benvenisty, a surgeon and director of the vascular laboratory at St. Luke's Hospital. In August, hoping to try a balloon procedure, Dr. Benvenisty sent him for an angiogram, a dye study that generates images of the arteries. But the test showed that a balloon was out of the question. Amputation was the only surgical option. So Dr. Benvenisty did what any doctor should: he laid out the options, pro and con. He told George that surgery was very risky and that the wounds did not heal properly in roughly 30 percent of below-the-knee amputations. A study of 704 such operations, published in The Archives of Surgery in 2004, found that patients were at risk for "significant morbidity and mortality." In George's case the odds were even longer: he was 94 and had suffered a mild heart attack during his angiogram. And then there was rehabilitation. At the very least, George would require two taxing months of aggressive physical therapy in a nursing facility.

What was the other option? Without surgery, Dr. Benvenisty told George, the vascular disease would probably kill him in a matter of months. I was among the many people to whom George spoke. Part of him clearly wanted to try surgery. After all, he told me, who does not want to live? But he spent even more time telling me why he thought surgery was too risky — and how even if it succeeded, he couldn't bear to be away from his frail 90-year-old wife, Dorothy, during his rehabilitation. "A few months is a long time when you get to be our age," he said. George's daughter, Ruth Pappas, recalls hearing mixed signals from him at first: "I don't want to go on," but "I haven't given up."

Ultimately, though, George chose hospice care over surgery. Ruth's husband, Tony Pappas, says George told him that even if the operation went well, he thought there would be complications and his life would not be prolonged. George chose home hospice. The hospice worker helped him go to the bathroom, keep clean and get in and out of bed. But he was not in hospice for long. He had already developed a fever, and after a few days he was worse, probably from a foot infection that had spread into his bloodstream. When the hospice physician proposed an antibiotic, George declined, saying, "I don't want to feel better." Ruth believes this was her father's way of saying he was ready to die. He did so later that night, quietly, in his sleep.

Dr. Benvenisty told me that in his experience, George was the exception to the rule. Most patients forge ahead — even those who swore never to have an amputation and those at high risk of dying from the procedure. I think George did the right thing, and perhaps I should have guided him even more in that direction. In the end, however, I was glad he made his own choice.

mortality outcomes, such as the inclusion of different causes of amputation, but there are additional factors to be considered, such as whether only people with a first amputation were included or also people with subsequent amputations. A review of mortality rates presented in literature is needed with the aim to look for any existing links between mortality outcomes and variables such as age at time of LLA. Special focus should be given to the population who survive 30 days but not longer than 12 months, and why the 30-day mortality rate differs so greatly from one population to another.

The decision process for people presenting with critical limb ischemia or life threatening infection is mostly approached from a surgical perspective, often with a focus on limb salvage. Outcomes of amputation surgery have also been considered mainly from a surgical/ medical perspective, for example healing time and survival rates, and only recently have patient factors, such as quality of life, come to be seen as important.[2,10,21,22] Rehabilitation and elderly care professionals could add important knowledge on rehabilitation prognosis and mobility potential and open further dialogue on quality of life and issues of importance to the elderly population. The current search for evidence-based decisions and discussion on when to amputate and at which level[1,23,24] would benefit from this wider team approach.

Amputation rehabilitation in the long term care setting

Amputation rehabilitation in the Dutch LTC setting is gaining increasing interest and it appears to offer a lot of positive opportunities. The focus on this setting will likely continue as a change to the funding of rehabilitation services is being implemented, taking effect in 2013. One of the benefits of rehabilitation in LTC is having access to clinicians with specialist skills for the elderly population. An interdisciplinary team approach to rehabilitation after LLA is vital with each member having an important role in maximising outcomes.[25,26] In the Dutch LTC setting, the team approach does not appear to have fully translated into care. The physiotherapist was largely responsible for all amputation related aspects, in consult with the rehabilitation physician and prosthetist. The occupational therapist in particular, was not involved in amputation rehabilitation with exception of arranging wheelchair prescriptions and a home visit before discharge (*chapter five*). This problem is not confined to our LTC setting or to the Netherlands, with a recent systematic review identifying just 2 studies considering rehabilitation of amputation for the older person from this professions perspective.[27] The studies included in that review were limited by methodological problems, however, there was some support that an increased frequency of occupational therapy sessions relates to increased use of a prosthesis. Occupational therapists are widely considered as integral or core members[28] to the functional outcomes achieved in amputation rehabilitation.[25,26] Despite these endorsements, there is little practical application or documented evidence, at least within the LTC setting.

Rehabilitation setting after LLA has mainly been looked at from the perspective of traditional rehabilitation center inpatient care. This setting yields best outcomes in terms of survival, a receipt of a prosthesis and better mobility, being more likely to return to independent living, greater medical stability, a lower number of subsequent amputations and a higher quality of life.[29-33] For the elderly population, more interest has been given to larger populations, namely people with stroke or orthopaedic disorders. Two recent studies on amputation rehabilitation in the LTC setting reported 57-65% of people returning home within one year, with pre-operative functional ability the main factor associated with this outcome.[7,34]

The conclusion of the qualitative study (*chapter five*) was that despite positive outcomes for patients with LLA, to a large extent, their care extends from a process of continuous problem solving, along with the energy and empathy of the clinicians involved. There is relative inexperience in treating the amputation population. Flexibility and informal communication styles between team members enables these patients to still achieve fairly good outcomes.[7,35,36] Unfortunately, this approach to care of people with LLA is largely unsustainable, when considered in the context of increasing demand for evidence in decision-making and a need for greater efficiency.

Research suggestions

A major limitation with research in the LTC setting to date is both the lack and choice of outcome measures used. For example, in the research mentioned earlier, a successful outcome of rehabilitation was defined as 'return to home'.[7,34] However, this does not necessarily equate to better outcomes of mobility, function or HRQOL, with return to home for this population also highly reliant on additional resources such as the availability of family / carers and accessibility to the home or it could even reflect a choice for palliative end-stage care. Outcome measures in the LTC setting for people with LLA are infrequently used (*chapter five*). Determining which measures are of importance for evaluating rehabilitation of the elderly person with LLA, and actually implementing these measures in the LTC setting, will add much needed support for continuing this service.

(Prosthetic) mobility

Following LLA, there is often a focus on prosthetic mobility. *Chapter seven* presented the numerous ways in which outcomes of prosthetic mobility have been defined in terms of prescription of a prosthesis, length of time worn or hours of use, an ability to perform certain skills or measuring the time to walk a determined distance and vice versa. More personalised definitions of a successful outcome are sought, but have not as yet been agreed upon. For example, Norvell et al. propose that mobility success after LLA needs to be considered "*relative to the impairment necessitating the surgical procedure, but also relative to the additional impairments that affect mobility at baseline.*"[37: p412] Prosthetic mobility for the elderly population is a difficult task and of all elderly people undergoing LLA, less than half manage this skill (*chapter seven*). Not only does prosthetic training require substantial effort from the patient themselves, but the rehabilitation team and prosthetist also invest a great deal of their time and energy. To see this effort reflected in a poor outcome is not only disappointing for the patient and clinicians,[38] but is also an inefficient use of rehabilitation resources.

Barriers to prosthetic mobility were desrcibed in publications from as early as the 1950's, which listed the clinical contra-indications for prosthetic ambulation:

"There are few absolute contraindications to prescription of a prosthesis: these are severe cardiovascular disease, inadequate motor coordination, and senile mental changes."[39: Grynbaum, 1956, p295]

"Basic requirements for satisfactory limb fitting in the aged:
1. An adequate stump.
2. Good general health - particularly in reference to cerebral, cardiac, pulmonary and renal function.
3. Opposite leg in good condition.
4. Amputee capable of unassisted crutch walking on the remaining leg.
5. Considerable initiative and perseverance."[40: McGoey, 1954, p471]

While preferred terminology has changed, the underlying principles of prosthetic prescription have not advanced much further and remain very much reliant on clinical experience.[41] High levels of intrinsic motivation, transtibial level amputation (as opposed to more proximal levels), greater preoperative function and better cognitive abilities are presented as important predictors for prosthetic mobility in the elderly population.[7,34,36,42] The 1-leg standing balance remains one of the best predictors for prosthetic walking ability.[7,42,43]

Research suggestions

Rather than looking at who should pursue prosthetic mobility, the problem could be approached from the opposite angle: which patients would be better enabled if directed toward learning other skills during their rehabilitation stay. A geriatric focus in the LTC setting could provide important differences compared to inpatient rehabilitation. In enabling the elderly person, non-prosthetic mobility also relates back to the level of amputation chosen with knee disarticulation or transfemoral levels prefered in cases where poor healing or knee contracture are considered a risk factor.[44]

There are few studies investigating non-prosthetic mobility (transfers and wheelchair skills) or functional outcomes in elderly people with LLA. This is an important gap with skills in non-prosthetic mobility essential for both prosthetic users and non-users alike. Existing instruments that cover the full spectrum of mobility (from 'bed bound' to 'no restrictions') are mostly unstandardised or sporadically used scales (*chapter seven*). Current wheelchair skills test are not amputee-specific and there may be important differences in sitting balance that could affect results when applying these tests. Falls related to wheelchair use are high even in younger amputation populations.[45] Energy requirements for wheelchair mobility are less than prosthetic ambulation in this population.[46] More effort to understand non-prosthetic mobility outcomes should be made, particularly in respect to enabling the elderly population.

Strengths and limitations

The research presented in this thesis made use of several types of study designs, each with its own strengths and limitations for answering our research questions. The elements specific to each design have been discussed as part of the individual chapters. Limitations and strengths of this thesis more generally are reported in this section.

Among the several study designs, different angles of the research problem were considered, including: what is currently known in literature (*chapter seven*); what clinicians' working in the field experience (*chapter five*); and how patients' themselves experience amputation and the months following (*chapter six*). However, a limitation of the research, as well as the focus of this discussion, is that we consider the research problem from one perspective only, the outcomes for the consumer. The cost-effectiveness of providing care needs to be considered in parallel. Many areas lend themselves to an economic-focussed discussion, for example: amputating earlier or not at all; funding of rehabilitation services in LTC; and insight to who will or will not achieve prosthetic mobility.

Despite the many aspects of rehabilitation and LTC for the elderly person with LLA that were addressed in this research, there are, of course, many additional factors of importance which were only briefly mentioned, in particular the availability of family/carers, functional outcomes and falls. These issues, common to all areas of elderly care and rehabilitation, should be kept in mind for their influence on the outcomes described.

We aimed to look in detail at the elderly population with LLA. However, it is clear that selection bias is a common theme through this work. While statistical methods such as those used in *chapter six* offer some advantages for the inevitable attrition in this population, nothing can replace good study designs, comprehensive reporting of populations and outcomes and improved coordination and collaboration from participating centres. Bias in research of elderly people is not unique to amputation research. The problem was recently highlighted in an important consensus statement on care of older people with diabetes by the American Diabetes Association and the American Geriatrics Society.[47] They push for the inclusion of older age groups in research, including randomised control trials, in order to fill the large gaps in understanding the unique needs of this population.[47] Bias is also described as characteristic of research conducted in the LTC setting.[48] As the global population continues to experience an increase in age, methods that include the elderly population with LLA are of growing importance.[49]

Noted throughout this thesis and highlighted in the systematic review, was the problem of inadequate reporting of included populations. We suggested in *chapter seven* that the minimal criteria to make a relatively informed conclusion from outcome studies are cause of amputation, level of amputation, sex and age of the participants/ population, with additional information dependent on the outcome of interest. For example, when looking at mortality rates, timing of the amputation is important. Specifically, does the population include only people undergoing their first amputation, or does it also include people undergoing a second or third amputation?

The problem of missing information was also described in *chapters two* to *four*. The study design, a retrospective review of medical records, was chosen as important details cannot be obtained from most national databases, which are fraught with limitations.[9,50,51] For example, the national database in the Netherlands is currently unable to differentiate between side of amputation. Therefore, when someone undergoes a transtibial level amputation followed by a transfemoral level amputation, it is not clear if the individual has a unilateral transfemoral amputation or a bilateral transtibial/transfemoral amputation, yet the difference in their potential outcomes and care can be substantial. Identifying cases that were incorrectly recorded in the national database offered another advantage. This occurred where a patient had been coded with 'transtibial amputation' when in fact the surgical record showed they had undergone amputation at a different level or the operation had been cancelled. Unfortunately, these omissions and errors could not be quantified due to different procedures for obtaining cases by each hospital.

Of course, a retrospective review of the medical files also introduced inevitable limitations. Most obvious was that for certain variables a substantial number of patients had missing information. This mostly concerned insight to additional factors we were interested in analysing. For example, smoking status was infrequently recorded despite it having a major role in both the need for amputation and healing rates after amputation.[19,52] Similarly, patients' weight was infrequently recorded preventing investigation, for example, of the impact of being over- or under- weight on mortality outcomes, and despite the importance of weight when considering prescription of prosthetic componentry. Another limitation of the information presented in the medical records, was that we were unable to differentiate between cause of amputation and this remained simply 'vascular, infection or diabetes related'. The underlying disease processes of these diagnoses differ and may have an influence on the choice of treatment and long term care. As we focussed on the 'elderly only' population, we felt this was a reasonable compromise to make.

Other authors have also questioned how to group or sample people with lower limb amputation.[53,54] Separating by age groups, but not cause of amputation, in the research in *chapter seven*, suggested that more information specific for the elderly population is needed irrespective of the underlying reason. There are advantages and disadvantages with any method chosen and the research question should be kept in mind when determining these criteria. What this again highlights is the importance of clearly reporting the included (and excluded) population characteristics. The International Society of Prosthetics and Orthotics have recently drafted recommendations for reporting populations with amputation and these should be considered when preparing research reports.[55]

Conclusions

The research presented in this thesis has looked at the elderly person with LLA, specifically how, and how well, the population is enabled through rehabilitation and LTC. It is clear that older age does not prevent someone achieving good outcomes after amputation. However, studying this population in isolation proved difficult. Some of these reasons are harder to avoid (high rates of death and drop out), while others were highlighted as needing improvement (reporting of included populations). A key finding was that, to a great extent, care is provided through the surgeons' and clinicians' best judgment and experience and remains a limitation to consistent decision-making. This includes decisions by the surgeon at the time of amputation through to rehabilitation decisions in LTC. The pre- and early- amputation research is highly surgically focussed and may benefit from increased input of the rehabilitation clinicians. Amputation rehabilitation for the elderly person must extend beyond replacement of the limb, encompassing psycho-social elements and alternative options for mobility. Currently, measures of non-prosthetic mobility are lacking and treatment from a wider group of the multidisciplinary team available in LTC (beyond the physiotherapist) should be implemented.

References

(1) Game F. Choosing life or limb. Improving survival in the multi-complex diabetic foot patient. Diabetes Metab Res Rev 2012;28 Suppl 1:97-100.

(2) Fiorito J, Trinidad-Hernadez M, Leykum B, et al. A tale of two soles: sociomechanical and biomechanical considerations in diabetic limb salvage and amputation decision-making in the worst of times. Diabet Foot Ankle 2012;3:10.3402/dfa.v3i0.18633 (early online).

(3) Fodor L, Sobec R, Sita-Alb L, et al. Mangled lower extremity: can we trust the amputation scores? Int J Burns Trauma 2012;2:51-58.

(4) Quon DL, Dudek NL, Marks M, et al. A qualitative study of factors influencing the decision to have an elective amputation. J Bone Joint Surg Am 2011;93:2087-2092.

(5) Busse JW, Jacobs CL, Swiontkowski MF, et al. (Evidence-Based Orthopaedic Trauma Working Group). Complex limb salvage or early amputation for severe lower-limb injury: a meta-analysis of observational studies. J Orthop Trauma 2007;21:70-76.

(6) Chan KM, Tan ES. Use of lower limb prosthesis among elderly amputees. Ann Acad Med Singapore 1990;9:811-816.

(7) Van Eijk M, 2012. Determinants of outcome in geriatric rehabilitation; the GRAMPS study. Thesis. Radboud University Nijmegen, the Netherlands.

(8) Feinglass J, Shively VP, Martin GJ, et al. How 'preventable' are lower extremity amputations? A qualitative study of patient perceptions of precipitating factors. Disabil Rehabil 2012;34:2158-2165.

(9) Jeffcoate WJ, van Houtum WH. Amputation as a marker of the quality of foot care in diabetes. Diabetologia 2004;47:2051-2058.

(10) Taylor SM, Kalbaugh CA, Cass AL, et al. "Successful outcome" after below-knee amputation: an objective definition and influence of clinical variables. Am Surg 2008;74:607-612.

(11) Kristensen MT, Holm G, Kirketerp-Moller K, et al. Very low survival rates after non-traumatic lower limb amputation in a consecutive series: what to do? Interact Cardiovasc Thorac Surg 2012;14:543-547.

(12) Remes L, Isoaho R, Vahlberg T, et al. Major lower extremity amputation in elderly patients with peripheral arterial disease: Incidence and survival rates. Aging Clin Exp Res 2008;20:385-393.

(13) Eskelinen E, Lepantalo M, Hietala EM, et al. Lower limb amputations in Southern Finland in 2000 and trends up to 2001. Eur J Vasc Endovasc Surg 2004;27:193-200.

(14) Pohjolainen T., Alaranta H. Ten-year survival of Finnish lower limb amputees. Prosthet Orthot Int 1998;22:10-16.

(15) Davenport DL, Ritchie JD, Xenos ES. Incidence and risk factors for 30-day postdischarge mortality in patients with vascular disease undergoing major lower extremity amputation. Ann Vasc Surg 2012;26:219-224.

(16) Vamos EP. Trends in lower extremity amputations in people with and without diabetes in England, 1996-2005. Diabetes Res Clin Pract 2010;87:275-282.

(17) Subramaniam B, Pomposelli F, Talmor D, et al. Perioperative and long-term morbidity and mortality after above-knee and below-knee amputations in diabetics and nondiabetics. Anesth Analg 2005;100:1241-1247.

(18) Aulivola B. Major lower extremity amputation: outcome of a modern series. Arch Surg 2004;139:395-399.

(19) Cruz CP, Eidt JF, Capps C, et al. Major lower extremity amputations at a Veterans Affairs hospital. Am J Surg 2003;186:449-454.

(20) Mayfield JA, Reiber GE, Maynard C, et al. Survival following lower-limb amputation in a veteran population. J Rehabil Res Dev 2001;38:341-345.

(21) Varu VN, Hogg ME, Kibbe MR. Critical limb ischemia. J Vasc Surg 2010;51:230-241.

(22) Landry GJ. Functional outcome of critical limb ischemia. J Vasc Surg 2007;45:A141-148.

(23) Attinger CE, Brown BJ. Amputation and ambulation in diabetic patients: function is the goal. Diabetes Metab Res Rev 2012;28 Suppl 1:93-96.

(24) Davis BL, Kuznicki J, Praveen SS, et al. Lower-extremity amputations in patients with diabetes: pre- and post-surgical decisions related to successful rehabilitation. Diabetes Metab Res Rev 2004;20:S45-50.

(25) Netherlands Society of Physical and Rehabilitation Medicine. Richtlijn amputatie en prothesiologie onderste extremiteit [Dutch] [Guidelines in lower extremity amputation and prosthetics]. VRA - Dutch Association of Rehabilitation Physicians; October 2012. Available online at http://www.revalidatiegeneeskunde.nl, accessed November 2012.

(26) British Society of Rehabilitation Medicine. Amputee and Prosthetic Rehabilitation – Standards and Guidelines, 2nd Edition; Report of the Working Party (Chair: Hanspal, RS). British Society of Rehabilitation Medicine. London. 2003.

(27) Spiliotopoulou G, Atwal A. Is occupational therapy practice for older adults with lower limb amputations evidence-based? A systematic review. Prosthet Orthot Int 2012;36:7-14.

(28) Broomhead P, Dawes D, Hale C, et al (eds). Evidence based clinical guidelines for the physiotherapy management of adults with lower limb prostheses; British Association of Chartered Physiotherapists in Amputation Rehabilitation. London. 2003

(29) Czerniecki JM, Turner AP, Williams RM, et al. The effect of rehabilitation in a comprehensive inpatient rehabilitation unit on mobility outcome after dysvascular lower extremity amputation. Arch Phys Med Rehabil 2012;93:1384-1391.

(30) Kurichi JE, Small DS, Bates BE, et al. Possible incremental benefits of specialized rehabilitation bed units among veterans after lower extremity amputation. Med Care 2009;47:457-465.

(31) Stineman MG, Kwong PL, Kurichi JE, et al. The effectiveness of inpatient rehabilitation in the acute postoperative phase of care after transtibial or transfemoral amputation: study of an integrated health care delivery system. Arch Phys Med Rehabil 2008;89:1863-1872.

(32) Dillingham TR, Pezzin LE. Rehabilitation Setting and Associated Mortality and Medical Stability Among Persons With Amputations. Arch Phys Med Rehabil 2008;89:1038-1045.

(33) Pezzin LE, Dillingham TR, MacKenzie EJ. Rehabilitation and the long-term outcomes of persons with trauma-related amputations. Arch Phys Med Rehabil 2000;81:292-300.

(34) Hershkovitz A, Dudkiewicz I, Brill S. Rehabilitation outcome of post-acute lower limb geriatric amputees. Disabil Rehabil 2012 (early online).

(35) Buijck BI, van Eijk MS, Zuidema SU, et al. Determinants of quality of life in older adults after lower limb amputation and rehabilitation in skilled nursing facilities. J Am Geriatr Soc. 2012;60:796-798.

(36) Zijp EM, Rasenberg EM, van den Bosch JS, [Rehabilitation of nursing home patients with a leg amputation. A retrospective study] [Dutch]. Tijdschr Gerontol Geriatr 1992;23:54-59.

(37) Norvell DC, Turner AP, Williams RM, et al. Defining successful mobility after lower extremity amputation for complications of peripheral vascular disease and diabetes. J Vasc Surg 2011;54:412-419.

(38) van Twillert S, Postema K, Geertzen JH, et al. Improving rehabilitation treatment in a local setting: a case study of prosthetic rehabilitation. Clin Rehabil 2009;23:938-947.

(39) Grynbaum BB, Gordon EE. Rehabilitation of the elderly amputee. J Chronic Dis 1956;4:292-295.

(40) McGoey PF. The choice of amputation in senile gangrene. Can Med Assoc J 1954;71:469-472.

(41) van der Linde H (2004) Prosthetic prescription in lower limb amputation. Development of a clinical guideline in the Netherlands. Thesis. University of Groningen, the Netherlands.

(42) Hamamura S, Chin T, Kuroda R, et al. Factors affecting prosthetic rehabilitation outcomes in amputees of age 60 years and over. J Int Med Res 09;37:1921-1927.

(43) Schoppen T, Boonstra A, Groothoff JW, et al. Physical, mental, and social predictors of functional outcome in unilateral lower-limb amputees. Arch Phys Med Rehabil 2003;84:803-811.

(44) Houghton AD, Taylor PR, Thurlow S, et al. Success rates for rehabilitation of vascular amputees: implications for preoperative assessment and amputation level. Br J Surg 1992;79:753-755.

(45) Dyer D, Bouman B, Davey M, et al. An intervention program to reduce falls for adult in-patients following major lower limb amputation. Healthc Q 2008;11:117-121.

(46) Chin T, Oyabu H, Maeda Y, et al. Energy consumption during prosthetic walking and wheelchair locomotion by elderly hip disarticulation amputees. Am J Phys Med Rehabil 2009;88:399-403.

(47) Kirkman MS, Briscoe VJ, Clark N, et al. Diabetes in Older Adults. Diabetes Care 2012 (Early online).

(48) Tilden VP, Thompson SA, Gajewski BJ, et al. Sampling Challenges in Nursing Home Research. J Am Med Dir Assoc 2012 (Early Online).

(49) Highsmith MJ. Barriers to the Provision of Prosthetic Services in the Geriatric Population. Topics in Geriatr Rehabil 2008;24:325-331.

(50) Rayman G, Krishnan ST, Baker NR, et al. Are we underestimating diabetes-related lower-extremity amputation rates? Results and benefits of the first prospective study. Diabetes Care 2004;27:1892-1896.

(51) Rommers GM, Vos LD, Groothoff JW, et al. Epidemiology of lower limb amputees in the north of The Netherlands: aetiology, discharge destination and prosthetic use. Prosthet Orthot Int 1997;21:92-99.

(52) Eneroth M. Factors affecting wound healing after major amputation for vascular disease: a review. Prosthet Orthot Int 1999;23:195-208.

(53) Kratz AL, Williams RM, Turner AP, et al. To lump or to split? Comparing individuals with traumatic and nontraumatic limb loss in the first year after amputation. Rehabil Psychol 2010;55:126-138.

(54) Dijkstra PU, Geertzen JH, Stewart R, et al. Phantom pain and risk factors: a multivariate analysis. J Pain Symptom Manage 2002;24:578-585.

(55) Lemaire E, Wong M (eds) ISPO Recommendation for Defining Participants in Prosthetics Research Draft. Available from http://www.ispoint.org/sites/default/files/archives/researchparticipantdataopenreview.pdf. Accessed Oct 2012.

English summary

In the Netherlands, most people undergoing a lower limb amputation (LLA) are over 65 years of age. Chronic peripheral vascular disease or diabetes mellitus has led to irreversible ischemia or a life threatening infection. Despite advances in preventative care, medical treatment and (peripheral) revascularisation procedures, in some cases, an amputation remains the best option for ending ongoing pain, hospitalisation and infection/ischaemia, and ultimately, enabling a person to live. It is the enabling a person to live that the research presented in this thesis focusses on. How, and how well, is the elderly population enabled from the decision to amputate and their subsequent rehabilitation and long term care (LTC)? We begin in *chapters two* and *three* with an investigation of incidence and mortality rates in the Northern Netherlands. The provision of rehabilitation for people with LLA in the LTC setting is then explored in *chapters four* and *five*. Two important outcomes for the elderly person with amputation – mobility and health related quality of life – are the focus of *chapters six* and *seven*. *Chapter eight* looks at the problem of bias in research of this population. The general discussion in *chapter nine* summarises the clinical implications of the findings of these chapters, from surgical decisions, rehabilitation setting, mobility and the importance of improving research and reporting of amputation populations.

The first chapters of this thesis present results from a historical cohort study of amputations performed in the Northern Netherlands in 2003 or 2004. Investigating population changes gives insight to the effectiveness of prevention programmes and need for rehabilitation services. *Chapter two* focussed on the incidence rates of amputation. Included were people who underwent a first major LLA (above the ankle) which was necessitated because of vascular disease or infection. The incidence of amputation was 8.8 (all-age) and 23.6 (≥45 years) per 100,000 person-years. When comparing to data from a matched study (setting, inclusion and methods) of the years 1991 and 1992, this incidence rate was found to be unchanged. For the cases in 2003-2004, a diagnosis of diabetes was recorded in 50% of the population. The incidence rate within the diabetic population was 151 per 100,000 person-years, giving a relative risk of amputation 12 times greater than people without diabetes. Reports from other Western economies have tended towards a decreasing rate of major amputation over time and a substantially lower relative risk in people with diabetes than seen in our setting. We propose that a follow up study with a recent cohort be performed to confirm the pattern of change in our region. Finding methods for reducing these incidence rates is of continued importance as diabetes prevalence increases and the global population ages. Consideration should be given to the provision of services from a range of areas including vascular surgery, diabetes care and multidisciplinary foot clinics.

Mortality rates after amputation are known to be high. This is attributed to both the older age of the population undergoing the procedure and the presence of multiple (cardiovascular) comorbidities. Looking at mortality rates in different (sub) populations can help in providing a prognosis to patients, as well as gaining insight into preventative and long term care needs. In *chapter three* we report 22% of all people died within 30 days of their first amputation, with cerebrovascular disease doubling the risk of death in this time frame. Longer term, mortality rates are more positive with 56% of people surviving at least one year and 24% surviving to 5 years, with odds of death within these time frames highest for people with renal disease. Mortality rates were not only investigated at different time points, but also by different combinations of important population characteristics including age, sex, the level of amputation and diagnosis of diabetes. With the exception of the oldest age group (85+ years), we found no substantial differences in the long term mortality rates. Conflicting results between our rates and other research may be due to population differences, such as inclusion of non-vascular amputations or people undergoing (partial) foot amputation. These procedures are more likely performed in people who are younger and in better general health than people who are at the point of needing amputation above the ankle. The variability in mortality rates emphasises the need for outcomes to be delineated by both the underlying cause and level of amputation (in addition to diabetes status), to avoid the bias resultant from populations with different causes and levels included.

After LLA, rehabilitation should be initiated as soon as possible. This is particularly important for the elderly population who can experience a rapid decline in their physical conditioning, which in turns leads to poorer outcomes in rehabilitation. Previous research has shown that being older, female, living alone and having LLA at a more proximal level increased the chance of discharge to LTC. In *chapter four* we report that in the Dutch setting, of all patients who survived the acute admission period, 55% were discharged to a LTC facility (*Dutch: verpleeghuis*) for their rehabilitation and the only factor associated with this outcome was older age. Although the overall number of people with LLA admitted to LTC was substantial, patients are spread across 34 different facilities in the 3 provinces. This dispersion of patients led to questions over the ability of clinicians to obtain and maintain amputation specific knowledge and skills.

To look further at this issue, we interviewed clinicians working in LTC facilities. From their perspective, we aimed to describe the current set up, barriers and potential for amputation rehabilitation in this setting. The findings, presented in *chapter five*, confirmed that the lack of people admitted with LLA led to subsequent difficulties in providing efficient or evidence-based rehabilitation. Most of the amputation aspects of rehabilitation lay with the physiotherapist with the wider multi-disciplinary team largely unutilised. Although other studies have reported positive rehabilitation outcomes for people with amputation in this setting, we suggest that the current set-up is largely unsustainable. A designated LTC facility for amputation rehabilitation in each region is presented as a solution but also smaller clinical changes are suggested, including improvements in communication and training.

Mobility in people with LLA is thought to be the key to independence and the basis of a higher quality of life (HRQOL). These outcomes are the focus of *chapters six* and *seven*. Change in health related quality of life over 18 months was analysed in a cohort of people with first LLA. The influence of age and walking ability on different HRQOL domains were investigated, along with a comparison to population norm values. Eighteen months after amputation, quality of life had improved significantly in 5 of 7 domains investigated – physical function, social function, pain, vitality and perceived change in health. Most change occurred in the first 6 months. The pattern of change over time differed only for physical function for people aged over 65 years compared to those younger. As this may have been related to the very small sample size, we also compared older and younger groups to population norm values of their respective age categories. These results supported the idea that there are age-specific differences in the domains affected by amputation, which should be explored further.

In a systematic review of mobility outcomes (*chapter seven*), we found advanced skills are achieved in selected populations of elderly people with LLA, including outdoor and community walking. However, when mobility is considered in unselected populations, inclusive of all people undergoing LLA, including those who die post-operatively, less than 50% of the elderly population were able to achieve a household level of prosthetic mobility. A range of different tools were used to assess mobility, and combined with poor reporting of included populations, it was difficult to compare the outcomes from the included studies. Measures of non-prosthetic mobility were limited to non-validated mobility scales that categorise people as being bed-bound or wheelchair dependent. The unique requirements that elderly people face in their rehabilitation, arising from multiple comorbid conditions and a short life expectancy, support a need for further investigation of mobility in this population.

Issues of population inclusion and selection bias were noted throughout the research presented in this thesis. In *chapter eight*, the extent of this problem was described in reference to a previously published prospective study on phantom pain. By comparing with the actual population who had LLA (derived from *chapter two*), we identified that more than 70% of potential inclusions to the phantom pain study had not been referred for inclusion. The missing population were, on average, 8 years older, more likely to have had LLA because of a vascular-related cause and there was a significant difference in one year survival between the groups (40% not referred versus 67% referred). When comparing the included and missing populations without 'reasonable non-inclusions' (i.e. we excluded all of the population who did not survive 12 months, who were most likely not referred to the study because of the severity of their condition), important differences in the age and level remained.

In *chapter nine*, the clinical implications of our findings are discussed. It is clear that older age does not prevent someone achieving good outcomes after amputation. However, studying this population in isolation proved difficult. Some of these reasons are hard to avoid (high rates of death and drop out), while others were highlighted as needing improvement (reporting of included populations). Many aspects of rehabilitation and LTC for the elderly person with LLA were addressed in this research but there are additional important factors which were only briefly mentioned, in particular the availability of family/carers, functional outcomes and falls and balance. Further, among the several study designs used in this research, we focussed on one perspective only, the 'consumer'. An economic perspective could add additional information for decisions. A key finding was that, to a great extent, care is provided through the surgeons' and clinicians' best judgment and experience and there are limitations to consistent decision-making. This includes decisions by the surgeon at the time of amputation through to rehabilitation decisions in LTC. The pre- and early- amputation research is mostly surgically focussed and may benefit from increased input of the rehabilitation team. Amputation rehabilitation for the elderly person extends beyond replacement of the limb, encompassing psycho-social elements and alternative options for mobility. Currently, measures and research of non-prosthetic mobility outcomes are lacking and treatment from a wider group of the multidisciplinary team available in LTC (beyond the physiotherapist) should be implemented.

Nederlandse samenvatting

Met dank aan Jaap van Netten en Maerian de Jong
voor de vertaling van deze samenvatting

In Nederland zijn de meeste mensen die een beenamputatie ondergaan ouder dan 65 jaar. Chronisch vaatlijden of diabetes mellitus heeft bij hen geleid tot onomkeerbare ischemie of een levensbedreigende infectie. Ondanks vooruitgang in preventieve zorg, medische behandeling en (perifere) revascularisatiemogelijkheden, is een amputatie in sommige gevallen de beste optie om langdurige pijn, ziekenhuisopnames en infectie/ischemie te beëindigen en daarmee leven mogelijk te maken. Het is dat 'mogelijk maken om te leven' waar het onderzoek dat in dit proefschrift wordt gepresenteerd op focust. Hoe, en in welke mate, wordt het de oudere met een amputatie mogelijk gemaakt om te leven, vanaf het moment dat de beslissing valt om te amputeren, de daaropvolgende revalidatie, en tenslotte de verpleeghuiszorg?

We beginnen in *hoofdstukken twee* en *drie* met een onderzoek naar de incidentie en de mortaliteit in Noord-Nederland. De revalidatievoorziening voor amputatiepatiënten in de verpleeghuiszorg wordt vervolgens onderzocht in de *hoofdstukken vier* en *vijf*. Twee belangrijke uitkomsten voor ouderen met een amputatie - mobiliteit en gezondheidsgerelateerde kwaliteit van leven – zijn de focus van *hoofdstukken zes* en *zeven*. *Hoofdstuk acht* bekijkt het probleem van 'bias' in het onderzoek van deze populatie. De discussie (*hoofdstuk negen*) vat de klinische implicaties van alle bevindingen samen, daarbij worden de chirurgische beslissingen, de revalidatiesetting, mobiliteit, het belang van beter onderzoek en het rapporteren van de populatie besproken.

In de *hoofdstukken twee* en *drie* van dit proefschrift worden resultaten gepresenteerd van een historische cohort-studie naar amputaties, uitgevoerd in Noord-Nederland in 2003 en 2004. Onderzoek naar veranderingen in de populaties geeft inzicht in de effectiviteit van preventieprogramma's en de behoefte aan revalidatie. *Hoofdstuk twee* focust op de incidentie van amputatie. Daarvoor werden personen geïncludeerd die voor het eerst een beenamputatie (boven de enkel) ondergingen vanwege vasculaire redenen of infecties. De incidentie van amputatie was 8,8 (alle leeftijden) en 23,6 ($\geq$ 45 jaar) per 100.000 persoon-jaren. In vergelijking met de data van een gelijke studie (setting, inclusie en methoden) van de jaren 1991 en 1992 was de incidentie niet veranderd. In de jaren 2003 en 2004 had 50% van de populatie diabetes mellitus. De amputatie incidentie was 151 per 100.000 persoon-jaren, leidend tot een relatief risico op amputatie dat 12 keer hoger is dan in personen zonder diabetes. Onderzoek in andere westerse economieën laten een afnemende incidentie van amputaties zien en een substantieel lager relatief risico voor patiënten met diabetes dan in onze setting wordt gevonden. We stellen voor dat een follow-up onderzoek in een recent cohort gedaan wordt om het patroon van (gebrek aan) verandering in onze regio te bevestigen. Het blijft van belang methoden te vinden om het aantal amputaties te verminderen, nu diabetes vaker voorkomt en de gehele bevolking ouder wordt. Daarbij staat aandacht voor zorg in meerdere disciplines, waaronder vaatgeneeskunde, diabeteszorg en multidisciplinaire voetklinieken, voorop.

Het is bekend dat de mortaliteit na een amputatie hoog is. Mortaliteit wordt toegeschreven aan zowel de hogere leeftijd van de patiënten als aan multipele (cardiovasculaire) comorbiditeit. Op basis van mortaliteit bij verschillende (sub) populaties kan patiënten een prognose gegeven worden over de noodzaak van preventieve en zorg op de lange termijn. In *hoofdstuk drie* rapporteren we dat 22% van de patiënten binnen 30 dagen na hun eerste amputatie is overleden, waarbij cerebrovasculaire ziekten het risico op overlijden in deze periode verdubbelen. Op de langere termijn zijn de cijfers betreffende de mortaliteit positiever; 56% van de patiënten overleeft het eerste jaar en 24% overleeft vijf jaar. De kans op overleven in deze tijdsperioden is het laagst voor mensen met een nierziekte. De mortaliteit werd niet alleen onderzocht op verschillende punten in de tijd, maar voor verschillende combinaties van populatiekarakteristieken, waaronder leeftijd, geslacht, amputatieniveau en de diagnose diabetes. Met uitzondering van de oudste leeftijdsgroep (85+) die een slechtere overlevingskans heeft, vonden we geen substantiële verschillen in de mortaliteit op lange termijn. Tegenstrijdige resultaten tussen onze en andere studies kunnen mogelijk verklaard worden door verschillen in populatie, zoals de inclusie van niet-vasculair gerelateerde amputaties of mensen die partiële voetamputaties ondergaan. Deze procedures worden vaker uitgevoerd bij mensen die jonger zijn en een betere algemene gezondheid hebben dan mensen die een amputatie boven de enkel ondergaan. De variatie in mortaliteit benadrukt het belang van gedifferentieerd rapporteren over de onderliggende oorzaak en amputatieniveau (naast het apart rapporteren van de diabetespopulatie), om 'bias' als gevolg van niet-vasculaire amputaties of verschillende amputatieniveaus te voorkomen.

Met revalidatie moet zo snel mogelijk na een amputatie worden begonnen. Dit is vooral belangrijk voor oudere patiënten die anders een snelle achteruitgang in hun fysieke conditie kunnen ervaren, wat vervolgens weer leidt tot slechtere revalidatieresultaten. Eerder onderzoek heeft aangetoond dat een hoge leeftijd, vrouwelijk geslacht, alleen wonen en een amputatie op een meer proximaal niveau de kansen op het ontslag naar een verpleeghuis voor revalidatie verhogen. In *hoofdstuk vier* rapporteren we dat van alle patiënten die de acute fase overleefd hebben, 55% naar een verpleeghuis ging voor revalidatie. De enige factor die hiermee samenhing was een oudere leeftijd. Ook al was het totale aantal patiënten dat naar een verpleeghuis ging hoog, in de drie noordelijke provincies zaten de patiënten verspreid over 34 verschillende faciliteiten. Deze spreiding leidt tot de vraag hoe clinici amputatiespecifieke kennis en vaardigheden verkrijgen en behouden.

Om dit verder te onderzoeken hebben we clinici in de verpleeghuizen geïnterviewd met als doel vanuit hun perspectief de setting, de barrières en het revalidatiepotentieel voor amputatiepatiënten in de verpleeghuizen te beschrijven. De resultaten, gepresenteerd in *hoofdstuk vijf*, bevestigen dat het kleine aantal amputatiepatiënten in ieder verpleeghuis leidt tot problemen in het geven van efficiënte en evidence based revalidatie. De meeste aspecten van de amputatierevalidatie liggen op het bord van de fysiotherapeut, waarbij de grotere mogelijkheden van het multidisciplinaire behandeling niet benut worden. Ondanks dat andere studies positieve resultaten van amputatierevalidatie in verpleeghuizen laten zien, stellen wij voor dat de huidige organisatie niet duurzaam te handhaven is. In iedere regio een verpleeghuis dat zich specialiseert in amputatierevalidatie is een oplossing. Ook kleinere veranderingen worden voorgesteld, waaronder verbeteringen in de communicatie en de training van clinici.

Mobiliteit van mensen met een amputatie wordt verondersteld de sleutel te zijn voor onafhankelijkheid en de basis voor een hogere kwaliteit van leven. Deze uitkomsten zijn de focus van *hoofdstukken zes* en *zeven*. Verandering in gezondheidsgerelateerde kwaliteit van leven na 18 maanden werd geanalyseerd in een cohort van mensen met een eerste beenamputatie. De invloed van leeftijd en loopmogelijkheden op verschillende gezondheidsgerelateerde aspecten van kwaliteit van leven werden onderzocht, samen met een vergelijking naar de normaalwaarden van de populatie. Achttien maanden na een amputatie was de kwaliteit van leven significant verbeterd in 5 van de 7 domeinen die onderzocht werden - fysieke functies, sociale functies, pijn, vitaliteit en ervaren verandering in gezondheid. De grootste verandering vond plaats in de eerste 6 maanden. Het patroon van verandering over de tijd verschilde alleen voor fysieke functie voor mensen ouder dan 65, in vergelijking met de mensen jonger dan 65. Omdat dit verschil mogelijk werd veroorzaakt door de zeer kleine onderzoeksgroep, vergeleken we ook oudere en jongere groepen met de populatie normaalwaarden. De resultaten ondersteunen het idee dat er leeftijdspecifieke verschillen zijn in de domeinen van kwaliteit van leven die beïnvloed worden door de amputatie. Deze verschillen zouden verder onderzocht moeten worden.

In een systematische review (*hoofdstuk zeven*) naar de uitkomsten op het gebied van mobiliteit vonden we dat geavanceerde vaardigheden bereikt werden in geselecteerde groepen van oudere mensen met een amputatie, waaronder het wandelen buitenshuis. Echter, als mobiliteit bekeken werd in niet geselecteerde populaties, inclusief alle mensen die een beenamputatie ondergaan en inclusief alle mensen die post-operatief overlijden, dan is slechts 50% van de oudere populatie in staat het niveau van mobiliteit binnen het huishouden te bereiken. Veel verschillende meetinstrumenten werd gebruikt om mobiliteit te meten, en in combinatie met het slechte rapporteren van de geïncludeerde populatie zorgde ervoor dat de uitkomsten van verschillende studies moeilijk te vergelijken waren. Meetinstrumenten van niet-prothese gerelateerde mobiliteit waren beperkt tot niet gevalideerde mobiliteit schalen die patiënten categoriseren als 'gebonden aan bed' of 'rolstoel afhankelijk'. De unieke behoeften die oudere mensen tijdens hun revalidatie hebben, als gevolg van de comorbiditeit en de korte levensverwachting, ondersteunen de noodzaak van verder onderzoek naar de mobiliteit van deze populatie.

Zaken als het includeren van de populatie en selectie bias werden beschreven in al het onderzoek gepresenteerd in dit proefschrift. In *hoofdstuk acht* wordt de grootte van dit probleem onderzocht, op basis van een eerder gepubliceerde prospectieve studie naar fantoompijn. Door de actuele populatie die geamputeerd werd (beschreven in *hoofdstuk twee*), ontdekten we dat meer dan 70% van de potentiële te includeren patiënten niet doorverwezen was. De ontbrekende populatie was gemiddeld 8 jaar ouder, had een grotere kans op een amputatie ten gevolge van een vasculair probleem. Bovendien was er een significant verschil in de overleving na een jaar tussen beide groepen (40% in de niet-verwezen groep versus 67% in de verwezen groep). Ook nadat we alle 'terechte niet-verwezen patiënten' (alle patiënten die binnen twaalf maanden overleden en die zeer waarschijnlijk niet verwezen werden vanwege hun slechte conditie) hadden geëxcludeerd, bleven er relevante verschillen bestaan op het gebied van populatiekarakteristieken tussen de geïncludeerde en de niet-geïncludeerde populatie.

In *hoofdstuk negen* worden de klinische implicaties van alle bevindingen besproken. Het is duidelijk dat een oudere leeftijd alleen het bereiken van goede uitkomsten van een amputatie niet in de weg hoeft te staan. Echter, het onderzoeken van deze geïsoleerde groep patiënten is moeilijk gebleken. Sommige redenen zijn moeilijk te vermijden (hoge percentages van overlijden en uitval), terwijl andere redenen in dit proefschrift zijn beschreven als belangrijke gebieden die verbetering behoeven (het rapporteren van de geïncludeerde populatie). Veel aspecten van revalidatie en verpleeghuiszorg voor de oudere amputatiepatiënt zijn in dit proefschrift aan bod gekomen, maar er zijn meer belangrijke factoren die in dit onderzoek slechts kort genoemd zijn. Vooral de beschikbaarheid van familie/verzorgenden, functionele uitkomsten, vallen en balans. Verder, de verschillende onderzoeksdesigns die in dit onderzoek gebruikt zijn, hadden allemaal een focus op slechts één perspectief, dat van de 'gebruiker'. Een economisch perspectief zou waardevolle informatie kunnen opleveren voor de beslissingen die genomen worden. Een belangrijke bevinding was dat de zorg voor het grootste deel geleverd wordt op basis van de best mogelijke inschattingen en ervaring van de chirurg en andere clinici, en dat er beperkingen zijn in het consistent nemen van dergelijke beslissingen. Dit bevat de beslissingen van de chirurg op het moment van amputatie tot de beslissingen tijdens de revalidatie in het verpleeghuis. Het onderzoek naar de fases voorafgaand en direct volgend op amputatie is sterk chirurgisch georiënteerd en kan profiteren van input van het revalidatie team. Amputatierevalidatie voor de oudere patiënt is meer dan het vervangen van een ledemaat, er moet ook rekening ophouden met psychosociale elementen en alternatieve opties voor mobiliteit. Op dit moment ontbreken meetmethoden en onderzoek naar niet-prothese gerelateerde mobiliteit. Ook de behandeling door een bredere groep van het multidisciplinaire team die in de verpleeghuizen beschikbaar is (i.e. meer dan alleen de fysiotherapeut) zou geïmplementeerd moeten worden.

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EXPAND

Extremities, Pain and Disability

Mission: EXPAND contributes to participation and quality of life of people with conditions and amputations of the extremities and musculoskeletal pain.

EXPAND focuses on two spearheads: research on the conditions and amputations of the extremities with emphasis on body functions and structures, activities and participations, and chronic pain and work participation. EXPAND contributes to Healthy Aging, the focus of the UMCG.