ISPO Report
Major Lower Limb Amputations Due to Vascular Disease: A Multidisciplinary Approach to Surgery and Rehabilitation

Karen L. Andrews; Malte Bellmann; Helena Burger; Joseph Czerniecki; Bernard Greitemann; Jan H. B. Geertzen; Andreas Hahn; Matthew Houdek; Anton Johannesson; Gert-Uno Larsson; Magnus Lilja; Saffran Moeller; Carolina Schiappacasse; Ernst Schrier; Harmen van der Linde; Harry Voesten; Saeed Zahedi

I. INTRODUCTION

Vascular disease is the most common cause of amputation, accounting for 82% of all amputations.[1] Although the incidence of amputation due to trauma and cancer has decreased,[1, 2] amputation due to vascular disease continues to increase. This report is specifically directed to the management of individuals with peripheral arterial disease (PAD) who are at risk or have undergone major lower limb amputation (above the ankle) and includes the amputation continuum from preoperative evaluation and limb salvage through surgical decision making, early postoperative rehabilitation, and residual limb healing. Assessment by a multidisciplinary team in the preoperative phase forms the basis for the policies to be followed after surgery and during the rehabilitation process. The involvement of multiple disciplines reduces the risk of complications during surgery and the postoperative phase.[3] In this report, we discuss:

- Evaluation and management of PAD and critical limb ischemia (CLI) prior to major lower limb amputation due to vascular disease
- Amputation surgery
- Postoperative dressings following amputation surgery
- Postoperative management in the immediate postoperative period
- Rehabilitation from amputation to initial prosthetic management
- Pain management following amputation
- Prosthetic prescription following lower extremity amputation due to vascular disease

This ISPO consensus report is realized thanks to ISPO International, Otto Bock, Protheor, Ossur, and Blatchford with the engagement and cooperation of the members of the ISPO consensus meeting February 2015, Basingstoke, UK. Dutch Evidence-Based Guidelines for Amputation and Prosthetics of Lower Extremity: Amputation Surgery and Postoperative Management. Part 1[4] and Dutch Evidence-Based Guidelines for Amputation and Prosthetics of the Lower Extremity: Rehabilitation Process and Prosthetics. Part 2[5] were published in 2015. Over the past few years, additional relevant papers regarding management of lower limb amputation due to vascular disease have been published. The ISPO International Consensus Group comprised of academicians, clinicians, and researchers was chosen to update the 2015 guidelines. The composition of the Consensus Group was based on profession, region of the world, and expertise. Members included surgeons (vascular and orthopedic), physicians (internal medicine and rehabilitation), prosthetists, therapists, engineers, and a psychologist all with expertise in amputation surgery and/or prosthetic rehabilitation. The goal of this report is to provide an updated international version of the previous Dutch guidelines. This report is created for care providers throughout the world who are involved in

the care of people with lower limb amputation due to vascular disease. Resources and expertise differ widely in many parts of the world. We hope that updating the Dutch guidelines to create an international report will help nations establish their own care directives.

II. METHODS
DATA SOURCES AND SEARCHES

In 2015, the Netherlands Society of Physical and Rehabilitation Medicine (VRA), a national society for medical specialists in rehabilitation medicine, and the Utrecht-Based Dutch Institute for Healthcare Improvement (CBO) developed the Dutch Guidelines for amputation and prosthetics of the lower extremities.

The recommendations in the 2015 Dutch guidelines[4, 5] were based on evidence from published scientific research. Relevant articles were identified by performing systematic searches in the Cochrane Library, Medline, Embase, PsycINFO and CINAHL. Languages were limited to Dutch, English, German, and French. Manual searches were also conducted. Search dates were between 1966 (Medline) and 1980 (Embase) and no later than January 2011. Additional information on the systematic review can be found in the Dutch Evidence-Based Guidelines for Amputation and Prosthetics of the Lower Extremity: Amputation Surgery and Postoperative Management.[4]

The current report was developed by a consensus process and is based on additional relevant references found through a consensus meeting February 2015, in Basingstoke, UK. We sought to capture the highest quality of literature available regarding major lower limb amputation due to vascular disease. The text was reviewed and revised by the consensus group. We formulated updated recommendations of key points for daily practice based both on available evidence and expert opinion.

The first draft of this report was presented in 2017 at the ISPO World Congress for public comment. Subsequent drafts were revised based on those comments. The updated recommendations are listed below.

III. EVALUATION OF THE PERSON WITH VASCULAR DISEASE PRIOR TO LOWER LIMB AMPUTATION

Dutch Guidelines:

-To prevent amputation, it is critical that patients with peripheral arterial disease (PAD) at risk of amputation are detected at an early stage. (Level 4)[4]

-To prevent amputation it is recommended that patients with critical limb ischemia receive a multidisciplinary evaluation and treatment. (Level 4)[4]

-All diabetic patients with ulcers should be assessed for PAD using objective tests, such as duplex ultrasound and ankle-brachial indices. (Level 4)[4]

-Early amputation may be indicated in critical limb ischemia, with the aim of achieving better long-term function and a lower risk of comorbidities.[6, 7](Level 4)[4]

-An amputation is indicated if there is: a severe (life threatening) infection, tissue loss due to extensive necrosis, intractable pain. (Level 4)[4]

-Immediate amputation should be considered in cases of acute ischemia and/or sepsis.[8] (Level 4)[4]

-If the vascular status is not yet established or if demarcation of the region for amputation has not yet taken place, it is advisable to postpone amputation. (Level 4)[4]

-In addition to the clinical assessment, anatomic localization of vascular disease can be obtained with segmental blood pressure or pulse volume recordings. (Level 4)[4]

-Arterial calcification may result in non-compressible vessels with the inability to obtain ankle brachial indices (ABIs). (Level 4)[4]

- When a discrepancy between clinical findings and non-invasive vascular studies arises, vascular imaging should be considered.[8] (Level 4)[4]

-Where arterial imaging is necessary for treatment decisions, the following imaging techniques are recommended: duplex examination, digital subtraction angiography (DSA), magnetic resonance angiography (MRA) and computed tomography angiography (CTA). (Level 4)[4]

-When revascularization is not an option or revascularization will not result in a functional limb, amputation should be considered. (Level 4)[4]

-The goal of an amputation is to achieve (initial) wound healing as distal as possible with the highest possible post-amputation function.[8] No clear criteria are given in the literature for the clinical assessment of the amputation level.[9] (Level 4)[4]

-When determining the level of amputation, preoperative mobility and the prospects for postoperative mobility should be taken into account. (Level 4)[4]

Updated Evidence:

Decision-making regarding limb salvage versus amputation remains complex. When an important decision like amputation needs to be made, the patient's opinion should be incorporated into the decision. Multidisciplinary evaluation and treatment (surgeon, anaesthesiologist, pain specialist, rehabilitation physician, and vascular medicine specialist) preoperatively is important for treatment of pain, cardiovascular risks, comorbidities, and to determine the level of amputation. The first step to evaluate the vascular status involves physical examination including skin temperature, capillary refill, venous refill, pulse exam and assessing ischemic changes (atrophy of the skin, hair loss, dystrophic nails, purpura, necrosis). In patients with PAD and diabetes, claudication may be masked due to neuropathy.

The European Consensus document defines critical limb ischemia (CLI) as persistently recurring ischemic rest pain or ulceration, or gangrene of a foot or toes lasting greater than two weeks.[10]

It is estimated that 5%-10% of patients with peripheral arterial disease older than 50 years develop CLI within five years.[11]

Critical limb ischemia is associated with high morbidity and mortality. Evaluating 13 studies enrolling 1,527 patients with a median follow up of 12 months, all-cause mortality was 22% and major amputation rate was 22%.[12] 30% of patients with CLI require amputation within the first year after diagnosis. The five-year mortality rate for CLI patients is 70%. Most of the deaths are cardiovascular related.[11]

Arterial disease can be demonstrated by either non-invasive or invasive vascular tests. The vascular laboratory plays an important role in non-invasive studies. The ABI is not accurate when the systolic blood pressure cannot be abolished using a blood pressure cuff. The incidence of non-compressible (artifactually high), calcified conduit arteries is highest in diabetic, elderly, and chronic renal failure patients. The resulting ABI values can be falsely elevated. Despite high recorded systolic pressure, these individuals may have severe disease. In this population, a greater importance should be attached to toe pressures and $TcPO_2$ measurements.[11,13] The use of transcutaneous oxygen pressure ($TcPO_2$) may provide an important tool to make clinical decisions regarding an appropriate level of amputation.[14]

According to TASC II[8] the following indicate CLI:

- Ankle pressure < 50 mm Hg
- Toe pressure < 30 mm Hg
- $TcPO_2$ < 30 mmHg

Revascularisation (surgical or endovascular) is effective in the prevention of amputation.[15] Because evidence indicates that blood flow to the lower limb improves in the first three weeks after revascularisation, deferred amputation following revascularisation is preferred.[16]

An amputation should be performed when a subsequent vascular reconstruction is no longer possible or if, despite successful revascularization, progressive ischemia is noted. In general more distal surgery provides a better functional outcome, but has increased risk of non-healing, re-ulceration, and re-amputation. Technical factors, aspects of wound healing, deconditioning and existing comorbidities are all factors that determine whether a patient is suitable for amputation.

In wet gangrene (whether local or generalised) immediate surgery is indicated to remove the infection. A guillotine amputation is used in this situation. Urgent amputation prevents further deterioration of the patient's clinical condition, resulting in an increased chance of recovery. A subsequent definitive amputation is then performed following recovery from sepsis syndrome. This leads to better results than a single intervention in this patient population.[17]

For individuals with end-stage renal disease (ESRD), revascularization is more expensive and less beneficial than in the general CLI population.[18] Two characteristics of individuals with end stage renal disease make limb salvage very challenging (1) limb salvage fails more frequently in the ESRD population than in non-ESRD critical limb ischemia; (2) the perioperative survival and long-term survival of patients with ESRD are both significantly lower than those of the non-ESRD CLI population.[19, 20] Studies suggest that local wound care and endovascular intervention may be more cost effective than primary amputation for individuals with critical limb ischemia and end-stage renal disease.[18, 21]

An important question is which subgroups of patients with critical limb ischemia would ultimately benefit more from amputation than revascularisation. It is important to weigh the chances of successful vascular reconstruction and subsequent mobility – against the chance of healing and mobility following initial amputation. Amputation, rather than revascularisation, may offer patients a more rapid return to an acceptable quality of life.

Evidence suggests that there is no significant difference in function at two years when comparing revascularization versus amputation, although limb salvage is associated with higher risk of complications, additional surgeries, and re-hospitalizations.[22] Some patients may weigh the risks of a reduced rate of healing of a distal amputation as acceptable if they have a higher likelihood of mobility. Others may prefer an amputation where the probability of primary healing is better and mobility may be adequate.[23]

Predicting whether a patient will use a prosthesis is a clinical judgement taking many factors (physical, medical, psychological, and social) into account. The perioperative consultation should address the likelihood of successful prosthetic fitting and use. This can assist the team to determine the optimal level of amputation.

At 1 year post-amputation, functional prosthetic use is reported in 47%-70% of persons with limb loss.[24-30] Persons with trans-tibial level amputation were more likely to be prosthetic ambulators (60-70%) than those with trans-femoral level amputation (40-50%).[27, 28] In one study, 5 years post-amputation, the number of prosthetic ambulators decreased to 17%.[25] The total one year mortality was 40% (17% among patients who received a prosthesis and 67% among those who did not prosthesis or had undergone reamputation).[30]

Chronic obstructive pulmonary disease, end-stage renal disease requiring hemodialysis, diabetes, hypertension, alcohol use disorder and history of treatment for anxiety or depression are all associated with worse functional outcomes.[27, 31] On the contrary, white race, being married and having at least a high school education are associated with better outcomes.[27]

The main factors associated with mobility are age, length of stay in a rehabilitation facility, and the mobility level prior to surgery.[29, 32] Wound complications,[32] a higher amputation level,[28, 33] older age[28, 29, 32, 33] and a low level of mobility before surgery often result in unsuccessful prosthetic fitting.[28, 29] Factors associated with functional status include age,[29], presence of diabetes mellitus,[34] standing balance and cognition.[29]

Patients undergoing lower extremity amputation due to vascular disease have often been functionally limited by peripheral arterial disease, foot ulcers, infections, and weight-bearing restrictions (sometimes for years prior to amputation). As a result, definitive management with amputation surgery can sometimes improve their function.

A subset of patients experience improvement in their functional mobility after amputation. Norvell reported that 37% of individuals with amputation returned to or exceeded their premorbid level of function at 1 year post-amputation.[31] Johnson also reported that many persons with unilateral trans-tibial amputation are able to maintain or improve their function after amputation.[35]

It has been suggested that persons with amputations comprise 2 distinct groups: the fit (often traumatic amputation); and the older, medically unfit patient who has a poorer prognosis.[36] Among this latter group, there is a great variation in functional outcome dependent on age, medical status and other factors. The ability to predict which among these patients are prosthetic candidates may reduce the costs and burden of care resulting from unsuccessful prosthetic fitting and allow earlier focus on interventions that will increase the patient's independence and quality of life.

Premorbid function is also predictive of post-amputation function.[35] Patients who are non-ambulatory prior to amputation are unlikely to resume ambulation after amputation.[24]

Every effort must be made to achieve initial wound healing at the trans-tibial level to preserve the knee. A trans-femoral level amputation increases the metabolic cost of ambulation. An initial trans-femoral level amputation (without prior vascular intervention) is performed in rare cases (non-ambulatory patients). The indication for this will be determined by:

- the risk of surgery due to medical comorbidities
- surgical options
- the patient's function and possible rehabilitation

With a knee flexion contracture, a knee disarticulation or long trans-femoral amputation may provide a superior option. Conversely, a knee disarticulation is an option worth exploring when a trans-femoral amputation is being considered.

If a patient is not a prosthetic candidate, they may be better served with a trans-femoral level amputation. For patients with limited mobility, dementia, end-stage renal disease and/or severe coronary artery disease; a knee disarticulation or trans-femoral amputation is considered.[28]

When prosthetic fitting patterns were examined for geriatric patients over 40 years, no marked changes in the rate of fitting or prosthetic wear occurred, despite technologic developments, advances in revascularization procedures, and provision of rehabilitation services. This suggests that a physiologic limit to successful prosthetic fitting may exist due to advanced age and comorbidity.[37]

IV. SURGICAL TECHNIQUE IN MAJOR LOWER EXTREMITY AMPUTATION DUE TO VASCULAR DISEASE

Dutch Guidelines:

-Good surgical technique (no excess soft tissue, no neuromas, a good residual limb shape, mobile scars and no joint contracture) helps ensure a 10-20% greater chance of postoperative mobility. An experienced surgeon achieves better results, both in terms of mobility and lower risk of re-amputation.[38] (Level 4)[4]

Updated Evidence:

Amputation surgery should be viewed as a reconstructive procedure carried out by an experienced, prosthetically aware, surgeon. The working group believes that patients facing

amputation require subsequent supervision and treatment by a multidisciplinary team in the hospital, with continued outpatient rehabilitation in a rehabilitation center, nursing home or at home.

Surgical technique including: use of a tourniquet; osseous length; residual limb length; trans-tibial skew, long posterior, or sagittal flaps; transtibial, trans-femoral and knee disarticulation level amputations; and bone bridge synostosis are discussed in the Dutch Guidelines.[4] Surgical technique varies between region and country. Obtaining consensus on optimal surgical technique would be challenging is beyond the scope of this project.

V. POSTOPERATIVE COMPLICATIONS FOLLOWING AMPUTATION SURGERY

Dutch Guideline:

-Complications can be divided into disorders that lead to delayed wound healing (wound edge necrosis, dehiscence and infection) and those that are more severe (progressive ischemia with extensive necrosis, infection, revision, venous thromboembolism, sepsis and death). (Level 4)[4]

Updated Evidence:

Robertson[39] reviewed the literature regarding the effectiveness of thromboprophylaxis in preventing venous thromboembolism in people undergoing major lower extremity amputation. Only two studies were included in this review, each comparing different interventions. There is inadequate evidence to make any conclusions regarding the most effective thromboprophylaxis regimen in patients undergoing lower limb amputation.

Wound healing is of primary importance after amputation due to the morbidity associated with delayed wound healing and re-amputation. Wound care, edema management, diabetic control, smoking cessation and adequate nutrition are all important factors. Optimally, wound healing takes 6-8 weeks after amputation. Amputations due to vascular disease may have a more prolonged course. Healing at 100 and 200 days was 55% and 83% for trans-tibial and 76% and 85% for trans-femoral amputations.[24]

Mortality after amputation is very high in the population with PAD. 30 day mortality after amputation is 8-10%.[24, 40, 41] 1 year survival is 60-70% and 5 year survival is 35% following amputation due to vascular disease.[40, 42] A cohort study by Stone[43] retrospectively evaluated 380 patients (median age 67 years) following recovery from trans-tibial or trans-femoral amputation. The exclusion criterion was amputation due to trauma. The results showed a perioperative mortality of 15.5% (n=59) in this population, with a prevalence of wound complications after 90 days of 13.4% (n=51). Reamputation was performed significantly more often in patients who underwent trans-tibial amputation, while patients with a trans-femoral amputation often underwent a local revision ($p = 0.0006$). The same result was seen in a study by Cruz;[44] in 229 patients (average age 68.8 years) who required amputation (trans-tibial (n=119), trans-femoral (n=177)), a significant difference in revision of the original amputation was seen in the group with a trans-tibial amputation ($P > 0.0001$).

Nehler[24] studied a cohort of 154 patients (median age 62 years) who had one or more amputation(s) (trans-femoral amputation (n=78), trans-tibial amputation (n=94)). Reasons for

exclusion were non-ambulatory, dementia, or neurologic disorders. The results showed a perioperative mortality of 10%. 57 revision surgeries were required (trans-tibial amputation (n=23); trans-femoral amputation (n=16); trans-femoral reamputation in 18 patients (19%)).

Campbell[45] retrospectively studied a cohort of 312 patients with one or more lower extremity amputation(s) (trans-tibial, n=192; trans-femoral, n=122; Gritti-Stokes, n=34; hip disarticulation, n=1). The study looked at the overall revision rate (12%) and perioperative mortality within 30 days (18%). Although no statistical analysis comparing the different levels of amputation was reported, individual percentages showed that the trans-tibial group had the highest revision percentage (19%), and perioperative mortality was highest in the groups that required trans-femoral or Gritti-Stokes amputation (both 24%).

Johannesson[46] prospectively followed 190 patients undergoing lower extremity amputation over a period of 4 years. The results showed that 27 patients died within one month of surgery, 24 patients required reamputation (16 trans-femoral, 8 trans-tibial), and 5 patients with trans-femoral amputation, required reamputation twice.

Certain comorbid conditions increase risk. Perioperative sepsis, congestive heart failure, renal failure and liver disease were associated with higher mortality in hospital, at 30 days and at 1 year.[40, 47] 1 year and 5 year survival was found to be comparable in patients with diabetes (69.4% and 30.9% survival at 1 and 5 years), but much worse in patients with either end-stage renal disease (51.9% and 14.4% survival at 1 and 5 years) or renal insufficiency (55.9% and 19.4% at 1 and 5 years).[40] Patients with renal insufficiency were also more likely to undergo repeat amputation within 30 days.[48]

Higher level of amputation is also associated with increased mortality. Mortality from in hospital to 5 years is higher for those with trans-femoral compared to trans-tibial amputation.[40, 47] 1 year survival was 75% in persons with trans-tibial compared to 50% with trans-femoral amputation. 5 year survival was 38% with trans-tibial level amputation compared to 23% with trans-femoral amputation.[40]

Given the high mortality after amputation due to vascular disease, it is important to identify appropriate interventions and rehabilitation goals to improve mobility, independence and quality of life early following amputation. Delayed wound healing will mean more time spent in the hospital, more medical appointments, and greater burden of care over many months. It is important to discuss prognosis and realistic goals with the patient and their family to avoid a prolonged period trying to heal a distal amputation or attempting prosthetic rehabilitation, if they are unlikely to be a functional prosthetic user. Some may be better served by a more proximal amputation, successful healing, and wheelchair mobility.

VI. POSTOPERATIVE DRESSINGS IN THE EARLY POSTOPERATIVE PERIOD

Dutch Guidelines:

-The benefits of soft dressings are ease of application, low cost and easy access to the wound. The drawbacks include: they become loose and fall off; they do not prevent joint contracture; they cause risk of a “choke” of the distal residual limb if too much compression is applied proximally and they do not protect the limb in the event of a fall. (Level 4)[4]

-Rigid dressings help optimize wound healing, control edema, shape the residual limb, prevent

contracture (when they extend above the knee), protect the limb and control pain. (Level 4)[4]

-There is a small difference in favour of the (semi-) rigid dressing (RD) in comparison with a soft dressing (SD) in terms of a reduction in the number of days to prosthetic fitting (Level 2)[4]

-A RD is favored in comparison with SD in the time required for wound healing.(Level 3)[4]

Updated Evidence:

Different types of dressings are used around the world (elastic bandage, socks, SD, RD, compression garments or liners) to help protect the limb and control edema. The advantages of the classic elastic stump dressing as described in the literature are based on the simplicity of this method, the minimal time required, the use of widely available materials and possibility for frequent wound inspection.[49, 50] Different kinds of soft or compressive dressings include self-adherent compressive bandage, figure of 8 compressive wrap, and a postoperative prosthetic sock with a garter belt suspension.

Known disadvantages are the experience required (in application of the dressing), high resting pressure, the potential for local or proximally generated pressures that may negatively affect healing, the required frequency (4 to 6 times daily) of application, the tendency of the dressings to loosen and sag and the limited protection of the amputation stump.[49, 50] A number of these disadvantages can be overcome by the use of elastic compression socks (stump shrinkers), or silicone liners, when tolerated, however these methods do not adjust to volume change. No comparative studies were found on this subject. The treatment team's experience with a particular method is of obvious importance.[50] Education is provided to optimize positioning and avoid dependent edema.

There is a considerable body of evidence in the literature in favor of rigid dressings applied directly after the amputation.[51] The comparison between a rigid removable dressing (RRD) and an elastic bandage on the reduction of stump volume was investigated by Janchai.[52] A clear but non-significant trend ($p = 0.064$) was observed in favour of the RRD, but only in the first 2 weeks of use. These findings are also supported by the systematic review by Nawijn,[53] which further notes that most studies were particularly weak in terms of patient numbers. Advantages of rigid dressings include edema management prevention of contracture (when they extend above the knee), and protection in case of a fall. Studies of rigid dressings show that they decrease time to prosthetic fitting compared to other management.[51, 54-56]

Although it is generally assumed (and reported in some descriptive and case studies) that rigid dressings achieve better pain reduction than elastic bandages, no significant evidence for this was found in the selected controlled trials. This may be due to the lack of power in these studies or the lack of suitably sensitive instruments to quantify postoperative pain.[49] Thus far, this pain-reducing effect has not been demonstrated.

The drawbacks of a non-removable plaster cast are that it requires weekly application by a skilled professional, prevents access to monitor the incision and is heavier and more costly than a soft dressing. A rigid removable dressing can be taken off to monitor the incision and is less heavy and costly than a non-removable rigid dressing.

A nonremovable rigid dressing allows the attachment of an immediate (or early)

postoperative prosthesis (pylon cast), which includes a connector, pylon and foot. The pylon cast has been purported to allow patients with trans-tibial amputations an opportunity for early ambulation without increased complications compared with other postoperative dressings.[57, 58] A study showed that despite a pylon cast, patients were mostly sedentary and had a low quality of life in the first six weeks after trans-tibial amputation.[59]

At the trans-femoral level, an early postoperative, provisional prosthesis can be used with a locking knee and toe-touch weight-bearing to avoid excess forces at the surgical incision.

The impact of early weight-bearing on wound healing is unclear. Potential complications include a pressure injury/ischemia if incorrectly applied and mechanical tissue trauma inside the cast.[49]

Before initiating any type of dressing, the team should be well prepared and trained. Before switching to using rigid dressings for postoperative management, all logistical obstacles should be overcome. If there is a lack of experience, choose the easiest method with least risk of complication.

For trans-tibial amputations, either a rigid or a soft dressing can be used. The consensus group recommends a rigid dressing as the treatment of choice during the early postoperative phase for persons with trans-tibial level amputations. When using a rigid dressing, compression is used, in the last few weeks, to shape the limb prior to prosthetic fitting. With trans-femoral level amputation, rigid dressings can be challenging (incontinence, suspension). Following trans-femoral amputation, typically soft dressings are used.

VII. THE REHABILITATION PROCESS FROM AMPUTATION TO INITIAL PROSTHETIC MANAGEMENT

Dutch Guidelines:

-Treatment should be consistent, consistently implemented, and follow a set framework or care plan. Information is a vital part of any medical treatment. Any information must be tailored to the specific needs of the individual and included in their medical record. (Level 4)[5]

-Optimal learning methods, coping styles, and skills should be determined during initial evaluation and reassessed during the course of rehabilitation. (Level 4)[5]

-Patients should be educated about stretching and positioning to avoid joint contracture. (Level 4)[4]

-Intensive physical therapy following lower limb amputation results in better load-bearing capacity and an improved 2-minute walk test, when compared to a less intensive treatment program.[60] (Level 3)[5]

-The multidisciplinary rehabilitation team determines the discharge destination following lower limb amputation based on the individual's expected function, social situation, and medical comorbidities. (Level 4)[5]

-Patients who receive inpatient rehabilitation after lower extremity amputation have a better 1-

year survival rate, greater success with prosthesis fitting, and are more likely to return home than patients not receiving inpatient rehabilitation.[42, 61, 62, 63] (Level 2)[5]

-Following amputation, a patient needs to adapt to an altered body image, postoperative management (possibly a prosthesis), and an altered future. (Level 3)[5]

-Social support positively influences the adjustment process.[64-68] (Level 3)[5]

-Cognitive decline reduces the chance of successful rehabilitation.[69] (Level 4)[5]

-Although the majority of patients who require amputation due to vascular disease are retired, some are working at the time of amputation. One year after the amputation, 42% of have resumed work.[70] and after more than one year 58-79% have returned to work or have stopped working for reasons unrelated to the amputation.[70-74] A subset of patients (approximately 30%) require adjustments in their work situation to return to work.[75] Of working patients, 60-80% resume work after lower extremity amputation. (Level 2)[5]

-Higher amputation level leads to poorer prognosis for return to work. (Level 3)[5]

Updated Evidence:

The main objective in the period from amputation to initial prosthetic fitting is to focus on recovery from the surgery, achieve medical stability, prevent complications and optimize mobility. This includes pain management, surgical site management, residual limb management (edema control, strengthening, and range of motion), and care of the contralateral limb.[50]

Maintaining knee mobility is of great importance in the postoperative phase. There is a tendency to keep the knee bent, particularly in the presence of postoperative pain. Education is provided to optimize positioning (avoid lying supine with a pillow under the knee). Dependent edema and knee flexion contractures can be prevented by using an elevated leg rest on the wheelchair, a residual limb support, and by educating the patient in proper positioning. To prevent hip flexion contracture, patients are educated to spend time prone with a pillow or towel under the anterior thigh (if tolerated).

Although the focus is usually on the amputated side, attention should also be paid to the contralateral side. It is important to ensure that the contralateral leg (heel) is protected against pressure ulcers, during surgery and postoperatively.

Specific attention should be paid to hip strengthening training. In a twice weekly hip strengthening program, the training group increased hip strength and decreased oxygen consumption compared to a control group, who continued their usual activities. Hip strength was reduced in the group not following the training program.[76] Another study showed improvement of functional performance and balance confidence following intense hip abductor strength training during an 8-week program of twice weekly hip abductor strength training or arm ergometry.[77]

The most frequently described adjustment issues are mood disorders and anxiety. In the course of rehabilitation, the adaptation process and associated psychosocial issues need to be considered.

Cognitive impairment appears to be more prevalent among persons with lower limb amputations than in the general population and is negatively associated with mobility, prosthetic use, and maintaining independence following amputation.[78] Cognitive screening prior to rehabilitation could assist in determining patients' suitability for a prosthesis versus wheelchair use and decision making for a specific rehabilitation program.[78]

The following factors are assessed: the patient's ability to return to their previous level of functioning; identification of resources previously used or those necessary to facilitate continuity of care; social/family support, psychological support; therapy; medical needs. The team works with social services to develop and implement the discharge plan. The discharge plan is documented in the medical record including the patient assessment and a plan for continuing care.

The relationship between shared decision-making and evidence-based practice is becoming increasingly recognized.[79] Shared decision-making provides a process for bringing evidence into the consultation and incorporating it into discussions with the patient, along with discussions about the patient's values and preferences. Shared decision-making may also help reduce the unwarranted variation in care.[80]

Discussions should take place not only in the presence of the patient, but also with the involvement of family members and other caregivers. Verbal information should be supported in other formats, as patients and their relatives (and other parties involved) often do not hear and/or remember everything. The format (oral, digital, leaflets) in which the information is provided will need to be tailored to the patient. Information resources should be developed at the local level.

Verbal education and printed materials are provided by various members of the rehabilitation team throughout the hospital stay. Education includes adjusting/adaptation to limb loss, optimizing functional mobility (bed mobility, wheelchair mobility, ambulation, and transfers), optimizing daily living skills, obtaining appropriate adaptive and durable medical equipment, caregiver support, communication with other care providers, decision-making on health risks, optimizing care options (including prosthetic fitting, sock management, prosthetic adjustments, prosthetic training, cardiovascular conditioning, risk factor prevention, and accessing emergency care if necessary).

The person with limb loss and their family are instructed in measures to avoid further limb loss, risk factors, the timeline for use of a prosthesis, fall prevention and management, home modifications, home safety, energy conservation, and expenditure, and the importance of follow up to prevent complications. It is useful to prepare a checklist detailing the minimum information that should be provided to the patient. This can be completed and supplemented by every practitioner involved in the treatment. Developing a single information dossier should be considered so that each discipline can see which items have already been discussed and what may still need attention. Since treatment involves multiple disciplines, it is advisable that items discussed are recorded in a manner that is clear to all disciplines. If the patient cannot safely function in their home environment after amputation, discharge to a rehabilitation setting is necessary.

Following lower limb amputation, discharge planning should be based on the degree of function, social situation, and the patient's health. A large population-based study in the U.S.[81] showed that 41% of patients with vascular disease requiring amputation are discharged to their homes, 37% to a skilled nursing facility, and 10% to a rehabilitation facility.

The discharge summary includes an acute medical history, rehabilitation medical history, description of the rehabilitation course, and ongoing care needs. The discharge summary outlines the plan for community-based services (pedorthotic services, foot care, health or psychosocial issues that require follow up). Also provided and documented in the medical record is information about consumer groups, and peer support (self-advocacy, financial assistance, emotional support, and support groups) including how to access them (phone numbers and names of contact persons), in the local community.

The discharge summary is reviewed by the patient and their family/support system. The discharge plan is updated throughout the course of the patient's stay and is reassessed frequently to ensure that the patient's continuing care needs are identified. A copy of the discharge summary is sent to the primary physician as designated by the patient and/or the healthcare facility to which the patient transitions.

VIII. PAIN MANAGEMENT FOLLOWING AMPUTATION

Dutch Guidelines:

-In addition to physical limitations, pain plays a major role (both stump pain and phantom pain) in determining the quality of life.[64, 69, 82-92] (Level 4)[4]

-Epidural or perineural administration of bupivacaine, compared with placebo, has no significant effect on the intensity or incidence of stump and phantom pain in the early perioperative period up to six months and long-term (12 months).[93, 94, 95] (Level 2)[4]

-Epidural treatment has a place in the perioperative management of pain. (Level 4)[4]

-Compared with placebo, gabapentin has no effect on the incidence and intensity of stump and phantom pain in the perioperative period up to 6 months.[96, 97] (Level 3)[4]

-Use of amitriptyline can be considered for patients with phantom pain. (Level 4)[4]

-Ketamine (epidural or intravenous), compared with placebo, has no significant effect on the incidence and intensity of stump and phantom pain in the perioperative period up to 6 months and long-term (12 months).[98, 99] (Level 2)[4] (Due to neurotoxicity, epidural infusion of ketamine cannot be recommended.)

Updated Evidence:

Careful consideration of several patient factors can improve success in medical therapy for phantom and postoperative pain. The patient's medical comorbidities should be considered. Limiting factors such as pulmonary, cardiovascular, renal, or hepatic impairment should be identified as these may influence medication choice.

Patients who undergo an amputation will experience moderate to severe acute postoperative

pain. In addition to oral and intravenous medications in the treatment of acute postoperative pain, epidural or perineural pain control may also be used.

In addition to acute pain following amputation, a considerable number of patients develop chronic pain syndromes. Phantom pain, experienced as painful sensations in the amputated limb, is a neuropathic pain syndrome probably caused by central and peripheral neural mechanisms. There is no evidence to outline the prevention of phantom pain.

Anticonvulsants are often used in the treatment of neuropathic pain. Perioperative administration of gabapentin appeared to have no effect on the incidence of phantom pain and chronic stump pain.[96] In a recent Cochrane Review,[100] these agents showed no benefit in the relief of phantom limb pain. In a small study by Bone,[97] gabapentin may have shown an effect on longstanding phantom pain. Pregabalin's mechanism of action is similar to gabapentin. No studies were found on the effect of pregabalin on phantom pain and chronic stump pain.

A study by Wilder-Smith[101] suggested that, in addition to tramadol, amitriptyline may be effective in patients with phantom pain. Amitriptyline and nortriptyline have been shown to be effective against neuropathic pain. Their role in the treatment of phantom pain has been poorly investigated.

A randomized double-blinded pilot study by Wu[102] showed that both Botox and Lidocaine/Depo-Medrol injected intramuscularly and subcutaneously at local tender points resulted in immediate improvement of residual limb pain (not phantom limb pain) and pain tolerance, which lasted for 6 months in persons with amputation who failed conventional treatments.

Medication side effects can be a barrier to treatment success. A frank conversation discussing common or serious side effects should be performed prior to starting a new treatment. Many of the treatment side effects can decrease over time due to progressive tolerance. Each medication should be maintained at the lowest effective dose. Topical medications, behavioral strategies, and physical modalities can be particularly beneficial in combination with other treatments due to their negligible side effect profiles.

While pain following amputation can prove difficult to treat, there are a variety of therapeutic options including behavioral therapies, physical modalities, topical and oral medications, and implantable devices. Mirror therapy (MT) has been shown to be an effective, non-pharmacologic, treatment for PLP.[103] Augmented Reality (AR) has the ability to create a high fidelity version of MT that may improve the effect and duration of pain reduction in patients experiencing PLP.

Pain research has shown that cognitive behavioral therapy is effective in the perioperative period. Third generation behavioral therapy (Acceptance and Commitment Therapy (ACT) and Mindfulness) also appear to be of benefit and indicate that future research into these treatment methods is necessary.

IX. PROSTHETIC PRESCRIPTION FOLLOWING LOWER LIMB AMPUTATION DUE TO VASCULAR DISEASE

Dutch Guidelines:

-Ideally, a prosthetic prescription should be generated with a multidisciplinary team including a physician familiar with rehabilitation requirements, a prosthetist, and a physical therapist. (Level 4)[5]

-The most fundamental question when developing a prosthetic prescription is the patient's need and their ability to use the prosthesis. The key point is the anticipated level of mobility with a prosthesis is the guiding factor in the choice of prosthetic components. (Level 4)[5]

-Choosing between the various components of a prosthetic prescription should be based on reliable information on the characteristics of these components. Using the product information provided by the manufacturer alone is insufficient. The determination of the specific characteristics and functional quality of a prosthesis should be based on clinical and biomechanical research. The use of clinically evaluated systems is recommended. (Level 4)[5]

-Baars, et al., concluded that silicone liners seem to lead to better suspension and better walking performance than a conventional supracondylar socket suspension.[104] (Level 2)[5]

-In a RCT involving 36 patients with trans-tibial amputation, no differences were found in the outcomes 'prosthetic function' and 'satisfaction' when comparing a total surface bearing socket (TSB) and a conventional patellar-tendon bearing (PTB) socket.[105] (Level 3)[5]

-Individuals with trans-femoral amputation using a microprocessor knee (MPK), are better able to walk down a slope.[106] (Level 3)[5]

-Persons with trans-tibial level amputation due to trauma walk at a higher speed with an energy-storing (dynamic response) foot.[107] No study was found in which a difference in patient satisfaction was reported with regard to a specific prosthetic foot.[107] (Level 2)[5]

Updated Evidence:

Prescribing a prosthesis is a process which involves assessment, production, delivery and evaluation of a prosthetic leg. Prescription and fitting processes vary significantly between countries. The way national public health insurances are organized also influence the processes and available choices.

Schaffalitzky[108] stresses the importance of psychosocial outcomes in prosthesis prescription and use. A limited improvement in physical capabilities may provide important gains in psychosocial outcomes and independence.

If the decision is made to prescribe a prosthesis, details of the prosthetic prescription including socket design, suspension, interface, pylon, knee, and foot components (with input from the prosthetist and the patient) is provided.

Prosthetic training should be arranged when the initial prosthesis is prescribed. Options include outpatient physical therapy, subacute rehabilitation, or inpatient rehabilitation. A well-fitting prosthesis with appropriate components, supervised training, and ongoing follow-up optimizes prosthetic use and function.

The individual with major limb loss must understand that successful prosthetic rehabilitation is a prerequisite for optimal performance. A state-of-the-art prosthesis will not provide optimal performance to a user who is not physically capable of taking advantage of its features. Conversely, optimal performance will not be achieved with a prosthesis that does not provide a level of technical sophistication that matches or challenges the user's physical capabilities.

There are significant limitations of the objective clinical knowledge available on the impact of different prosthetic components on performance with a prosthetic leg. Further, it is challenging to predict an individual's response to a specific component on clinical variables alone. Therefore, empiric knowledge and individual judgement remain indispensable to determine the appropriate prosthetic prescription. The measurement and documentation of clinical performance is recommended.

The socket is where the prosthesis and the body connect. It is the most critical element in prosthetic design. Unlike the plantar tissues of the intact foot, residual limb soft tissues are not accustom to bearing loads.[109] Loads imparted on the residual limb by the prosthetic socket can cause wounds and other skin conditions. This is problematic as treatment may require stopping the use of the prosthesis. To help cushion the transfer of load between the prosthetic socket and residual limb, soft prosthetic liners have been used. High-quality research is needed to inform decisions about liner prescription based on user experience.[110]

Microprocessor controlled knee components have been investigated over the last decade. Independent systematic reviews by Samuellson, et al.,[111]; Highsmith, et al.,[112] suggest that hydraulic microprocessor knees (MPKs) are associated with improved patient satisfaction, safety, energy consumption, and are cost effective. A systematic review by Kannenberg, et al.,[113] concludes that the benefits of a MPK are also apparent with subjects of limited mobility. As MPKs vary in type,[114-116] different designs maybe associated with different effects.[117, 118] A systematic review by Sawyers, et al., found moderate evidence of improved confidence, mobility, and decreased cognitive demands. They also concluded that no evidence could be found where non-microprocessor knees were associated with clinical advantages over MPKs. Larger observational studies suggest that the benefits of the MPK are not limited by age, mobility grade, etiology, BMI, and other clinical variables.[119, 120]

In a Cochrane Review on the effectiveness of ankle foot mechanisms, Hofstad, et al., concluded that in trans-tibial amputations, there appears to be greater stride length with a dynamic response foot in comparison with a conventional fixed prosthetic foot. At high activity levels, there also seems to be a better gait efficiency.[121]

Hydraulic and microprocessor controlled feet (MPF) have recently become available in some countries. Such devices are associated with a reduction of internal stress of the amputated limb[122] and optimize pressure distribution at the residual limb.[123] They are also associated with an increase in toe clearance[124, 125] which may contribute to a reduction in the risk of falling. Patients reported feeling safer during ramp descent.[126]

There are limitations in the objective clinical knowledge available on the impact of various prosthetic components on performance with a prosthetic leg. In addition, it is challenging to predict an individual's response to a specific component on clinical variables alone. Empiric

knowledge and individual judgement remain indispensable to determine the appropriate prosthetic prescription. The measurement and documentation of clinical performance is recommended. Specific issues of prosthetic components/prescription are beyond the scope of this report.

The rehabilitation consultant will attempt to optimize the patient's achievable level of function. This depends on both the amputation level and premorbid function.[28] When indicated, the demands of a patient's workplace should be taken into account when prescribing a prosthesis.

X. CONCLUSION

The Dutch Guidelines[4, 5] established that there are gaps in knowledge and need for future research regarding amputation and prosthetic rehabilitation. As our consensus group met to expand the Dutch Guidelines for a larger audience, these gaps are again apparent. The rehabilitation process and the value of multidisciplinary treatment need to be further delineated. The opinion of the working group is that the rehabilitation process for a person with major lower limb amputation due to vascular disease is best accomplished with a comprehensive, multidisciplinary, specialized treatment team.

REFERENCES

1. Dillingham TR, Pezzin LE and MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. *South Med J*. 2002 Aug; 95: 875-83.
2. Ephraim PL, Dillingham TR, Sector M and et al. Epidemiology of limb loss and congenital limb deficiency: a review of the literature. *Arch Phys Med Rehabil*. 2003 May; 84: 747-61.
3. The Rehabilitation of Lower Limb Amputation Working Group and Department of Veterans Affairs Department of Defense. VA/DOD Clinical Practice Guideline for Rehabilitation of the Lower Limb Amputation. Version 1.0. 2007.
4. Geertzen JH, H. vdL, Rosenbrand K and et al. Dutch evidence-based guidelines for amputation and prosthetics of the lower extremity: Amputation surgery and postoperative management. Part 1. *Prosthet Orthot Int*. 2015 Oct; 39: 351-60.
5. Geertzen JH, van der Linde H, Rosenbrand K and et al. Dutch evidence-based guidelines for amputation and prosthetics of the lower extremity: Rehabilitation process and prosthetics. Part 2. *Prosthet Orthot Int*. 2015 Oct; 39: 361-71.
6. Tennant J, McClelland M and Miller J. Breaking Down the Barrier from Multidisciplinary to Interdisciplinary Care: A Case Study in a High Risk Foot Clinic. *Primary Intention: The Australian Journal of Wound Management*. 2004 Aug; 12: 127-30.
7. Parvin S. Do we waste time trying to save some feet: the positive amputation. *Diab*. 2003; 6: 90-2.
8. Wohlgemuth WA, Freitag MH, Wölfle KD and et al. Incidence of major amputations, bypass procedures and percutaneous angioplasties (PTA) in the treatment of peripheral arterial occulsive disease in a German referral center 1996-2003. *Rofo*. 2006 Sep; 178: 906-10.
9. Davis BL, Kuznicki J, Praveen SS and et al. Lower-limb amputation in patients with diabetes: Pre- and post-surgical decisions related to successful rehabilitation. *Diabetes Metab Res Rev*. 2004 May-Jun; 20 Suppl 1: S45-50.
10. Conrad MF, Crawford RS, Hackney LA and et al. Endovascular management of patients with critical limb ischemia. *J Vasc Surg*. 2011 Apr; 53: 1020-5.
11. Norgren L, Hiatt WR, Dormandy JA and et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Eur J Vasc Endovascular Surg*. 2007; 33 Suppl: S1-S75.
12. Abu Dabrh AM, Steffen MW, Undavalli C and et al. The natural history of untreated severe or critical limb ischemia. *J Vasc Surg*. 2015 Dec; 62: 1642-51.
13. deGraaf JC, Ubbink DT, Legemate DA and et al. Evaluation of toe pressure and transcutaneous oxygen measurements in management of chronic critical leg ischemia: a diagnostic randomized clinical trial. *J Vasc Surg*. 2003 Sep; 38: 528-34.
14. Arsenault KA, Al-Otaibi A, Devereaux PJ and et al. The use of transcutaneous oximetry to predict healing complications of lower limb amputations: a systematic review and meta-analysis. *Eur J Vasc Endovascular Surg*. 2012 Mar; 43: 329-36.
15. Hinchliffe RJ, Brownrigg JR, Andros G and et al. Effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral artery disease: a systematic review. *Diabetes Metab Res Rev*. 2016 Jan; 32: 1036-44.
16. Caselli A, Latini V, Lapenna A and et al. Transcutaneous oxygen tension monitoring after successful revascularization in diabetic patients with ischaemic foot ulcers. *Diabet Med*. 2005 Apr; 22: 460-5.

17. Tisi PV and Callam MJ. Type of incision for below knee amputation. *Cochrane Database Syst Rev*. 2004: CD003749.
18. Barshes NR, Kougas P, Ozaki CK and et al. Cost-effectiveness of revascularization for limb preservation in patients with end-stage renal disease. J Vasc Surg 2014 Aug, 60(2): 369-74.
19. Albers M, Romiti M DLN and et al. An updated meta-analysis of infrainguinal arterial reconstruction in patients with end-stage renal disease. *J Vasc Surg*. 2007 Mar; 45: 536-42.
20. Gajdos C, Hawn MT, Kile D and et al. The risk of major elective vascular surgical procedures in patients with end-stage renal disease. *Ann Surg*. 2013 Apr; 257: 766-73.
21. Bradbury AW, Adam DJ, Bell J and et al. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: A survival prediction model to facilitate clinical decision making. *J Vasc Surg*. 2010 May; 51: 52S-68S.
22. Bosse MJ, MacKenzie EJ, Kellam JF and et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. *N Engl J Med*. 2002 Dec; 347: 1924-31.
23. Dillon MP and Fatone S. Deliberations about the functional benefits and complications of partial foot amputation: do we pay heed to the purported benefits at the expense of minimizing complications? *Arch Phys Med Rehabil*. 2013 Aug; 94: 1429-35.
24. Nehler MR, Coll JR, Hiatt JG and et al. Functional outcome in a contemporary series of major lower extremity amputations. *J Vasc Surg*. 2003 Jul; 38: 7-14.
25. McWhinnie DL, Gordon AC, Collin J and et al. Rehabilitation outcome 5 years after 100 lower-limb amputations. *Br J Surg*. 1994 Nov; 81: 1596-9.
26. Pohjolainen T, Alaranta H and Wikstrom J. Primary survival and prosthetic fitting of lower limb amputees. *Prosthet Orthot Int*. 1989 Aug; 13: 63-9.
27. Czerniecki JM, Turner AP, Wiliams RM and et al. The development and validation of the AMPREDICT model for predicting mobility outcome after dysvascular lower extremity amputation. *J Vasc Surg*. 2017 Jan; 65: 162-71.
28. Taylor SM, Kalbaugh CA, Blackhurst DW and et al. Preoperative clinical factors predict postoperative functional outcomes after major lower limb amputation: an analysis of 553 consecutive patients. *J Vasc Surg*. 2005 Aug; 42: 227-35.
29. Schoppen T, Boonstra A, Groothoff JW and et al. Physical, mental, and social predictors of functional outcome in unilateral lower-limb amputees. *Arch Phys Med Rehabil*. 2003 Jun; 84: 803-11.
30. Johannesson A, Larsson GU, Ramstrand N and et al. Outcomes of a standardized surgical and rehabilitation program in transtibial amputation for peripheral vascular disease: a prospective cohort study. *Am J Phys Med Rehabil*. 2010 Apr; 89: 293-303.
31. Norvell DC, Turner AP, Williams RM and et al. Defining successful mobility after lower extremity amputation for complications of peripheral vascular disease and diabetes. *J Vasc Surg*. 2011 Aug; 54: 412-9.
32. Munin MC, Espejo-De Guzman MC, Boninger ML and et al. Predictive factors for successful early prosthetic ambulation among lower-limb amputees. *J Rehabil Res Dev*. 2001 Jul-Aug; 38.
33. Fletcher DD, Andrews KL, Butters MA and al. e. Rehabilitation of the geriatric vascular amputee patient: a population-based study. *Arch Phys Med Rehabil*. 2001 Jun; 82: 776-9.
34. Traballsei M, Brunelli S, Pratesi L and et al. Prognostic factors in rehabilitation of above knee amputees for vascular diseases. *Disabil Rehabil*. 1998 Oct; 20: 380-4.

35. Johnson VJ, Kondziela S and Gottschalk F. Pre and post-amputation mobility of trans-tibial amputees: correlation to medical problems, age and mortality. *Prosthet Orthot Int*. 1995 Dec; 19: 159-64.
36. Houghton AD, Taylor PR, Thurlow S and et al. Success rates for rehabilitation of vascular amputees: implications for preoperative assessment and amputation level. *Br J Surg*. 1992 Aug; 79: 753-5.
37. Fletcher DD, Andrews KL, Hallett JW Jr and et al. Trends in rehabilitation after amputation for geriatric patients with vascular disease: implications for future health resource allocation. *Arch Phys Med Rehab*. 2002 Oct; 83: 1389-93.
38. Awopetu AI, Moxey P, Hinchliffe RJ and et al. Systematic review and meta-analysis of the relationship between hospital volume and outcome for lower limb arterial surgery. *Br J Surg*. 2010 Jun; 97: 797-803.
39. Robertson L and Roche A. Primary prophylaxis for venous thromboembolism in people undergoing major amputation of the lower extremity. *Cochrane Database Syst Rev*. 2013 Dec 16; 12: CD010525.
40. Aulivola B, Hile CN, Hamdan AD and et al. Major lower extremity amputation: outcome of a modern series. *Arch Surg*. 2004 Apr; 139: 395-9; discussion 9.
41. Collins TC, Johnson M, Daley J and et al. Preoperative risk factors for 30-day mortality after elective surgery for vascular disease in Department of Veterans Affairs hospitals: is race important? *J Vasc Surg*. 2001 Oct; 34: 634-40.
42. Dillingham TR and Pezzin LE. Rehabilitation setting and associated mortality and medical stability among persons with amputations. *Arch Phys Med Rehabil*. 2008 Jun; 89: 1038-45.
43. Stone PA, Flaherty SK, Aburahma AF and et al. Factors affecting perioperative mortality and wound-related complications following major lower extremity amputations. *Ann Vasc Surg*. 2006 Mar; 20: 209-16.
44. Cruz CP, Eidt JF, Capps C and et al. Major lower extremity amputations at a Veterans Affairs hospital. *Am J Surg*. 2003 Nov; 186: 449-54.
45. Campbell WB, Marriott S, Eve R and et al. Factors influencing the early outcome of major lower limb amputation for vascular disease. *Ann R Coll Surg Engl*. 2001 Sep; 83: 309-14.
46. Johannesson A, Larsson GU and Oberg T. From major amputation to prosthetic outcome: a prospective study of 190 patients in a defined population. *Prosthet Orthot Int*. 2004 Apr; 28: 9-21.
47. Bates B, Stineman MG, Reker DM and et al. Risk factors associated with mortality in veteran population following transtibial or transfemoral amputation. *J Rehabil Res Dev*. 2006 Nov-Dec; 43: 917-28.
48. O'Hare AM, Feinglass J, Reiber GE and et al. Postoperative mortality after nontraumatic lower extremity amputation in patients with renal insufficiency. *J Am Soc Nephrol*. 2004 Feb; 15: 427-34.
49. Smith DG, McFarland LV, Sangeorzan BJ and et al. Postoperative dressing and management strategies for transtibial amputations: a critical review. *J Rehabil Res Dev*. 2003 May-Jun; 40: 213-24.
50. Geertzen JHB and Rietman JS (eds). Amputatie en prothesiologie van de onderste extremiteit. *NV Den Haag: Boom Lemma*. 2008.
51. Churilov I, Churilov L and Murphy D. Do rigid dressings reduce the time from amputation to prosthetic fitting? A systematic review and meta-analysis. *Ann Vasc Surg*. 2014 Oct; 28: 1801-8.

52. Janchai S, Boonhong J and Tiamprasit J. Comparison of removable rigid dressing and elastic bandage in reducing the residual limb volume of below knee amputees. *J Med Assoc Thai*. 2008 Sep; 91: 1441-6.
53. Nawijn SE, van der Linde H, Emmelot CH and et al. Stump management after trans-tibial amputation: a systematic review. *Prosthet Orthot Int*. 2005 Apr; 29: 13-26.
54. Wu Y, Keagy RD, Krick HJ and et al. An innovative removable rigid dressing technique for below-the-knee amputation. *Am Correct Ther J*. 1980 Nov-Dec; 34: 169-75.
55. Johannesson A, Larsson GU, Oberg T and et al. Comparison of vacuum-formed removable rigid dressing with conventional rigid dressing after transtibial amputation: similar outcome in a randomized controlled trial involving 27 patients. *Acta Orthop*. 2008 Jun; 79: 361-9.
56. Sumpio B, Shine SR, Mahler D and et al. A comparison of immediate postoperative rigid and soft dressings for below-knee amputations. *Ann Vasc Surg*. 2013 Aug; 27: 774-80.
57. Ali MM, Loretz L, Shea A and et al. A contemporary comparative analysis of immediate postoperative prosthesis placement following below-knee amputation. *Ann Vasc Surg*. 2013 Nov; 27: 1146-53.
58. Mazari FA, Mockford K, Barnett C and et al. Hull early walking aid for rehabilitation of transtibial amputees--randomized controlled trial (HEART). *J Vasc Surg*. 2010 Dec; 52: 1564-71.
59. Samuelsen BT, Andrews KL, Houdek MT and et al. The impact of immediate postoperative prosthesis on patient mobility and quality of life after transtibial amputation. *Am J Phys Med Rehab*. 2017 Feb; Am J Phys Rehabil: 2.
60. Rau B, Bonvin F and de Bie R. Short-term effect of physiotherapy rehabilitation on functional performance of lower limb amputees. *Prosthet Orthot Int*. 2007 Sep; 31: 258-70.
61. Kurichi JE, Small DS, Bates BE and et al. Possible incremental benefits of specialized rehabilitation bed units among veterans after lower extremity amputation. *Med Care*. 2009 Apr; 47: 457-65.
62. Stineman MG, Kwong PL, Kurichi JE and 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 Oct; 89: 1863-72.
63. Schaldach DE. Measuring quality and cost of care: evaluation of an amputation clinical pathway. *J Vasc Surg*. 1997 Mar; 15: 13-20.
64. Asano M, Rushton P, Miller WC and et al. Predictors of quality of life among individuals who have a lower limb amputation. *Prosthet Orthot Int*. 2008 Jun; 32: 231-43.
65. Boutoille D, Feraille A, Maulaz D and et al. Quality of life with diabetes-associated foot complications: comparison between lower-limb amputation and chronic foot ulceration. *Foot Ankle Int*. 2008 Nov; 29: 1074-8.
66. Deans SA, McFadyen AK and Rowe PJ. Physical activity and quality of life: A study of a lower-limb amputee population. *Prosthet Orthot Int*. 2008 Jun; 32: 186-200.
67. Desmond DM and MacLachlan M. Coping strategies as predictors of psychosocial adaptation in a sample of elderly veterans with acquired lower limb amputations. *Soc Sci Med*. 2006 Jan; 62: 208-16.
68. Williams RM, Ehde DM, Smith DG and et al. A two-year longitudinal study of social support following amputation. *Disabil Rehabil*. 2004 Jul-Aug; 26: 867-74.
69. Larner S, van Ross E and Hale C. Do psychological measures predict the ability of lower limb amputees to learn to use a prosthesis? *Clin Rehabil*. 2003 Aug; 17: 493-8.

70. MacKenzie EJ, Bosse MJ, Kellam JF and et al. Early predictors of long-term work disability after major limb trauma. *J Trauma* 2006 Sep; 61: 688-94.
71. Schoopen T, Boonstra A, Groothoff JW and et al. Employment status, job characteristics, and work-related health experience of people with a lower limb amputation in The Netherlands. *Arch Phys Med Rehabil*. 2001 Feb; 82: 239-45.
72. Schoopen T, Boonstra A, Groothoff JW and et al. Factors related to successful job reintegration of people with a lower limb amputation. *Arch Phys Med Rehabil*. 2001 Oct; 82: 1425-31.
73. Fisher K, Hanspal RS and Marks L. Return to work after lower limb amputation. *Int J Rehabil Res*. 2003 Mar; 26: 51-6.
74. Hebert EJ and Ashworth NL. Predictors of return to work following traumatic work-related lower extremity amputation. *Disabil Rehabil*. 2006 May 30; 28: 613-8.
75. van der Sluis CK, Hartman PP, Schoppen T and et al. Job adjustments, job satisfaction and health experience in upper and lower limb amputees. *Prosthet Orthot Int*. 2009 Mar; 33: 41-51.
76. Nolan L. A training programme to improve hip strength in persons with lower limb amputation. *J Rehabil Med*. 2012 Mar; 44: 241-8.
77. Pauley T and Devlin M. A single-blind, cross-over trial of hip abductor strength training to improve Timed Up & Go performance in patients with unilateral, transfemoral amputation. *J Rehabil Med*. 2014 Mar; 46: 264-70.
78. Coffey L, O'Keeffe F, Gallagher P and et al. Cognitive functioning in persons with lower limb amputations: a review. *Disabil Rehabil*. 2012; 34: 1950-64.
79. Hoffmann TC, Légaré F, Simmons MB and et al. Shared decision making: what do clinicians need to know and why should they bother? *Med J Aust*. 2014 Jul; 201: 35-9.
80. Mulley AG, Trimble C and Elwyn G. Stop the silent misdiagnosis: patients' preferences matter. *BMJ*. 2012 Nov 8; 345.
81. Dillingham TR, Pezzin L and Mackenzie E. Discharge destination after dysvascular lower-limb amputations. *Arch Phys Med Rehabil*. 2003 Nov; 84: 1662-8.
82. Coffey L, Gallagher P, Horgan O and et al. Psychosocial adjustment to diabetes-related lower limb amputation. *Diabet Med*. 2009 Oct; 26: 1063-7.
83. Donovan-Hall MK, Yardley L and Watts RJ. Engagement in activities revealing the body and psychosocial adjustment in adults with a trans-tibial prosthesis. *Prosthet Orthot Int*. 2002 Apr; 26: 15-22.
84. Cheung E. Psychological distress in workers with traumatic upper or lower limb amputations following industrial injuries. *Rehabilitation Psychology*. 2003 May; 48: 109-12.
85. Darnall BD, Ephraim P, Wegener ST and et al. Depressive symptoms and mental health service utilization among persons with limb loss: results of a national survey. *Arch Phys Med Rehabil*. 2005 Apr; 86: 650-8.
86. Hawamdeh ZM, Othman YS and Ibrahim AI. Assessment of anxiety and depression after lower limb amputation in Jordanian patients. *Neuropsychiatr Dis Treat*. 2008 Jun; 4: 627-33.
87. Horgan O and MacLachlan M. Psychosocial adjustment to lower-limb amputation: a review. *Disabil Rehabil*. 2004 Jul 22-Aug 5; 26: 837-50.
88. Mayer A, Kudar K, Bretz K and et al. Body schema and body awareness of amputees. *Prosthet Orthot Int*. 2008 Sep; 32: 363-82.
89. Murray CD and Fox J. Body image and prosthesis satisfaction in the lower limb amputee. *Disabil Rehabil*. 2002 Nov 20; 24: 925-31.

90. Singh R, Hunter J and Philip A. The rapid resolution of depression and anxiety symptoms after lower limb amputation. *Clin Rehabil*. 2007 Aug; 21: 754-9.
91. Singh R, Ripley D, Pentland B and et al. Depression and anxiety symptoms after lower limb amputation: the rise and fall. *Clin Rehabil*. 2009 Mar; 23: 281-6.
92. Zidarov D, Swaine B and Gautheir-Cagnon C. Quality of life of persons with lower-limb amputation during rehabilitation and at 3-month follow-up. *Arch Phys Med Rehabil*. 2009 Apr; 90: 634-45.
93. Nikolajsen L, Ilkjaer S, Christensen JH and et al. Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. *Lancet*. 1997 Nov 8; 350: 1353-7.
94. Pinzur MS, Garla PG, Pluth T and et al. Continuous postoperative infusion of a regional anesthetic after an amputation of the lower extremity. A randomized clinical trial. *J Bone Joint Surg Am*. 1996 Oct; 78: 1501-5.
95. Boonstra AM, van Duin W and Eisma W. Silicone suction socket (3S) versus supracondylar PTB prosthesis with Pelite liner: transtibial amputees' preference. *Prosthet Orthot Int*. 1996; 8: 96-9.
96. Nikolajsen L, Finnerup NB, Kramp S and et al. A randomized study of the effects of gabapentin on postamputation pain. *Anesthesiology*. 2006 Nov; 105: 1008-15.
97. Bone M, Critchley P and Buggy DJ. Gabapentin in postamputation phantom limb pain: a randomized, double-blind, placebo-controlled, cross-over study. *Reg Anesth Pain Med*. 2002 Sep-Oct; 27: 481-6.
98. Wilson JA, Nimmo AF, Fleetwood-Walker SM and et al. A randomised double blind trial of the effect of pre-emptive epidural ketamine on persistent pain after lower limb amputation. *Pain*. 2008 Mar; 135: 108-18.
99. Hayes C, Armstrong-Brown A and Burstal R. Perioperative intravenous ketamine infusion for the prevention of persistent post-amputation pain: a randomized, controlled trial. *Anaesth Intensive Care*. 2004 Jun; 32: 330-8.
100. Alvair MJ, Hale T and Dungca M. Pharmacologic interventions for treating phantom limb pain. *Cochrane Database Syst Rev*. 2016 Oct 14; 10: CD006380.
101. Wilder-Smith CH, Hill LT and Laurent S. Postamputation pain and sensory changes in treatment-naive patients: characteristics and responses to treatment with tramadol, amitriptyline, and placebo. *Anesthesiology*. 2005 Sep; 103: 619-28.
102. Wu H, Sultana R, Taylor KB and et al. A prospective randomized double-blinded pilot study to examine the effect of botulinum toxin type A injection versus Lidocaine/Depomedrol injection on residual and phantom limb pain: initial report. *Clin J Pain*. 2012 Feb; 28: 108-12.
103. Morgan SJ, Friedly JL, Amtmann D and et al. Cross-Sectional Assessment of Factors Related to Pain Intensity and Pain Interference in Lower Limb Prosthesis Users. *Arch Phys Med Rehab*. 2017 Jan; 98: 105-13.
104. Baars EC and Geertzen JH. Literature review of the possible advantages of silicon liner socket use in trans-tibial prostheses. *Prosthet Orthot Int*. 2005 Apr; 29: 27-37.
105. Selles RW, Janssens PJ, Jongenengel CD and et al. A randomized controlled trial comparing functional outcome and cost efficiency of a total surface-bearing socket versus a conventional patellar tendon-bearing socket in transtibial amputees. *Arch Phys Med Rehabil*. 2005; 86: 154-61; quiz 80.
106. Hafner BJ, Willingham LL, Buell NC and et al. Evaluation of function, performance, and preference as transfemoral amputees transition from mechanical to microprocessor control of the prosthetic knee. *Arch Phys Med Rehabil*. 2007 Feb; 88: 207-17.

107. van der Linde H, Hofstad CJ, Geurts AC and et al. A systematic literature review of the effect of different prosthetic components on human functioning with a lower-limb prosthesis. *J Rehabil Res Dev*. 2004 Jul; 41: 555-70.
108. Schaffalitzky E, Gallagher P, Maclachlan M and et al. Understanding the benefits of prosthetic prescription: exploring the experiences of practitioners and lower limb prosthetic users. *Disabil Rehabil*. 2011; 33: 1314-23.
109. Dudek NL, Marks MB, Marshall SC and et al. Dermatologic conditions associated with use of a lower extremity prosthesis. *Arch Phys Med Rehabil*. 86: 659-63.
110. Richardson A and Dillion MP. User experience of transtibial prosthetic liners: a systematic review. *Prosthet Orthot Int*. 2017; 41: 6-18.
111. Samuellson. Controlled knee components (MPKs) are associated with improved patient satisfaction 2012.
112. Highsmith MJ, Kahle JT, Bhoomi DR and et al. Safety, energy efficiency and cost efficiency of the C-leg for transfemoral amputees: a review of the literature. *Prosthet Orthot Int*. 2010; 34: 362-77.
113. Kannenberg A, Zacharias B and Probsting E. BeBenefits of microprocessor-controlled prosthetic knees to limited community ambulators: systematic review. *J Rehabil Res Dev*. 2014; 51: 1469-96.
114. Bellmann M, Schmalz T and Blumentritt S. Comparative biomechanical analysis of current microprocessor-controlled prosthetic knee joints. *Arch Phys Med Rehabil*. 2010 Apr; 91: 644-52.
115. Bellmann M, Schmalz T, Ludwigs E and et al. Immediate effects of a new microprocessor-controlled prosthetic knee joint: a comparative biomechanical evaluation. *Arch Phys Med Rehabil*. 2012 Mar; 93: 541-9.
116. Thiele J, Westebbe B, Bellmann M and et al. Designs and performance of microprocessor-controlled knee joints. *Biomed Technol (Berl)*. 2014 Feb; 59: 65-77.
117. Hafner BJ and Askew RK. Physical performance and self-report outcomes associated with use of passive, adaptive, and active prosthetic knees in persons with unilateral, transfemoral amputation: Randomized crossover trial. *J Rehabil Res Dev*. 2015; 52: 677-700.
118. Prinsen C, Nederhand MJ, Olsman J and et al. Influence of a user-adaptive prosthetic knee on quality of life, balance confidence, and measures of mobility: a randomised cross-over trial. *Clin Rehabil*. 2015 Jun; 29: 581-91.
119. Hahn A and Lang M. Effects of Mobility Grade, Age, and Etiology on Functional Benefit and Safety of Subjects Evaluated in More Than 1200 C-Leg Trial Fittings in Germany. *JPO*. 2015; 27: 86-94.
120. Hahn A, Lang M and Stuckart C. Analysis of clinically important factors on the performance of advanced hydraulic microprocessor-controlled EXO prosthetic knee joints based on 899 trial fittings. *Medicine (Baltimore)*. 2016 Nov; 95: e5386.
121. Hofstad C, Linde H, Limbeek J and et al. Prescription of prosthetic ankle-foot mechanisms after lower limb amputation. *Cochrane Database Syst Rev*. 2004: CD003978.
122. Portnoy S, Kristal A, Gefen A and et al. Outdoor dynamic subject-specific evaluation of internal stresses in the residual limb: Hydraulic energy-stored prosthetic foot compared to conventional energy-stored prosthetic feet. *Gait Posture*. 2012 Jan; 35: 121-5.
123. Wolf SI, Alimusaj M, Fradet L and et al. Pressure characteristics at the stump/socket interface in transtibial amputees using an adaptive prosthetic foot. *Clin Biomech*. 2009 Dec; 24: 860-5.

124. Johnson L, De Asha AR, Munjal R and et al. Toe clearance when walking in people with unilateral transtibial amputation: effects of passive hydraulic ankle. *J Rehabil Res Dev*. 2014; 51: 429-37.
125. Rosenblatt NJ, Bauer A, Rotter D and et al. Active dorsiflexing prostheses may reduce trip-related fall risk in people with transtibial amputation. *J Rehabil Res Dev*. 2014 51: 1229-42.
126. Fradet L, Alimusaj M, Braatz F and et al. Biomechanical analysis of ramp ambulation of transtibial amputees with an adaptive ankle foot system. *Gait Posture*. 2010 Jun; 32: 191-8.