Dysvascular lower limb amputation: incidence, survival and pathways of care

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CHAPTER 1 – General Introduction

Generally, when people think of those confronted with lower limb amputation (LLA), they imagine a relatively young person struck with the tragedy of losing a limb due to an accident or worse—as the consequence of war. They imagine persons with amputation overcoming the odds and through “blood, sweat and tears” resuming their life using a prosthesis. This thesis does not deal with the aforementioned group of persons. This thesis will focus on persons undergoing lower limb amputation (LLA) due to diabetes mellitus (DM) and/or peripheral arterial disease (PAD), who constitute the overwhelming majority (90-95%) of newly occurring LLA in the western societies. We will refer to this population as dysvascular amputation patients.

A steadfast adage in biomedical sciences is “more research is needed”. Although junior researchers are often instructed by supervisors to avoid repeating this mantra in their academic work, euphemisms for “more research is needed” are found in the introduction and discussion sections of nearly all peer reviewed research articles. But, for more research, more funding is needed. Funding for medical research is a zero sum game: the amount of money (and time) to go around is finite. When asked, people tend to agree that all patient populations should deserve equal consideration in the advancement of medical science. Although some diagnoses seem to be more equal in importance than others. In 2018, the Dutch KWF Cancer Society and the Dutch Heart Foundation proudly—and justly so—spent €69 million² and €20 million³ on cancer and heart disease related research respectively. Allocated funding for amputation related research has been negligible when compared. Consequently, the available body of evidence within the field of amputation care remains limited compared to diseases with more public appeal. The paucity of research data about dysvascular amputation patients poses considerable challenges for healthcare professionals aiming to apply evidence-based practice in amputation care. Ultimately, this is disadvantageous for the standards of care for persons confronted with LLA. In solving a problem, one should first try to ascertain what is, before attempting to state what ought to be. This thesis focuses on contributing to an evidence-based framework for healthcare professionals in the Netherlands involved in the multidisciplinary treatment of persons with LLA, in order to facilitate decision-making by providing epidemiological data to supplement clinical observations and expertise. The aim of this thesis is to answer two questions pertaining to persons undergoing dysvascular LLA: who are they; and what happens to them after the amputation?

Incidence

The most recent study of newly occurring dysvascular LLA in the Netherlands estimated the incidence in 2003 as 8.8 per 100,000 person-years.⁴ For reference: in 2003 the incidence of myocardial infarction in the Netherlands was estimated between 150 to 210 per 100,000 person-years.⁵ For international comparison: in 2011 the worldwide incidence of LLA was reported to range from 3.6 to 69.4 per 100,000 person-years.⁶ We should notice the strikingly large variation of incidence rates in the
literature and that LLA is a rare occurrence on a population level. Chapter 2 zooms in on incidence rates in the Northern region of the Netherlands. Updated incidence rates and patient characteristics are presented, and potential trends in time spanning two decades are explored, using a cohort of persons undergoing LLA in 2012 and 2013.

**Survival**

Dysvascular LLA is inherently irreversible. It is often regarded a necessary evil, to be performed when other options to preserve the limb have been exhausted. Patients, their families and healthcare professionals are disappointed that diseases have led to loss of a person’s limb. Unfortunately, the disconcerting medical situation does not end with an amputation. Historically, LLA has been associated with “abysmal” survival rates, as up to 47% do not survive the first year after amputation. To put matters in perspective and with the caveat that direct comparison of survival rates ought to be interpreted with caution: all types of malignancies combined, the average 1-year mortality rate due to cancer in the period 2001-2010 in the Netherlands was estimated to be 26%. Among the survivors of amputation, the troubles do not necessarily end: in some cases subsequent LLA on the ipsilateral or/and contralateral limb are unfortunately required. Chapter 3 will focus on mortality and reamputation rates in the geographical cohort. Different subpopulations among persons undergoing LLA will be explored, and the role of potential risk factors associated with mortality and reamputation rates will be investigated.

**Pathways of care**

Many different healthcare professionals are typically involved in the treatment of (to be) LLA patients, prior to and following an amputation: general physicians, (vascular) surgeons, endocrinologists, elderly care physicians and rehabilitation physicians. Multimorbidity is a serious concern among LLA patients; hence, other specialists may also be involved such as cardiologists, neurologists and nephrologists. The small absolute number of cases on a population level and each medical speciality having access to their own medical databases only, produces a *Fog of War* in the pathways of care among persons undergoing LLA. Because of this, healthcare professionals are limited to their personal observations within the confines of their speciality and healthcare facilities, no one being able to observe the clinical course at different stages on a population level. The current literature supports this notion: to my knowledge there are no sources providing an aerial view for the LLA population at different stages and clinical settings prior to and after LLA. That is, previous studies have focused on either hospital, inpatient rehabilitation or skilled nursing facility settings only. Chapter 4 will target three questions pertaining to persons undergoing LLA: where do they come from; where do they go after the amputation; and are they able to return to home eventually? The intricacies in the pathways of care

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* A term used in military operations describing the uncertainty of situational awareness, the adversary’s capabilities and the actual conditions in the battlefield.
will be illustrated, contextual information of the Dutch health care system as it relates to amputation care will be presented, and factors associated with persons’ chances of resuming independent living will be explored.

**Diabetic foot ulceration**

Chapter 5 presents a departure from the amputation cohort. It will focus on Diabetic foot ulceration (DFU) and evaluate the potential merits of a new type of conservative treatment aimed at optimising DFU healing and ultimately preventing amputation. The relatively new total contact softcast (TCS) will be compared to the traditionally applied total contact cast (TCC) with regard to time to ulcer healing and ulcer healing rates.

In this thesis, several clinical observations and hypotheses will be put to the test. A non-exhaustive overview of the hypotheses is presented in Box I, including the respective chapters in which they are discussed in detail. In the General Discussion (Chapter 6) we will recapitulate and reflect upon the hypotheses introduced in the General Introduction.
References

Box 1. Clinical observations, questions and hypotheses.

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**Item I**  
I hypothesize that, as the treatment of DM and PAD has improved in the past two decades, LLA will have become necessary less frequent.

**Item II**  
A clinical observation in the Netherlands is that persons undergoing LLA “keep getting older”.

**Item III**  
I expect that, mortality rates after major* LLA are still very high: one in four persons will not survive the first year after amputation.

**IVa**  
Given that the dysvascular LLA population constitutes persons with pronounced multimorbidity:
- In line with previous studies, I expect that older age, more severe cardiac and renal disease are associated with higher mortality rates;
- Based on the current literature, I am uncertain whether chronic pulmonary disease, cerebrovascular disease, alcohol abuse, autoimmune disease or use of immunosuppressive medication are associated with mortality,
- I hypothesize that DM patients (type I and II) requiring insulin treatment to be worse off in terms of mortality compared to those with DM requiring oral medication only or no DM.

**IVb**  
Surgeons and patients want to avoid LLA as much as possible. They will strive to preserve as much of limb length as it is possible. I hypothesize that more proximal level of amputation is indicative of more severe disease, and will therefore be associated with higher mortality rates.

**IVc**  
In many cases, prior to the eventual major LLA, several revascularisation operations and/or minor LLA are performed. I hypothesize that those undergoing a major LLA without any history of revascularization or minor LLA are generally more physically fit, and therefore have slightly better odds of survival.

**VII**  
A minor LLA is bad, a major LLA is worse in every sense. Surgeons and patients want the major LLA to be the last LLA. I expect that reamputation rates after a major LLA are considerably lower than that of minor LLA (which are about 25%).

**VIII**  
At this time, rates of persons returning home after LLA on the short and long terms are largely unknown. Based on clinical observation, I expect that a majority of persons are discharged to home directly after hospitalization, whereas a small minority does not return to home eventually.

**IX**  
In the Netherlands, dedicated rehabilitation for elderly persons has seen considerable growth in the past decade. Based on post-stroke and orthopaedic injury research, I expect that geriatric rehabilitation in skilled nursing facilities is associated with better odds of return to home after LLA compared to being discharged to care only nursing homes.

**X**  
Based on design characteristics and clinical observations, I expect TCS to be associated with somewhat faster time to healing than, and at least similar healing rates to TCC among patients treated for DFU.

DFU: diabetic foot ulcer; DM: diabetes mellitus; PAD: peripheral arterial disease; LLA: lower limb amputation; TCC: total contact cast; TCS: total contact softcast.

* Major LLA defined as: from ankle disarticulation and more proximal levels.