Chapter 1: General introduction and outline

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In recent years, the medical community has been subject of increasing scrutiny with respect to quality of care in a complex playing field of patient associations, medical insurance providers and politicians, against a backdrop of continuing budgetary limitations. Moreover, it is to be expected that this critical appraisal of outcomes and the relation between costs, results and their effects on health-related quality of life will be intensified over the years to come.

With the introduction of the free market principle in health care and the allowance of competition between care providers within the publicly financed - Dutch health care system in January of 2006 [1], physicians and hospitals have been progressively compelled to allow assessment of their efficiency by outside parties by means of nation-wide audits, registries and the implementation of volume criteria. [2] At the same time, it has become a broadly supported perception that spending of health care funds increasingly has been lacking transparency and consistency. Clearly, more than ever before, health care finance, cost-effectiveness and quality of care have become principal subjects within national budget debates.

In the era of market driven yet still by enlarge publicly financed health care, vascular surgeons, just as anyone, will have to demonstrate that they deliver the best product for the best price, in order to be granted the privilege to supply specific health care products. Also, the influence of patient interest groups is growing. One of the instruments in the assessment of quality of care is the volume of care parameter; another is the registration of complications and mortality associated with different types of treatment [3-6]. It has been hypothesized that these types of hospital and patient related information will aid the care consumer to make a well-founded choice between health care providers.
Outcome measures and their limitations

Vascular surgical practice is commonly divided in six main areas: aortic repair, carotid surgery, haemodialysis access surgery, peripheral arterial reconstruction, venous surgery and a miscellaneous category of diseases less frequently seen, including thoracic outlet syndrome, hyperhidrosis and deep venous thrombosis of the upper and lower extremities. Within these specific areas of vascular care, comparison of outcomes between providers is hampered by heterogeneity, both between and within the populations compared. Although patients suffering from aortic aneurysm and carotid disease still may be fairly comparable, the population of patients with peripheral arterial occlusive disease is commonly very heterogeneous, with different (combinations of) comorbidities, different levels of severity and different clinical manifestations. Many factors influence outcome such as various regimens of preoperative diagnosis, different surgical techniques applied and a range of post-operative care and follow up protocols. On top of this, literature shows us that the beneficial effect of all of current diagnostic and therapeutic modalities on clinical status and especially patient related outcome measures (PROMS, such as health-related quality of life) are far from undisputed. [7-11] It has been shown to be exceptionally difficult to quantify the effect of our treatments, let alone to reproduce our results; unequivocal evidence is simply lacking. Ultimately, all these factors lead to the mere impossibility to perform any valuable comparison that would justify a conclusion as to what is best for our patients. In the category of vascular patients with ‘miscellaneous’ diseases, this is even truer; the relative rarity of these afflictions is an additional stumbling block on the way to reach consensus over diagnostic and therapeutic strategies.

The currently available tools to measure the efficacy of our treatment modalities typically are not broadly applicable, inaccurate and therefore unreliable, especially when measuring PROMS, such as quality of life.
Examples of frequently used tools are the SF-36 health questionnaire, the Euroqol EQ-5D, the Visual Analogue Scale (VAS) for pain, the Walking Impairment Questionnaire, the VascuQol questionnaire, the DASH upper extremity functional outcome questionnaire and the Barthel Index. [12-17]

First, disease or patient group specific tools are best to obtain an adequate and precise reflection of a specific type of patient’s health status. On the other hand, a more generally applicable tool may be preferred to enable researchers to compare their patients with more diverse groups of patients later on. We are facing the following dilemma: do we prefer a very specific tool that provides us with the utmost precise measurement of our patient group, but makes it impossible to compare our group with others (because there are no patient groups alike)? Or, alternatively, do we settle for a more generic, less specific type of tool that gives us less information about our individual patient, but at least allows comparison with other patient groups (assessed with a similar lack of detail)? This reality is frequently illustrated by patients who are very satisfied with their treatment even though it failed to relieve their symptoms, while others are not at all satisfied with their treatment, even though it was a demonstrable technical success.

On a larger scale, differences exist between patient groups, e.g. various hospital populations: some hospitals do treat more severe cases than others. This case-mix has a presumably significant – but largely unidentified and unknown - influence on the outcomes of different medical centers, in terms of complication rates and mortality.

Necessity of audits and quality of care assessments

Regular auditing is necessary to guard the quality of care we provide. Particularly for treatment of conditions from the ‘miscellaneous’ category (that is, relatively rare afflictions for which evidence based treatments are lacking), for example, the neurogenic thoracic outlet syndrome, it is very
important to critically review our own results; we should at all cost avoid exposing patients to disproportionate risks of adverse events and toxicity by giving them treatments that are not supported by solid evidence. Registration in an audit is the only way to detect these risks.

Aim of the thesis

The aim of this thesis is to investigate several methods of quality control, the use of tools measuring PROMS and costs in the diagnostic and therapeutic process, in patients with peripheral arterial disease and patients with thoracic outlet syndrome.

Outline

I. Thoracic Outlet Syndrome
   1. Neurogenic Thoracic Outlet Syndrome (N-TOS)
   2. Deep venous thrombosis of the upper extremity (Paget-Schroetter Syndrome)

II. Peripheral Arterial Disease
   1. Diagnostics
   2. Cost-utility analysis of diagnostics
   3. Intraoperative quality control
   4. Surgical site infection after prosthetic grafting
   5. Long-term follow up after bypass grafting
   6. Treatment of critical ischemia
   7. Management of phantom pain after major amputation
**Ad. I-1.** In **Chapter 2** we assess quality of life and functional capacity of the upper extremity in a group of patients diagnosed with the neurogenic thoracic outlet syndrome. It is hypothesized that patients with N-TOS suffer from brachial plexus compression by musculature, ligaments and bones in the upper thoracic aperture, leading to pain, paraesthesia, hypaesthesia, anaesthesia, muscle atrophy and loss of strength leading to different degrees of disability, varying from mild complaints to complete inability to work and welfare dependence. Diagnosis is hampered by the fact that no diagnostic tools are available to confirm the clinical diagnosis; it is impossible to prove its presence and it is also impossible to objectify any effect that may result from therapy. Imaging and functional tests such as EMG or MRI are useless. One of the treatment options available is costoclavicular decompression by first rib resection; another option is physiotherapy. First rib resection has an uncertain outcome and can result in serious complications, whereas physiotherapy may also have disappointing results but has no complications. It has been hypothesized that the chronic nature of N-TOS makes it very resistant to all types of therapy, as is commonly seen in a variety of chronic complex pain syndromes. Some believe that a certain psychosocial predisposition may play a role. In this group of patients, outcomes are heavily influenced by patient selection; N-TOS is a condition that is diagnosed based on clinical information only. So, which patient actually is suffering from N-TOS, and which patient only looks like he is suffering from N-TOS?

Data on a group of patients with N-TOS, treated with first rib resection or physiotherapy, were retrieved retrospectively and compared with a group of healthy individuals matched for age and gender. Quality of life is measured with the EuroQol questionnaire and function was measured with the QuickDASH questionnaire. Also, pain (VAS-score) and the degree of relief of symptoms are measured. Aim of this study is to identify any association between different treatments, quality of life and functional outcome.
Ad. I-2. In Chapter 3 we investigated the effect of thrombolysis and first rib resection on quality of life in patients suffering from spontaneous deep arm vein thrombosis. Spontaneous deep arm vein thrombosis is a fairly rare condition. It is known that indwelling venous catheters and paraneoplastic effects may lead to thrombosis in the upper extremity, but the pathogenesis of spontaneous deep arm vein thrombosis is not clear. It is generally accepted that vigorous upper extremity labour may cause arm vein thrombosis by repetitive trauma to the subclavian vein due to crushing of the vessel between the first rib and the clavicle. It is also hypothesized that muscle hypertrophy in the upper thoracic aperture (subclavicular muscle, scaleneus muscles, minor pectoral muscle) may lead to compression and subsequent thrombosis, as is sometimes seen in athletes or bodybuilders.

Deep arm vein thrombosis is associated with the occurrence of the ill-defined post-thrombotic syndrome, consisting of complaints such as fatigue, pain, swelling, discomfort, impaired function and – in extreme cases – ulceration. This post-thrombotic syndrome is held responsible for the disability and the loss of quality of life in – often young and active - patients who were treated for deep arm vein thrombosis, successfully or not. There are no tests available to objectify its presence.

Current treatment options for deep arm vein thrombosis are administration of oral anticoagulants, catheter guided thrombolysis, first rib resection or a combination of these. Although the literature shows an on-going trend towards a more and more aggressive approach in these patients, probably because of the feared post-thrombotic syndrome, evidence in terms of quality of life is far from uniform.

In this study, patients treated with anticoagulants, thrombolysis and thrombolysis combined with first rib resection were asked to rate their quality of life and record their symptoms that are related to the post-thrombotic syndrome.
Goal of this study is to determine the relation between different treatment regimens and the occurrence of symptoms associated with PTS, and to assess differences in QoL.

Ad. II-1. Chapter 4 focuses on the clinical utility of magnetic resonance angiography (MRA) as a minimally invasive alternative to digital subtraction angiography (DSA) in patients with peripheral arterial occlusive disease. Goal was to evaluate the use of MRA as a first choice imaging tool for treatment planning in patients with PAOD. The question we intended to answer is whether MRA can compete with other imaging modalities as an independent tool in preparation for a therapeutic intervention. In order to do so, we collected clinical information, MRA images and follow up data on 128 consecutive patients with manifestations of PAOD, between August 2003 and June 2004. The use of additional imaging, deemed necessary because MRA did not get us the information we thought we needed (duplex, DSA), was recorded. To assess its clinical utility, we compared pre-treatment MRA-findings with intraoperative findings or findings during percutaneous intervention: is the actual situation indeed reflected by the predictions that MRA provided? Is MRA over – or underestimating reality? Does MRA present us with unforeseen situations, does it confront us unfavourable surprises when we are in the middle of a procedure? Is additional imaging frequently required or can we do the job with only MRA as our map?

Ad. II-2. In Chapter 5 we have taken an economic point of view on imaging in PAOD. We performed a cost-utility analysis of MRA and DSA; how much quality of life do we gain per euro spent and is there a difference in QoL benefits between patients preoperatively assessed with MRA and DSA? To answer this question, 79 patients out of a cohort of 200, enrolled in an earlier randomized diagnostic trial that compared diagnostic accuracy between MRA and DSA in patients with PAOD, filled out a QoL questionnaire before and 4 months after randomization. Additionally, other
variables influencing QoL, such as comorbidities, and type of treatment were recorded. We look at changes in QoL within each group (those analyzed with MRA and DSA, respectively) over time, and we compare the changes over time between groups. We also make an effort to determine the exact amount of money spent on each patient, from the time they were included, until 4 months later. Also, a revealing insight was gained in the differences and ways money was spent within those two groups. Bootstrap analysis is used to make an estimate on the relative difference in QoL gained or lost per euro spent, and to make a modest suggestion as to which imaging modality to pick, from a cost-utility perspective.

Ad. II-3. Chapter 6 is about intraoperative functional bypass evaluation. It is reasonable to assume that an immediately well performing bypass will have a better life span than a bypass that has a mediocre performance at best from the start. It is a known fact that poor flow is associated with imminent bypass failure. Many methods of intraoperative bypass evaluation are currently in use, including routine completion angiography (which many surgeons will consider a hassle), the somewhat crude and widely interpretable technique of pulse palpation (obviously requiring great experience), duplex ultrasonography, continuous wave Doppler and volume flowmetry. This section discusses intraoperative volumetric flow measurements (VMF) as a means of quality control: does a certain flow within a vein graft tell us something about the risk of bypass failure later on, and can we determine an minimal flow that will warrant bypass patency to some extent? To answer this question, a group of 273 consecutive patients undergoing infrainguinal vein grafting were studied, of which 103 had an intraoperative VMF. We compared patients with and without VMF, to see if the use of VFM predicts a better patency, or maybe bypass failure and whether VFM leads to immediate bypass revision. 30-day postoperative revision rates between these groups were also compared. A receiver operating characteristic curve was made in an attempt to identify a VFM cut-off point, associated with bypass failure.
Ad. II-4. Wound complications pose a risk to all patients undergoing surgery. Despite numerous efforts, surgical wound infections still occur in a considerable number of patients, varying by the type of surgery they had. Especially in patients receiving foreign material implants, infection causes significant morbidity and mortality. The incidence of wound complications in individual hospitals now has become a quality parameter used by insurance companies and government health inspection agencies in the Netherlands. For some hospitals, this has led to intensified scrutiny and monitoring by the National Health Inspection, illustrating the widely shared sense of urgency associated with this complication. Chapter 7 includes an investigation of a much feared post-operative complication: surgical site infection after prosthetic vascular graft implantation and prosthetic graft infection. It has been amply stated that surgical site infection is a multifactorial phenomenon, that cannot be dealt with by means of a simple, one-way solution. In order to define risk factors for groin wound infection after prosthetic vascular reconstruction, the data of 202 consecutive patients were subjected to univariate comparison to detect significant differences in patient variables between those with and without infection, and a multivariate analysis to identify variables associated with the occurrence or absence of infection. Special interest is aimed at the role of the duration of intravenous antibiotic prophylaxis and the use of antibiotic impregnated grafts.

Ad. II-5. In Chapter 8 we assess the outcomes of above knee prosthetic bypass grafting, discussing both patient-oriented outcomes (quality of life, walking ability) and physician-oriented outcomes (patency, amputation rate, survival).

Traditionally, the primary focus of investigations on bypass grafting has been on bypass patency, a physician oriented outcome. In this study we make an attempt to assess the effect of bypass grafting, bypass occlusion, bypass salvage and bypass revision on two patient-oriented outcome parameters: quality of life and walking ability.
For this study, we prospectively included 140 patients that needed femoropopliteal bypassgrafting with prosthetic conduits. Long term QoL and Walking ability were assessed with questionnaires. From the perspective of QoL and walking ability the effect of bypass failure, the relationship and discrepancies between patient and physician-oriented outcomes and the necessity of bypass surveillance, revision and salvage are discussed.

Ad. II-6. By means of a systematic review, in Chapter 9 we discuss the relation between quality of life and treatment of patients with critical limb ischemia and try to shed some light on the issue of primary amputation versus revascularisation in this population of very fragile vascular patients. It seems obvious that some patients are better off with an immediate amputation and a quick return home, rather than a far-fetched attempt at revascularisation of some kind, with the risk of all sorts of near-lethal and lethal complications, maybe leading to some degree of disability or dependence. However, patient selection for either treatment option has proven to be difficult at times; revascularisation in patients with CLI is not rarely followed by revascularisation failure and subsequent amputation, of which the outcome is far worse than the outcome of primary amputation. What use is a salvaged limb that only has limited function, or a salvaged limb that severely limits the functioning of the patient? Patient selection appears to be of pivotal importance in the resolvement of this issue.

Ad. II-7. The final section, Chapter 10, is about pain management after lower extremity amputation in PAOD patients. Amputees are often suffering from phantom pain, which is sometimes very resistant to analgesic therapy. The only know effective treatment is the administration of opioids, but this is often insufficient. Some of these patients in despair will resort to different types of self-help measures. Anecdotally, wrapping or rubbing the amputation stump with aluminium foil is said to result in some degree of pain relief. In order to determine the effect of aluminium
wrapping of the stump, a randomized, double-blind, placebo-controlled cross-over trial is performed.

This thesis demonstrates the use of a variety of methods to assess quality of care in groups of patients for which sound evidence is absent. The effect of both diagnostic and therapeutic modalities on the quality of care are studied, using different instruments, covering different types of patient- and physician related outcome measures.
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