THE MANGLED LOWER LEG

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THE MANGLED LOWER LEG

Fracturen van het onderbeen met ernstig weke-delenletsel

(met een samenvatting in het Nederlands)

PROEFSCHRIFT

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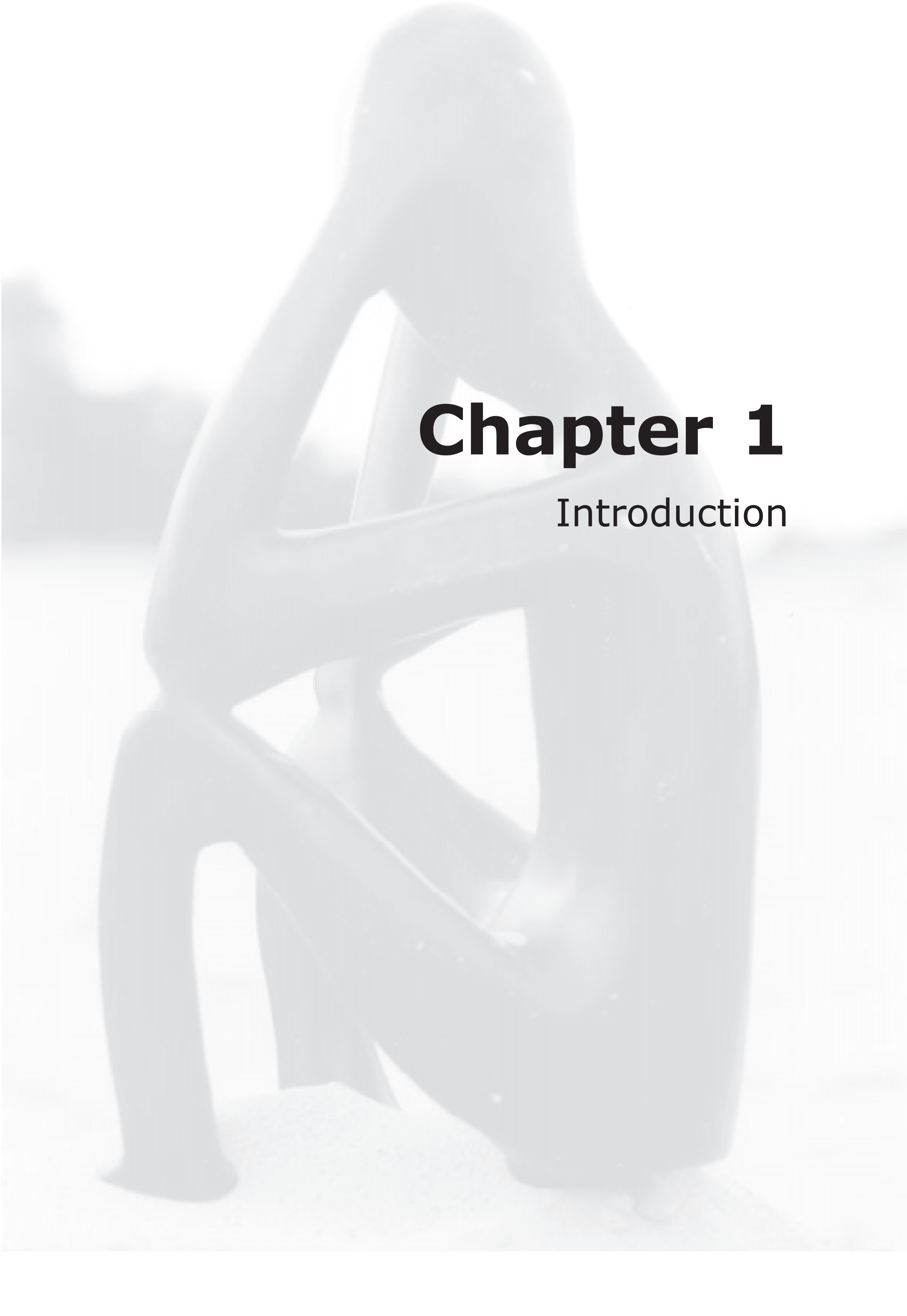
Contents



Chapter 1

Introduction

Until late in the nineteenth century the mortality from open fractures was high - mainly due to sepsis after infection. Theodor Billroth, the famous surgeon, reported in 1881 that 46 of 93 patients with an open fracture of the lower leg whom he treated in Zurich, died.[1] Gunshot wounds were particularly notorious and though generally treated with immediate amputation, most of these victims did not survive. It is recorded that in the American Civil War (1861-1865), the overall mortality rate after nearly 30.000 amputations was in the order of 30%, for above-knee amputations it reached 54%.[2] In the Franco-Prussian War (1870-1871), the death rate from open fractures was 41%, while for open fractures of the knee this rate was even 77%.[2] With the growing understanding of bacterial contamination and cross infection, the introduction of antisepsis and aseptic surgery, the advances in operative fracture stabilisation and, more recently, the various options for bone and soft-tissue reconstruction (table 1), the problems from open fractures have been greatly reduced. The emphasis came from life saving via limb salvage on restoration of limb function and preservation of quality of life.

Table 1. *Overview of major advances in (open) fracture treatment in the last two centuries.*

Year	**Innovation / foundation**	**Author**
1840	External fixation of fractures	Malgaigne
1844 / 1846	Narcosis with nitrous oxide / ether	Wells / Morton
1852	Plaster-of-Paris impregnated bandage	Mathyssen
1864	Modern bacteriology	Pasteur
1867	Antiseptic surgery	Lister
1880	Aseptic surgery	Von Bergmann
1886	Plate fixation of fractures	Hansmann
1886	Intramedullary ivory pegs to secure fixation of fractures	Bircher
1915	Tube pedicle tissue flap	Gilles
1928	Discovery of antibiotics (penicillin)	Fleming
1938	(Metallic) intramedullary nailing of fractures	Küntscher
1940	Cancellous bone grafting	Abbott
1949	Compression fixation of fractures	Danis
1958	Formation of the Arbeitsgemeinschaft für Osteosynthesefragen	Müller et al.
1969	Bone distraction osteogenesis	Ilizarov
1970	Antibiotic-impregnated polymethylmethaacrylate (PMMA)	Buchholz
1973	Microvascular tissue transplantation	Daniel

At the present time, the majority of open tibial fractures are caused by traffic accidents. In the Netherlands, approximately 5.000 patients annually are admitted to hospital with a lower leg fracture - both as an isolated injury and as part of "polytrauma".[3] It is estimated that open fractures account for 10% of this total.[4] The improvements in treatment of mangled lower legs have opened the door to therapeutical options, previously unavailable to the surgeon. Multidisciplinary approaches have been responsible for some remarkable successes in terms of limb salvage and have improved the outlook for patients with a mangled extremity.[5,6] However, in spite of these spectacular results, there are still patients who are better of with primary amputation.[7-9] If in these cases salvage is nevertheless attempted, after a long period of untreatable infections and ischemic problems, the decision has to be made for secondary amputation as yet. These patients generally undergo several complex operations, and suffer more and more severe complications than patients with a primary amputation.[8,9]

The aim of this thesis was to answer the following questions:

1. Is it possible to predict outcome in individual patients with a mangled lower leg?
2. What are the short-term consequences of the chosen treatment?
3. How is the long-term outcome of successful salvage and amputation?
4. What are the influences of smoking on the healing of open tibial fractures?
5. How are the results of treatment of infected segmental defect pseudarthrosis of the tibia?

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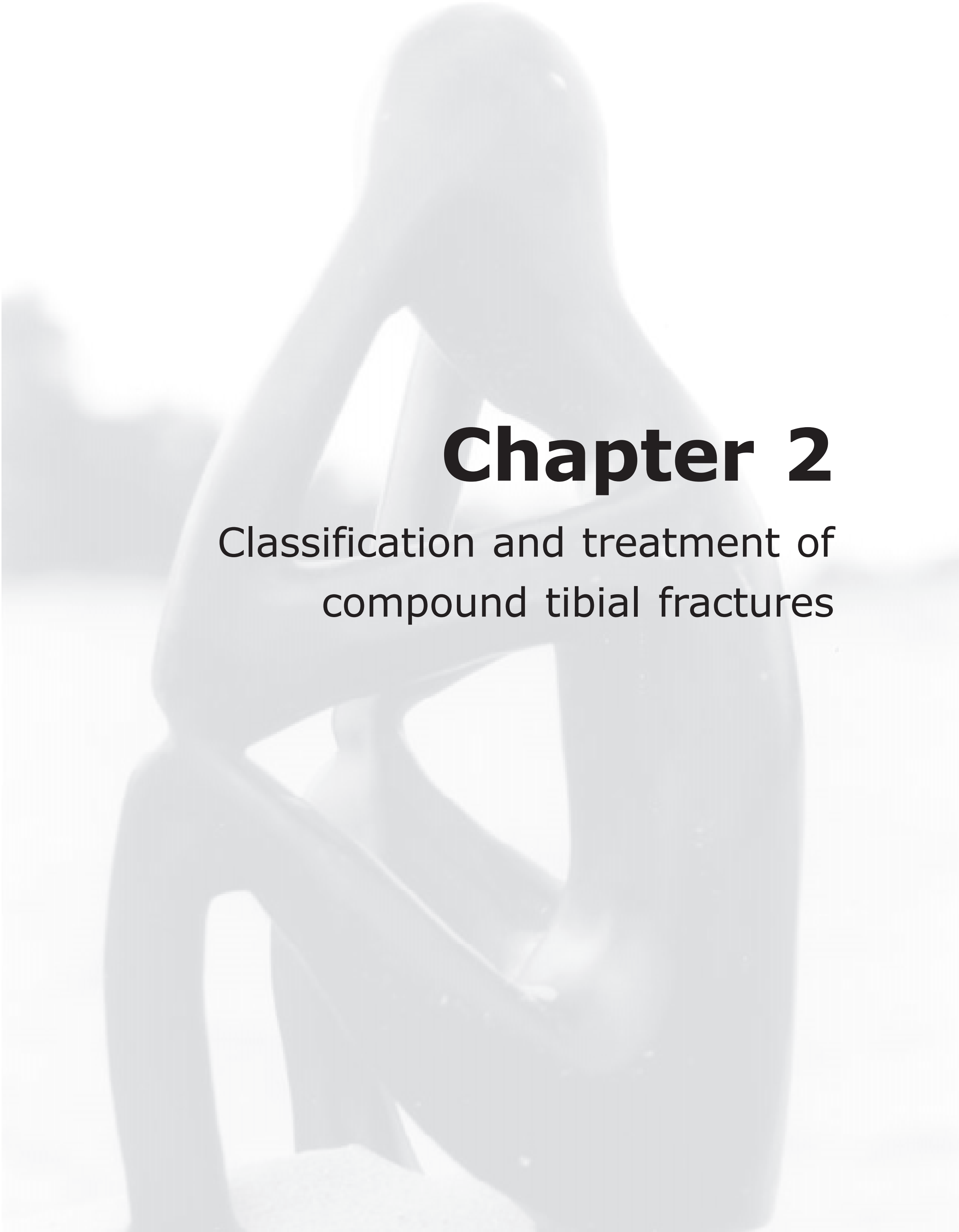


Chapter 2

Classification and treatment of compound tibial fractures

CLASSIFICATION OF FRACTURES

The successful management of fractures is based on sound surgical principles with stepwise procedures tailored to the individual needs and specific circumstances. Early explicit determination of fracture type and severity of the soft-tissue injury with clear definitions will aid the discussion and expedites decision-making and treatment planning. Moreover, it facilitates prediction of outcome of the injuries (prognosis) and simplifies comparison of results. Fracture classifications have been used since the time of Hippocrates to facilitate the care of broken bones,[1] but its number has grown strongly over the past decades. Today, a fracture in any anatomical region of the skeleton can be classified into one of the many different classifications. We will discuss the most commonly used classification systems for (tibial) fractures and associated soft-tissue injury.

Fractures

The *AO Comprehensive Classification of Fractures of Long Bones*, originated by Müller et al., provides a universally accepted scheme of fracture classification.[2] This system consists of five parts: the first digit represents the bone segment, which defines the involved bone; the second digit represents the segment of bone where the fracture is located (proximal, diaphyseal, or distal); the third digit (letter) defines the type of fracture (simple, wedge, or comminuted); the fourth digit defines the group or fracture pattern (spiral, oblique, transverse); and the fifth digit defines the subgroup, which allows for certain features unique to each bone to be categorised (figures 1 and 2).[2,3] The AO Classification is very well applicable to all diaphyseal fractures and to most epi- or metaphyseal fractures. In figure 3, the classification for tibial/fibular shaft fractures is shown as an example.

Figure 1. *The AO Classification uses a five-character alpha-numeric coding system. The first two numbers indicate the location, whereas the remaing letter and two numbers describe the morphologic characteristics of the fracture.*[2]

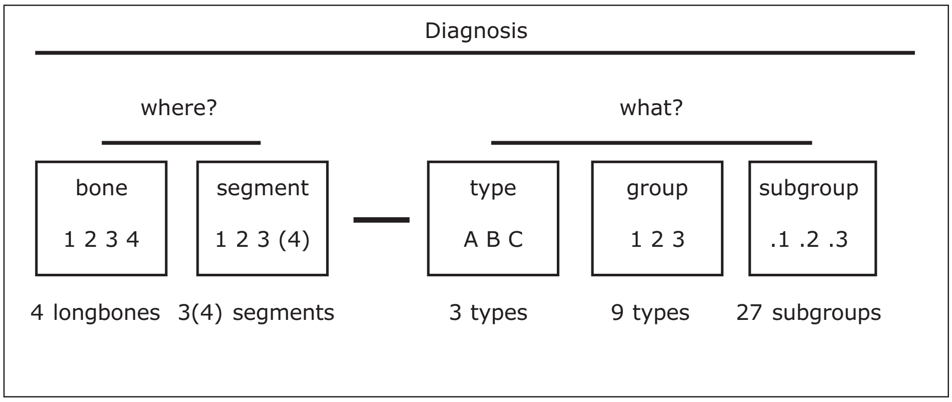


Figure 2. *The location codes for the AO Classification. Each long bone is numbered (1-4) and divided into proximal, diaphyseal, and distal segments, providing the first two number in the code.*[2]

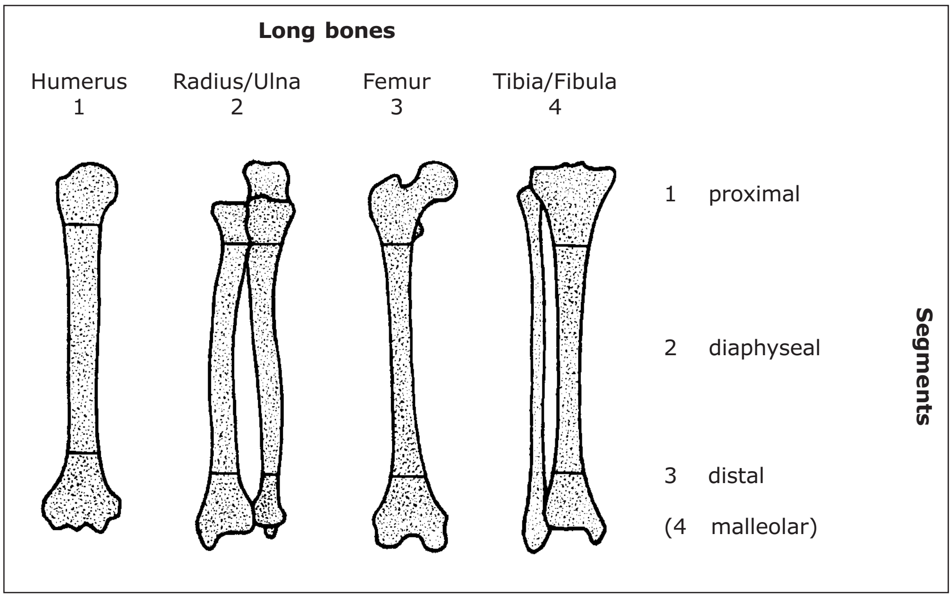
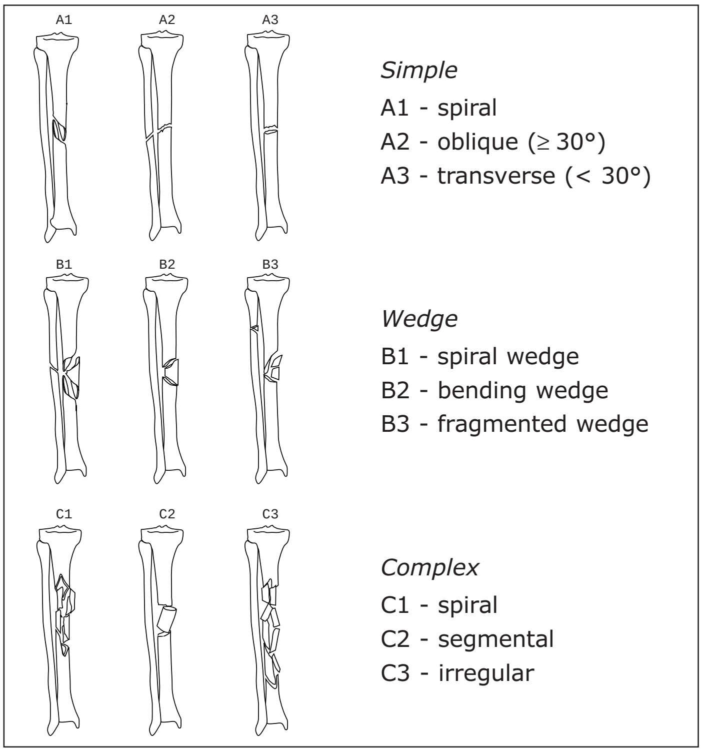


Figure 3. *AO Classification for tibial/fibular shaft fractures (longbone group 4).*[2]



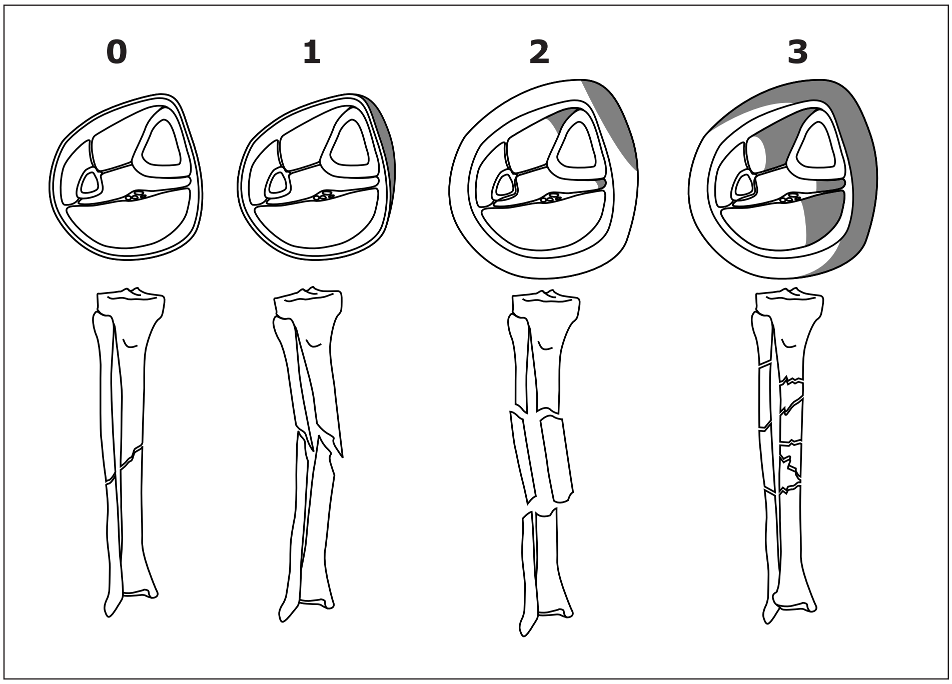
Soft-tissue injury (closed fractures)

Closed fractures with or without associated soft-tissue injury are not the topic of this thesis. However, even if there is no open wound or visible blood loss, the soft-tissue damage may be impressive. Therefore, skin lesion alone is not a marker of soft-tissue injury severity. In 1982, Tscherne and Oestern proposed a classification system for closed extremity fractures with concomitant soft-tissue injury, which is well accepted nowadays (table 1 and figure 4).[4]

Table 1. *Tscherne-Oestern classification for soft-tissue damage in closed fractures.*[4]

Type	Description
0	Minimal soft-tissue damage. Indirect violence. Simple fracture patterns. Example: torsion fracture of the tibia in skiers.
1	Superficial abrasion or contusion caused by pressure from within. Mild to moderately severe fracture configuration. Example: pronation fracture-dislocation of the ankle joint with soft-tissue lesion over the medial malleolus.
2	Deep contaminated abrasion associated with localised skin or muscle contusion. Impending compartment syndrome. Severe fracture configuration. Example: segmental "bumper" fracture of the tibia.
3	Extensive skin contusion or crush. Underlying muscle damage may be severe. Subcutaneous decollement. Decompensated compartment syndrome. Associated major vascular and/or nerve injury. Severe or comminuted fracture configuration.

Figure 4. *Tscherne-Oestern Classification for soft-tissue damage in closed fractures.*[4]



Soft-tissue injury (open fractures)

The widely cited *Gustilo Classification* of compound fractures in Grades I, II and III from 1976 was in 1984 extended with a subclassification of Grade III fractures, reflecting the severity or energy absorption of the fracture area in addition to the size of the open wound (table 2 and figure 5).[5,6] From daily practice we know that it is hard to classify open fractures consistently. This was shown by Brumback and Jones, who proved that agreement among orthopaedic surgeons was only 60% (based on photographs) regarding the classification of compound fractures ranging from Grade II to Grade IIIC, with large interobserver variation leading to poor reliability and reproducibility.[7] Moreover, there is significant variability in injury severity within each specific (sub)group. Because of this variability, the treatment options and prognosis for fractures within one group may differ strongly.

Figure 5. *The Gustilo Classification of open fractures.*[5,6]

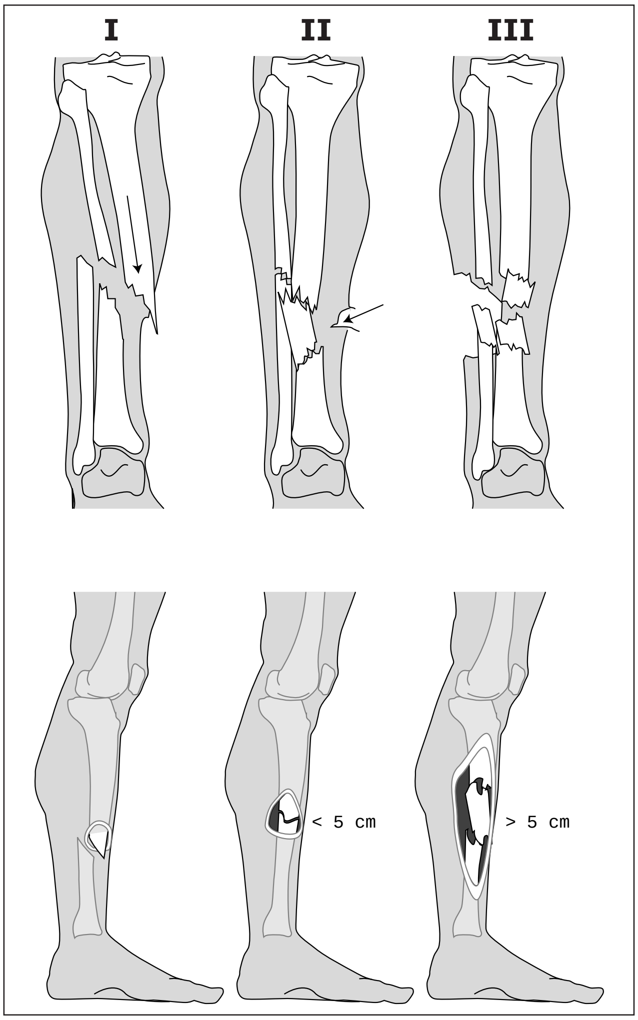


Table 2. *The Gustilo Classification of open fractures.*[5,6]

Grade	Description
I	A fracture with a clean cutaneous wound less than 5 cm in length.
II	A fracture with laceration greater than 5 cm in length lacking any severe soft-tissue damage.
III	A fracture with extensive soft-tissue damage and …
A	... adequate coverage of the fracture by soft tissues despite extensive cutaneous lacerations or flaps. High-energy trauma irrespective of wound size.
B	... more extensive injury to and contamination of the soft tissues, periostal stripping and soft-tissue gaps are present.
C	... any open fracture with an arterial injury requiring repair regardless of degree of soft tissue disruption.

CURRENT TREATMENT OF COMPOUND TIBIAL INJURIES

The principal goals in treating open fractures are to promote bony union and to restore function, to avoid complications such as infection, and to minimise both surgical and anaesthesiologic risks.[8] Open fractures of the tibia are among the most difficult to treat, because of the poor soft-tissue cover and delicate blood supply.[9] The management of open tibial fractures is to be based on a stepwise approach, starting with initial wound debridement and fracture stabilisation, followed by early soft-tissue coverage, and various forms of secondary surgery on broad indication.

Wound debridement and decompression

Adequate debridement (i.e. the removal of dirty, poorly vascularised and dead tissue) is the key to success in treating open fractures. Healthy soft tissues with a sufficient (micro)circulation are essential for wound healing and the defence against micro-organisms.[10-13] If in doubt about the result of the initial procedures, 24 to 48 hours later re-assessment and re-debridement must be performed. These steps need to be repeated until remaining bone and soft tissues are viable: it requires courage to create large defects in order to prevent infection and to promote healing capacity.

A high index of suspicion must be maintained for compartment syndrome. In the past, it was believed that open fractures do not present with compartment syndrome because of the misconception that the associated soft-tissue injury (with torn fascial layers) will decompress compartments by definition. This is not correct, nowadays we know that compartment syndromes do develop in the presence of an open fracture.[14,15] In the first place, because compartments may remain closed despite the severity of the injury, secondly because the contents of compartments are inhomogeneous structures. This means that the musculature in a compartment may have been partially decompressed as a result of overlying fascial damage, but that adjacent parts of the muscle may still be enclosed in an intact fascial envelope and consequently develop a high compartment pressure.[16] Outcomes of tissue-pressure measurements are not always reproducible and there is disagreement regarding the tissue pressure level at which a fasciotomy for decompression should be performed. In the light of the disastrous outcome of a missed compartment syndrome, decompression should be performed on a broad indication: prevention is much better than cure.

Fracture stabilisation

Immediate and adequate fracture stabilisation are important in preventing infection. Immobilisation of the bone in its anatomical position restores alignment of the neurovascular and muscular structures. By doing this, inflammatory responses are decreased, venous return is improved, and further soft-tissue and neurovascular damage from abnormal motion is prevented.[17] Many methods have been described for stabilisation of tibial fractures, including (un)reamed intramedullary nails, plates, and external fixation.

Internal fixation

Intramedullary nails. Intramedullary (IM) nails act as internal splints and are from a biomechanical point of view in an ideal, i.e. central position. There is evidence that IM nails in general are better than external fixators in the treatment of open tibial shaft fractures. Bhandari et al. published a meta-analysis of five randomised trials (n = 396 patients) comparing these two methods of fracture stabilisation.[9,18-22] The risks of deep infection, re-operation and non-union with nails - inserted without reaming - in comparison with external fixators were, respectively, 0.51, 0.69, and 0.60 (no significant differences). Unreamed nails offered significant advantages in reducing the risks of superficial infection (rr 0.24) and mal-union (rr 0.42).[18] Direct comparisons between reamed IM nailing and external fixation were not available. These authors compared reamed and unreamed tibial nailing as well, by analysing two randomised trials (n = 132 patients).[14,18,23] Reamed IM nails did not significantly decrease the risk of re-operation when compared with unreamed nails (rr 0.75). Moreover, reaming did not significantly alter the risks of deep infection or of non-union in comparison with non-reaming (respectively, rr 0.70 and 1.02). However, the use of reamed nails significantly reduced the risk of implant failure (rr 0.32).[18]

Plates and screws. Plate fixation offers good fracture stability allowing early limb mobility especially when there is no bone loss or extensive comminution. Plates are useful to buttress reduction of displaced intra-articular fractures and can be used to fix open metaphyseal fractures, because limited additional periosteal stripping is required for plate application.[24] In comparison with external fixation, plates are favoured with regard to prevention of mal-union. However, they score worse regarding deep infection and failure of fixation.[18,25] If plating is performed, care must be taken not to strip soft tissues from the bone unnecessarily in order not to jeopardise its vascularity.

External fixation

Traditionally, external fixation was preferable for grade IIIB and grade IIIC open tibial fractures because of concerns regarding the implantation of metal implants into a contaminated field. In general, external fixation is biomechanically less stable compared with internal fixation and is associated with more problems like pin-track infection, longer time to fracture union, malunion, and practical problems of access for the microvascular surgery and skin grafting.[9,26,27] Because it is a quick procedure, external fixation remains the most suitable option in desperate situations.

Antibiotics

The value of antibiotic prophylaxis in preventing infection of contaminated or compromised wounds is undisputed. However, classical experiments by Burke proved antibiotics only to be effective if adequate blood and tissue levels are present at the moment of bacterial inoculation.[28] In this respect, antibiotic prophylaxis in accidental wounds is always too late by definition. While in closed fractures antibiotics are administered before the potential contamination during surgery, open fractures will be contaminated at the time of accident. In these cases it is a matter of dispute as to whether preoperative administration of antibiotics is prophylaxis in its true sense and as such it is better to speak of early therapy. This explains why the value of antibiotics to prevent infection after operative therapy of closed fractures is proven,[29] while the results of studies in open fractures are still inconclusive.[30-33] In our institution, no antibiotics are administered to patients presenting with a grade I open tibial fracture. In grade II and IIIA open fractures, a single dose (broad-spectrum) cephalosporin (Cefazolin®) is used; for grade IIIB and IIIC open fractures an aminoglycoside (Gentamycin®) is added.

Soft-tissue reconstruction

Because without a healthy musculo-cutaneous envelope fracture healing is strongly jeopardised, adequate coverage is an essential part of treatment in fractures with concomitant soft-tissue defects. Superficial or small defects are best covered with (split) skin grafts or fascio-cutaneous flaps. In larger defects, cover should be achieved with a muscle flap because of its plastic properties (filling up dead space), its excellent vascular and trophic qualities and its resistance to infection.[11,34] The gastrocnemius and soleus muscles are most frequently used as pedicled flaps in the lower leg, and the latissimus dorsi, the rectus abdominus and the gracilis muscles for free muscle transfers. An important factor is the timing of soft-tissue coverage. The ideal interval between the injury and soft-tissue reconstruction with a flap should be such as to ensure a good general condition of the patient, the certainty of proper wound debridement, and the most convenient conditions for the transfer.[35] Nowadays, the recommendation is to perform flap surgery as soon as possible after revision and bone fixation.[36-38] Early cover not only reduces the risk of infection, but also improves blood supply to the healing bone.[9] Godina has reported that early (<72 hours) reconstruction results in less free flap failures and infections, enhancing bone healing and reducing hospitalisation time.[35]

Secondary surgery

In patients with severely comminuted and segmental fractures, early (prophylactic) bone grafting (at 4 to 10 weeks) is recommended. Grafting immediately at the time of wound closure will cause additional dissection and bears the risk that the graft will dissolve or become infected.[17] Moreover, in comminuted fractures it is not clear in which specific level bone should be applied. The most suitable method for restoration of moderate bone loss (up to 6 cm) is the use of cancellous bone grafts. For larger defects, segmental bone transport or even a free vascularised fibular transfer should be considered.[39-44]

Conclusions

Open tibial fractures are challenging therapeutical problems. They bear a high risk on complications and are a major source of morbidity. The management of these fractures can only be successful if tailored to the individual needs and specific circumstances. A consequent step-by-step approach is imperative, starting with proper fracture classification followed by the planning of several subsequent procedures. Four cornerstones are essential: 1) vigorous and repeated debridement; 2) immediate fracture stabilisation using different methods depending on the fracture type and site, the soft-tissue condition and contamination, the condition of the patient, and personal preference; 3) early soft-tissue reconstruction and; 4) secondary surgery to promote fracture healing and/or to reconstruct skeletal defects if needed.

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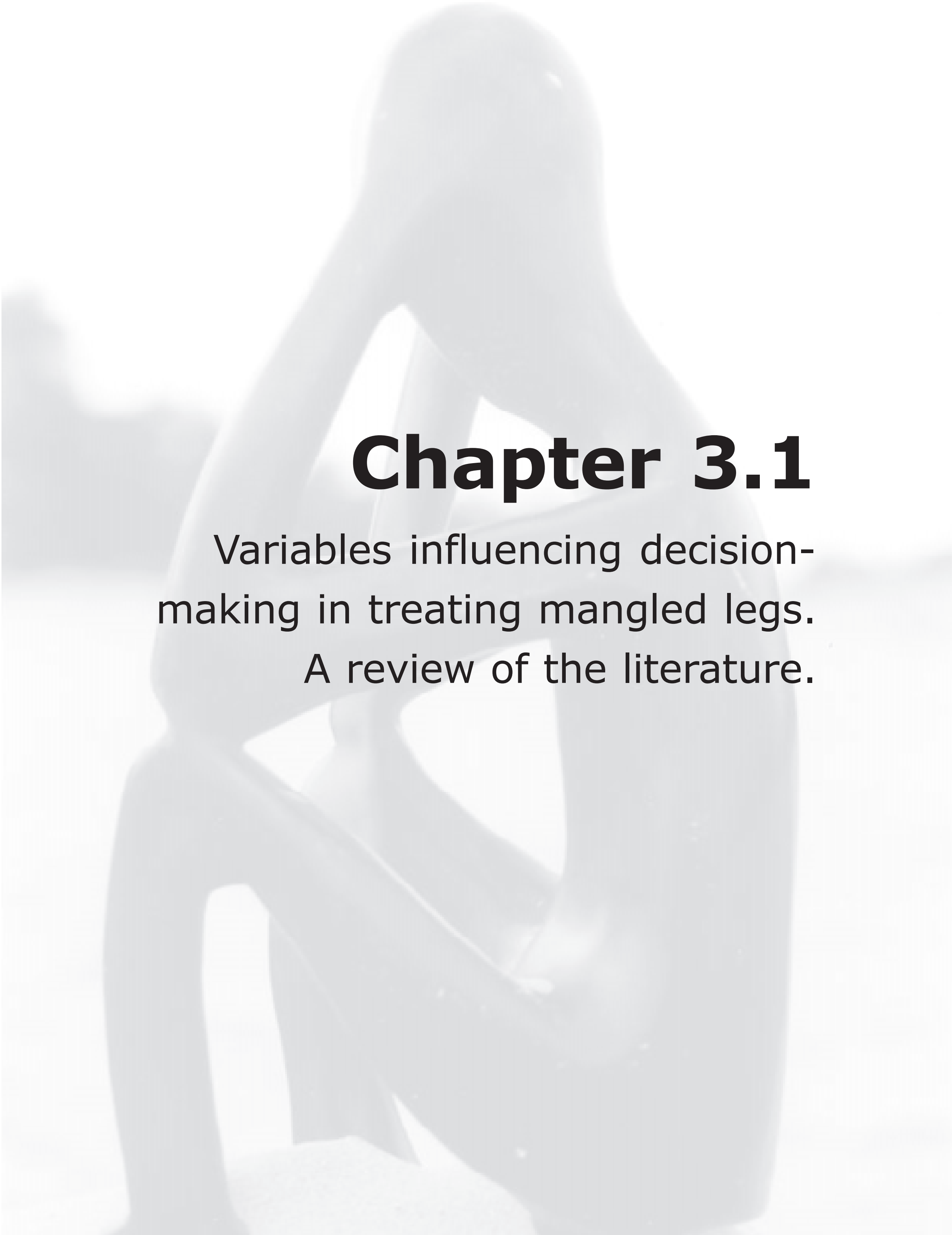

Chapter 3.1

Variables influencing decision-making in treating mangled legs. A review of the literature.

Introduction

The management of a mangled lower extremity is a topic of ongoing debate. While several decades ago most of these legs had to be amputated, nowadays most are potentially salvageable. The major decision in these fractures is not whether one *can* but whether one *should* attempt salvage.[1] This decision is often clearly mandated by the nature and extent of the lower-extremity injury and the patient as a whole.[2] Many factors have been considered as being significant in the functional outcome of lower extremity fractures with associated soft-tissue injury and some play a decisive role in the choice between an attempt at salvage and primary amputation. In this chapter, these factors will be discussed successively.

Patient-related factors

Age

The patient's age is an important consideration in treating mangled legs. It has a significant effect on long-term prognosis related to trauma in general,[3] but also to specific injury types, primarily because older patients have an increased likelihood of medical co-morbidity[4] and inactivity[5]. A study by Gaston et al. on isolated tibial fractures (both open and closed) treated by intramedullary nailing, showed that age was predictive of time to union and therewith to full weight-bearing.[5] In relating to mangled legs, most authors believe that an age over 50 years is strongly disadvantageous.[6] Of course, the physiologic age and the status of the loco-regional vasculature of the limb are more significant than chronological age.

Co-morbidity

Underlying disease, such as diabetes mellitus and bleeding disorders, can delay the healing process and lead to complications. Severe pulmonary disease or congestive heart failure can make a lengthy operation unduly risky, whereas osteoporosis increases the risk of mechanical instability after osteosynthesis. Pre-existing vascular disease may further compromise the blood supply to the injured bone and soft tissues and delay revascularisation. In general, pre-existing diseases alone will not alter management, but in combination with other influencing factors - such as an high age - it does.

Smoking behaviour

Smokers may encounter several difficulties during the recovery of a severe lower extremity injury. They need a significant longer time to fracture union than nonsmokers and have a higher incidence of delayed union.[7,8] In case of microvascular surgery, smoking significantly increases the rate of postoperative complications, with wound infection, muscle necrosis, and skin graft loss being more common.[9-11] Several studies - mainly performed in elective procedures by plastic surgeons - have demonstrated positive effects of cessation on short term.[12-14] It is likely that such advantages can be found in smoking patients treated for an open tibial fracture, who refrain smoking after the accident and persevere the full rehabilitation course, too.[10,11]

Local trauma-related factors

Mechanism of injury

The mechanism of injury is an indicator of the severity of the initial injuries. It says whether the trauma was blunt or penetrating, and indicates the amount of energy absorbed by tissues.[15] In high-energy trauma (for example a traffic accident or a fall from height), there is a much higher risk on complex fractures with severe damage to the soft tissues than in low-energy trauma (for example a sports accident).

Fracture pattern

The degree to which skeletal stability is destroyed is one of the crucial aspects in the ultimate fate of a damaged lower extremity. Comminuted (AO type C) fractures tend to give more complications and need longer healing than simple (AO type A) or wedge (AO type B) fractures.[16-18] With increasing displacement of fracture fragments, periostal stripping and stronger comminution the healing capacity is impaired.[5] In 1984, Gustilo proved the difference in the rate of bony union between displaced and non-displaced Grade III open tibial fractures to be statistically different ($p<0.005$).[19]

Soft-tissue injury

Extensive soft-tissue injury has clearly been shown to be a major prognostic indicator.[16,20] Serious direct muscle damage, and the following progressive muscle necrosis, may lead to extremity loss despite functioning major vessel revascularisation. Muscle not only provides the coverage at the traumatised area, but augments vascularisation of the fracture site and helps overcome wound contamination and infection. Therefore, it is important to restore large soft-tissue defects on short term. Nowadays, local pedicled flaps and free muscle flaps improve the ability to salvage complex wounds.[21,22] In both open and closed tibial fractures, there is a high risk on compartment syndrome due to an increased tissue pressure. Even in the most severe open fractures, complete fasciotomies are to be performed consequently and on broad indication.

Vascular injury

Open tibial fractures with relevant arterial injury (Grade IIIC according to Gustilo) have a poor prognosis. Amputation rates in this group range from 20% to 75%.[23] To save an extremity, it is imperative that there be early recognition and treatment of arterial injury. Miller and Welch have documented in a canine model a salvage rate of greater than 90% with ischemic periods of less than 6 hours. Their limb salvage rates were less than 50% with ischemia of greater than 12 hours.[24] In these injuries, there is a high risk on compartment syndrome, due to the interrupted blood flow and massive bleeding. Therefore, fasciotomies have to be performed in a large number of cases.

Neurological injury

Disruption of the posterior tibial nerve leads to complete loss of the protective sensitivity of the foot sole, with a high risk of neuropathic ulcers. According to several authors, this is a functional liability significant enough to warrant primary amputation.[20,25-28] However, recently Jones et al. showed that high-energy trauma in association with an insensate foot at the time of admission indeed results in substantial long-term impairment, but that this impairment is independent of treatment with or without amputation.[29] These investigators questioned therefore the validity of the insensate foot as an indicator for primary amputation. Moreover, tibial nerve grafting has been documented to restore plantar sensation in selected cases.[30-32]

Ipsilateral injury

If there is an additional severe injury to the ipsilateral extremity, an individual approach - tailored to the specific situation - needs to be chosen. It may preclude reasonable function even if the limb is salvageable.[6] If an unreconstructible foot is present, amputation must be strongly considered.[20]

Contamination

Especially (open) tibial fractures caused by high-energy trauma present with gross contamination. A shock wave creates severe stripping of soft tissue, followed by a momentary vacuum, which sucks debris into the limb. A small wound may conceal a completely degloved bone with particulate material embedded deep within it. Because of the high risk on infection, all necrotic and contaminated tissue must be debrided adequately.

General trauma-related factors

Injury severity

Patients presenting with a mangled leg may have associated (life-threatening) injuries, such as an intracranial haematoma or intra-abdominal bleeding from a ruptured liver or spleen. Time-consuming attempts to preserve the lower limb may lead to increased mortality.[33] Because in the management of polytrauma patients the adage "life before limb" is valid, primary amputation might be indicated so operative time can be minimised and intra- or post-operative management facilitated.[20,33]

Shock

Most polytrauma patients have major bleedings and present in shock. Because of the consequential peripheral vasoconstriction, the tissue perfusion in the lower leg will be further minimised. This may lead to irreversible ischemia and cellular death, threatening the injured limb. To minimise complications, an early and aggressive effort at volume restoration with fluid and blood products to restore systemic perfusion is essential. The administration of vaso-active drugs might have the same consequences.

Hypothermia

Hypothermia influences treatment dramatically and has a profound effect on outcome. It disturbs hemostasis by diminishing platelet function, influencing the coagulation cascade, and exerting an effect on the fibrinolytic system.[34] Eventually, this will lead to uncontrolled coagulopathy and hemorrhage, with a major risk at compartment syndrome and peri-operative complications. In case of severe hypothermia, patients are best treated by acute amputation.

Decision-making

All the above-mentioned variables have been implicated as being important in the process of decision-making for the treatment of a patient with a mangled leg. The ideal situation is one, which allows identification of those patients who will benefit from attempts at limb salvage, and those for whom primary amputation is the correct choice. Usually the individual prognosis is not known, due in part to the unique nature of the injury and the limited personal experience of most (orthopaedic) surgeons. In recent decades, a number of predictive indices in the form of scoring systems - based on some the factors discussed in this chapter - have been developed in order to assist the surgeon in decision-making.[16,17,27,35-37] In general, these scoring systems lack sensitivity. Therefore they have limited clinical value and cannot be used as a reliable criterion for decision-making.[38]

Large prospective studies have to be done that try to define clear guidelines to help decide which severely damaged extremities are best handled by immediate amputation and which by attempt at salvage. This would allow both patients and their doctors to avoid prolonged, costly, and fruitless salvage procedures when such a course is not indicated.[1] Until such a more rigid protocol is developed, decision-making for the treatment of mangled lower legs must rely upon a flexible approach that considers the array of the previously discussed variables.

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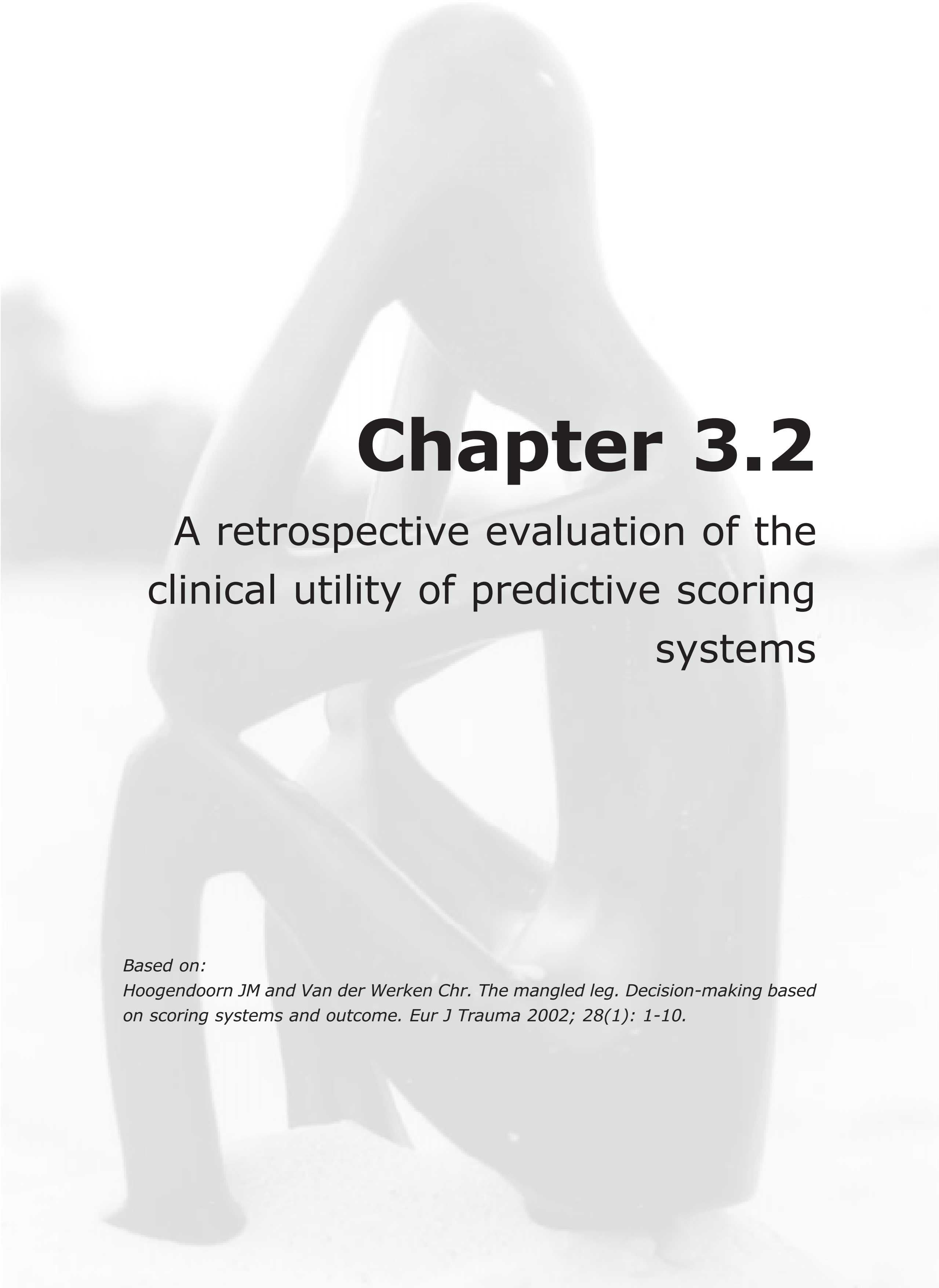

Chapter 3.2

A retrospective evaluation of the clinical utility of predictive scoring systems

Based on:
Hoogendoorn JM and Van der Werken Chr. The mangled leg. Decision-making based on scoring systems and outcome. Eur J Trauma 2002; 28(1): 1-10.

Abstract

Objective
Evaluation of the utility of scoring systems as predictors of salvage or amputation in open tibial fractures with severe soft-tissue damage.

Design
Retrospective study.

Patients and methods
Fifty-seven patients (age >15 years), all treated in the University Medical Centre Utrecht between 1992 and 1997, were included. An analysis of the patients' notes was performed to gather data on type of injury, clinical and operative findings and final outcome. With these data the MESI (Mangled Extremity Syndrome Index), the PSI (Predictive Salvage Index), the HFS (Hannover Fracture Scale), the LSI (Limb Salvage Index), the MESS (Mangled Extremity Severity Score) and the NISSSA (nerve injury, ischemia, soft tissue injury/contamination, skeletal injury, shock/blood pressure, age) were calculated for all patients. To examine the discriminant validity of the six lower-extremity injury-severity scores, the sensitivity, the specificity, the positive predictive value (PPV), and the negative predictive value (NPV) were calculated.

Results
Thirty-nine patients underwent a successful attempt at salvage, in 12 patients amputation was performed primarily (within 1 week after presentation) and in 6 patients secondarily. Sensitivity, specificity, PPV and NPV were respectively 28%, 97%, 83% and 75% for MESI, 56%, 85%, 63% and 80% for PSI, 67%, 85%, 67% and 85% for HFS, 67%, 95%, 86% and 86% for LSI, and 67%, 92%, 80% and 86% for both MESS and NISSSA. In 8 patients 4 or more scoring systems predicted incorrectly.

Conclusions
The present study did not support the utility of any of the scoring systems for discriminating between limbs requiring amputation and those likely to be salvaged successfully. They lack sensitivity and, consequently, limbs eventually requiring amputation would be at risk for a delay in the procedure. Therefore these scores have limited clinical value and cannot be used as a reliable criterion on which decision-making for the treatment of mangled legs is based.

Introduction

The objective of therapy in patients with severe injuries to the extremities is the salvage of a functional limb. When this goal is not obtainable, early amputation can avoid costly attempts at salvage that may subject the patient to significant morbidity and in some cases mortality.

In the literature, many factors influencing initial treatment have been described.[1] Several authors have developed predictive scoring systems based on these objective criteria to establish a dividing line between limb salvage and amputation.[2-7] By graduating the factors composing these systems, subscores can be given. If the total score (i.e. the sum of the subscores) exceeds the threshold, primary or early amputation should be strongly considered. Six of the more commonly used scoring systems are the MESI (Mangled Extremity Syndrome Index)[3], the PSI (Predictive Salvage Index)[5], the HFS (Hannover Fracture Scale)[6], the LSI (Limb Salvage Index)[2], the MESS (Mangled Extremity Severity Score)[4], and the NISSSA (nerve injury, ischemia, soft tissue injury/contamination, skeletal injury, shock/blood pressure, age)[7] (Appendix, tables A1-6).

The originators of the respective scoring systems validated these by demonstrating high rates of sensitivity and specificity in predicting limb salvage. However, most scores were based on retrospective studies, with small sample sizes, and are affected by the clinical bias of the index developers.

We report the results of an independent, retrospective evaluation of six predictive scoring systems designed to assist in the decision to salvage or amputate a severely injured lower limb.

Patients and methods

In the period 1992-1997, 63 patients (>15 years old) with a Gustilo grade III open tibial fracture were treated at the University Medical Centre Utrecht. The choice of treatment was based on clinical impressions, taking into account the previously discussed decision-making variables. None of the six mentioned scoring systems was used. Six patients, who deceased during the initial stay in hospital due to associated injuries, have been excluded from analysis.

The study group consisted of 43 men (75%) and 14 women, with an average age of 43 years. Thirteen (23%) fractures were classified as Gustilo grade IIIA, 25 (44%) as grade IIIB and in 19 (33%) cases there were associated significant arterial injuries, making it grade IIIC open fractures.

In 45 patients, limb salvage was attempted, while 12 patients underwent primary amputation (i.e. within one week after presentation). Mean age did not differ between both groups (43.1 versus 40.8 years), nor did the mean Injury Severity Score

(29.9 versus 28.0). Six of the 45 patients in whom limb salvage was attempted, underwent secondary amputation. The reasons were infected pseudarthrosis (3 patients), necrosis of free muscle transfers (2 patients) and ischemic necrosis of the sole of the foot (1 patient). The average number of days to secondary amputation was 175 (8-596). The mean age of the patients undergoing secondary amputation was significantly higher than that of the patients with a successful attempt at salvage (60.8 versus 40.4 years). The patients undergoing primary amputation had significant more serious injuries than the patients with a successful reconstruction or secondary amputation, as appears from the higher number of grade IIIC open fractures. The grade IIIA : IIIB : IIIC ratio was 12(31%) : 21(54%) : 6(15%) for patients with a successful reconstruction, 1(17%) : 3(50%) : 2(33%) for patients undergoing secondary amputation, and 0 : 1(11%) : 11(89%) for patients undergoing primary lower leg amputation.

An analysis of the patients' notes and X-rays was performed to gather data on type of injury, clinical and operative findings and final outcome. With these data the MESI[3], the PSI[5], the HFS[6], the LSI[2], the MESS[4], and the NISSSA[7] were calculated for all patients. Mangled extremity scores for groups of patients were reported as the mean. Student's t-test was used to compare groups with significance inferred at $p<0.05$. To examine the discriminant validity of the six lower-extremity injury-severity scores, the sensitivity, the specificity, the positive predictive value (PPV), and the negative predictive value were calculated. Sensitivity was defined as the index's probability that limbs requiring an amputation will have scores at or above the threshold; specificity was defined as the index's probability that salvaged limbs will have scores below the threshold; PPV measures the incidence of amputation if amputation was predicted; and NPV measures the incidence of salvage if salvage was predicted. All calculations were performed by using SPSS for Windows (version 8.0).

Results

In table 1 the mean values of the studied predictive scoring systems are shown for the patients undergoing primary amputation, secondary amputation or a successful attempt at salvage. The recommended amputation-threshold scores published for the scoring systems were used.

Table 1. *Mean values of the predictive scoring systems for patients undergoing primary amputation, secondary amputation or a successful attempt at salvage.*

	MESI	PSI	HFS	LSI	MESS	NISSSA
Range	3-75	3-15	1-39	0-13	1-14	0-16
Threshold	20	8	15	6	7	9
Primary amputation	23.6	7.9	22.0	8.3	7.5	10.5
Secondary amputation	12.5	6.5	12.5	4.8	6.2	7.8
Successful attempt at salvage	10.2	5.4	10.8	4.1	4.8	6.1

Figures 1-6 display the observed and predicted limb salvage and amputation frequencies for each of the six scoring systems. In conjunction with these figures, table 2 presents the sensitivity, specificity, positive predictive value, and negative predictive value for each of the indices. The sensitivity ranged from 28% (MESI) to 67% (HFS, LSI, MESS, and NISSSA), the specificity from 85% (PSI and HFS) to 97% (MESI). The positive predictive value ranged from 63% (LSI) to 86% (PSI) and the negative predictive value from 75% (MESI) to 85% (LSI, MESS and NISSSA).

Figure 1. *Limb salvage & amputation by MESI.*

		Observed		
		amp	***salv***	
Predicted	***amp***	5	1	6
	salv	13	38	51
		18	39	

Figure 2. *Limb salvage & amputation by PSI.*

		Observed		
		amp	***salv***	
Predicted	***amp***	10	6	16
	salv	8	33	41
		18	39	

Figure 3. *Limb salvage & amputation by HFS.*

		Observed		
		amp	***salv***	
Predicted	***amp***	12	6	18
	salv	6	33	39
		18	39	

Figure 4. *Limb salvage & amputation by LSI.*

		Observed		
		amp	***salv***	
Predicted	***amp***	12	2	14
	salv	6	37	43
		18	39	

Figure 5. *Limb salvage & amputation by MESS.*

		Observed		
		amp	***salv***	
Predicted	***amp***	12	3	15
	salv	6	36	42
		18	39	

Figure 6. *Limb salvage & amputation by NISSSA.*

		Observed		
		amp	***salv***	
Predicted	***amp***	12	3	15
	salv	6	36	42
		18	39	

Table 2. *Cross-validation summary.*

Scoring system	**Sensitivity**	**Specificity**	**PPV**	**NPV**
MESI	0.28 (5/18)	0.97 (38/39)	0.83 (5/ 6)	0.75 (38/51)
PSI	0.56 (10/18)	0.85 (33/39)	0.63 (10/16)	0.80 (33/41)
HFS	0.67 (12/18)	0.85 (33/39)	0.67 (12/18)	0.85 (33/39)
LSI	0.67 (12/18)	0.95 (37/39)	0.86 (12/14)	0.86 (37/43)
MESS	0.67 (12/18)	0.92 (36/39)	0.80 (12/15)	0.86 (36/42)
NISSSA	0.67 (12/18)	0.92 (36/39)	0.80 (12/15)	0.86 (36/42)

Table 3. *Characteristics of the patients in whom four or more of the scoring systems predicted incorrectly*

Patient	Age	ISS	Days to amputation	MESI	PSI	HFS	LSI	MESS	NISSSA	Comments
A	47	50	9	**15** *	**5**	**10**	**4**	**5**	**7**	Associated injuries ("life before limb")
B	33	34	2	**18**	**6**	20	**5**	**5**	**7**	Associated injuries ("life before limb")
C	53	20	596	**8**	**6**	**10**	**5**	**6**	**7**	Complication (infected pseudarthrosis)
D	66	20	8	**11**	**5**	**9**	**4**	**6**	**7**	Complication (failure of free tissue transfer)
E	74	21	370	**10**	**6**	**12**	**5**	**6**	**8**	Complication (infected pseudarthrosis)
F	32	34	1	**8**	**6**	**9**	**9**	8	8	Complication (misjudged arterial injury with subsequent iriversible ischemia)
G	52	21	n/a	**23**	**9**	**21**	**9**	**9**	**13**	Grade IIIC open fracture with injuries to the aa. tib post, tib ant and peroneus; venous bypass (v. saphena magna). Moreover, contused n. tib post.
H	29	50	n/a	17	**8**	**20**	5	**7**	**9**	Severe polytrauma (mostly injuries to the ipsilateral extremity)

* **Bald scores** represent incorrect predictions

In six patients, four or more of the scoring systems predicted salvage, nevertheless amputation had to be performed. The characteristics in table 3 show that in two of these cases major associated injuries were of overriding importance (patients A and B), in three cases the presence of complications (patients C, D, and E), and misjudgement of an arterial tear with subsequent ischemia in the latter (patient F). In two patients, four or more of the scoring systems predicted amputation, but salvaged was successfully attempted (patients G and H).

Discussion

The severely injured lower extremity presents a challenge in surgical management. Many controversies have developed in the literature regarding what criteria justify limb salvage attempts for severely injured lower extremities. Several predictive scoring systems have been proposed to objectify the regional injury severity of the limb in order to assist the surgeon in decision-making.[2-7] Ideally, a scoring system would be 100% sensitive and 100% specific. A high sensitivity is important to guard against inappropriate delays in amputation when the limb is ultimately not salvageable. High specificity is important to ensure that only a small number of salvageable limbs are incorrectly assigned a score above the decision threshold.

We studied and compared the most widely described scoring systems: the MESI (Mangled Extremity Syndrome Index)[3], the PSI (Predictive Salvage Index)[5], the HFS (Hannover Fracture Scale)[6], the LSI (Limb Salvage Index)[2], the MESS (Mangled Extremity Severity Score)[4], and the NISSSA (nerve injury, ischemia, soft-tissue injury/contamination, skeletal injury, shock/blood pressure, age)[7].

Mangled Extremity Severity Index (MESI)

The MESI – the first published scoring system (1985) – was the result of a retrospective study in only 17 patients (including five patients with upper extremity injury).[3] The authors awarded points to the severity of the lower extremity injury (integument, nerve, vessel and bone), the Injury Severity Score (ISS), the extent and duration of ischemia, age, co-morbidity and shock (table A1). The investigators found that a MESI score of 20 was the dividing line below which limb salvage was predictable and above which 100% of their patients required amputation. However, in our study we found that the MESI tends to underestimate the lower limb injury (table 2, figure 1). Disadvantages are that the fracture localisation and associated injuries to the ipsilateral extremity (foot) are not taken into account. The MESI comprises many components that are important in the decision-making process, but it is also a complex scoring system that eventually fails in predictive value and practical applicability. In several other publications, similar comments were made.[8-10]

Predictive Salvage Index (PSI)

The PSI is the result of (retrospective) outcome analysis of the treatment of 21 lower extremity fractures with significant vascular comprise, in 1987, by Howe et al.[5] The investigators found that limb salvage is not related to the presence of shock, damage to veins or associated injuries. Determining factors were the time interval between accident and operation, the level of arterial injury, and the severity of damage to muscles and bones. Thus, these four variables compose the PSI (table A2). Compared with the MESI, the PSI contains fewer variables and seems easier in use. However, in daily practice it is difficult to interpret the degree of severity of the soft-tissue injuries, because the PSI does not give a clear description of the grades 'mild', 'moderate' and 'severe'.[8,10] Moreover, our study shows a too low sensitivity and specificity of respectively 56% and 85% (table 2). Evaluation of the PSI by Bosse et al., based on data collected as part of a large prospective, multicentre study (the Lower Extremity Assessment Project (LEAP)), confirmed these findings.[11]

Hannover Fracture Scale (HFS)

The HFS, proposed by Südkamp et al. in 1989, comprises many parameters: fracture type, size of bone defect, severity of soft-tissue injury, extent and duration of ischemia, nerve injury, contamination, the severity of the total of injuries, and the period between accident and operation (table A3).[6] Although the HFS seems to be a combination of the most "logical" variables, it still has a low sensitivity, so that in too many patients, amputation will be delayed unnecessarily (table 2).[11] Besides, the scoring system is difficult in use because of the large amount of parameters and because the soft-tissue injury has to be defined so precisely that it is hardly feasible.

Limb Salvage Index (LSI)

In 1991, Russell et al. published the LSI, based on a retrospective study of the results of treatment of 70 open tibial fractures with arterial injury.[2] The score is based on seven criteria: arterial, nerve, bone, skin, muscle, and deep venous injury as well as ischemic time (table A4). In previous publications, varying sensitivities and specificities have been reported.[8,11,12] Although the LSI is very detailed, relevant parameters such as age and associated injuries are not taken into account. Another drawback is that the outcome of the initial reconstructive procedures must be known, before the surgeon can score the variable 'skin'. For example, the variable describes primary closure, split-thickness skin grafting, and flap closures. Especially in injuries with severe tissue-loss, management of skin lacerations can change frequently due to necessary debridement of necrotic tissue. Therefore, we support Bonanni et al., who have the opinion that the LSI can not be used in the acute decision-making process.[8]

Mangled Extremity Severity Score (MESS)

The MESS, described by Johansen et al. in 1990, is based on four clinical variables (table A5).[4] Because it has few variables, does not need extensive operative evaluation, and seems easy to apply, it is probably the most widely used and referenced predictive index.[8,11-14] The emphasis on gunshot and penetrating injuries (mechanism of treatment) makes this scoring system more applicable in the United States than in Europe. When applied to our data, the MESS predicted amputation with a sensitivity of 67% and a specificity of 92% (table 2).

Nerve injury, Ischemia, Soft-tissue injury, Skeletal injury, Shock, and Age of patient Score (NISSSA)

In 1994, McNamara et al. designed the NISSSA -a modification of the MESS-, by adding more weight to the soft-tissue and skeletal injury (table A6).[7] In their hands, this new scoring system gave an improved sensitivity (82%) and specificity (92%) in predicting amputation. Unfortunately, this improvement could not reproduced by us and other investigators (table 2, figure 6).[11,13]

The present study did not support the utility of any of the scoring systems for discriminating between limbs requiring amputation and those likely to be salvaged successfully. The Limb Salvage Index had the highest sensitivity and specificity (respectively 0.67 and 0.95), but even this scoring system predicted falsely in eight of 57 (14%) patients. In six patients the injuries resulted in amputation in stead of the predicted successful limb salvage and in two patients vice versa. In the majority of these cases, three or more of the other scoring systems predicted wrongly too. In four of the wrongly predicted amputations, the (secondary) amputation had to be performed due to complications (table 3, patient A, C, D, and E), which even the best scoring systems cannot foresee. A greater number of variables does not create a more reliable scoring system. The Hannover Fracture Scale, a combination of 12 'logical variables', for example has lower sensitivity and specificity than the Mangled Extremity Severity Score, consisting of only four variables.

Conclusions

Overall, the scoring systems for discriminating between limbs requiring amputation and those likely to be salvaged successfully lack sensitivity. Consequently, mangled limbs eventually requiring amputation would be at risk for a delay in the procedure. Therefore scoring systems have limited clinical value and cannot be used as a reliable criterion on which decision-making for the treatment of mangled legs is based.

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Appendix

Table A1. *Mangled Extremity Syndrome Index (MESI)*[3]

Type	Characteristics	Points
Injury Severity Score	0-25 25-50 >50	1 2 3
Integument	Guillotine Crush/burn Avulsion/degloving	1 2 3
Nerve	Contusion Transection Avulsion	1 2 3
Vascular	Artery Transected Thrombosed Avulsed Vein	1 2 3 1
Bone	Simple Fx* Segmental Fx Segmental-comminuted Fx Segmental-comminuted Fx with bone loss < 6cm* Segmental Fx intra-extra articular Segmental Fx intra-extra articular with bone loss < 6cm*	1 2 3 4 5 6
Lag time	(1 point for every hr>6)	
Age	40-50 years 50-60 years 60-70 years	1 2 3
Pre-existing disease		1
Shock		2

Fx = fracture; * bone loss greater than 6cm, add 1

Table A2. *Predictive Salvage Index (PSI)*[5]

Type	Characteristics	Points
Level of arterial injury	Suprapopliteal Popliteal Infrapopliteal	1 2 3
Skeletal injury	Mild Moderate Severe	1 2 3
Soft-tissue injury	Mild Moderate Severe	1 2 3
Timespan between accident and arrival at OR	< 6 h 6-12 h > 12 h	0 2 4

OR = operating room

Table A3. *Hannover Fracture Scale*[6]

Type	Points
A Fracture	
AO Type A	1
AO Type B	2
AO Type C	4
Bone loss	
< 2 cm	1
> 2 cm	2
B Soft tissues	
Skin (laceration, contusion)	
none	0
< ¼ circumference	1
¼ - ½ circumference	2
½ - ¾ circumference	3
> ¾ circumference	4
Soft-tissue loss	
none	0
< ¼ circumference	1
¼ - ½ circumference	2
½ - ¾ circumference	3
> ¾ circumference	4
Deep soft tissues (muscle, tendon, ligaments); contusion or defect	
none	0
< ¼ circumference	1
¼ - ½ circumference	2
½ - ¾ circumference	3
> ¾ circumference	4
Amputation	
none	0
subtotal guillotine	1
subtotal crush	2
total guillotine	3
total crush	4

Type	Points
C Artery	
normal	0
incomplete ischemia (capillary refill +)	1
complete ischemia	
< 4 h	2
4-8 h	3
> 8 h	4
D Nerve	
palmar-plantar sensibility	
yes	0
no	1
finger-toe motor activity	
yes	0
no	1
E Contamination	
foreign body	
none	0
little	1
massive	2
bacterial contamination	
none	0
aerobe, 1 species	2
> 1 species	3
anaerobe	2
aerobe-anaerobe	4
F Associated injuries	
monotrauma, PTS 1	0
PTS 2	1
PTS 3	2
PTS 4	4
G Start of operation(tissue score>2)	
6-12 h	1
> 12 h	3

Table A4. *Limb Salvage Index (LSI)*[2]

Location	Extent of injury	Points
Artery	Contusion, intimal tear, partial laceration or avulsion (pseudo-aneurysm) with no distal thrombosis and palpable pedal pulses; complete occlusion of one of three shank vessels or profunda	0
	Occlusion of two or more shank vessels, complete laceration, avulsion or thrombosis of femoral or popliteal vessels without palpable pedal pulses	1
	Complete occlusion of femoral, popliteal, or three of three shank vessels with no distal runoff available	2
Nerve	Contusion or stretch injury; minimal clean laceration of femoral, peroneal, or tibial nerve	0
	Partial transection or avulsion of sciatic nerve; complete or partial transection of femoral, peroneal, or tibial nerve	1
	Complete transection or avulsion of sciatic nerve; complete transection or avulsion of both peroneal and tibial nerves	2
Bone	Closed fracture one or two sites; open fracture without comminution or with minimal displacement; closed dislocation without fracture; open joint without foreign body; fibula fracture	0
	Closed fracture at three or more sites on same extremity; open fracture with comminution or moderate to large displacement; segmental fracture; fracture dislocation; open joint with foreign body; bone loss < 3cm	1
	Bone loss > 3cm; Type IIIB or IIIC fracture	2
Skin	Clean laceration, single or multiple, or small avulsion injuries, all with primary repair; first degree burn	0
	Delayed closure due to contamination; large avulsion requiring SSG or flap closure. Second and third degree burns	1
Muscle	Laceration or avulsion involving a single compartment or single tendon	0
	Laceration or avulsion involving two or more compartments; omplete laceration or avulsion of two or more tendons	1
	Crush injury	2
Deep vein	Contusion, partial laceration, or avulsion; complete laceration or avulsion if alternate route of venous return is intact; superficial vein injury	0
	Complete laceration, avulsion, or thrombosis with no alternate route of venous return	1
Warm ischemia time	<6 hours	0
	6-9 hours	1
	9-12 hours	2
	12-15 hours	3
	>15 hours	4

SSG = split skin graft

Table A5. *Mangled Extremity Severity Score (MESS)*[4]

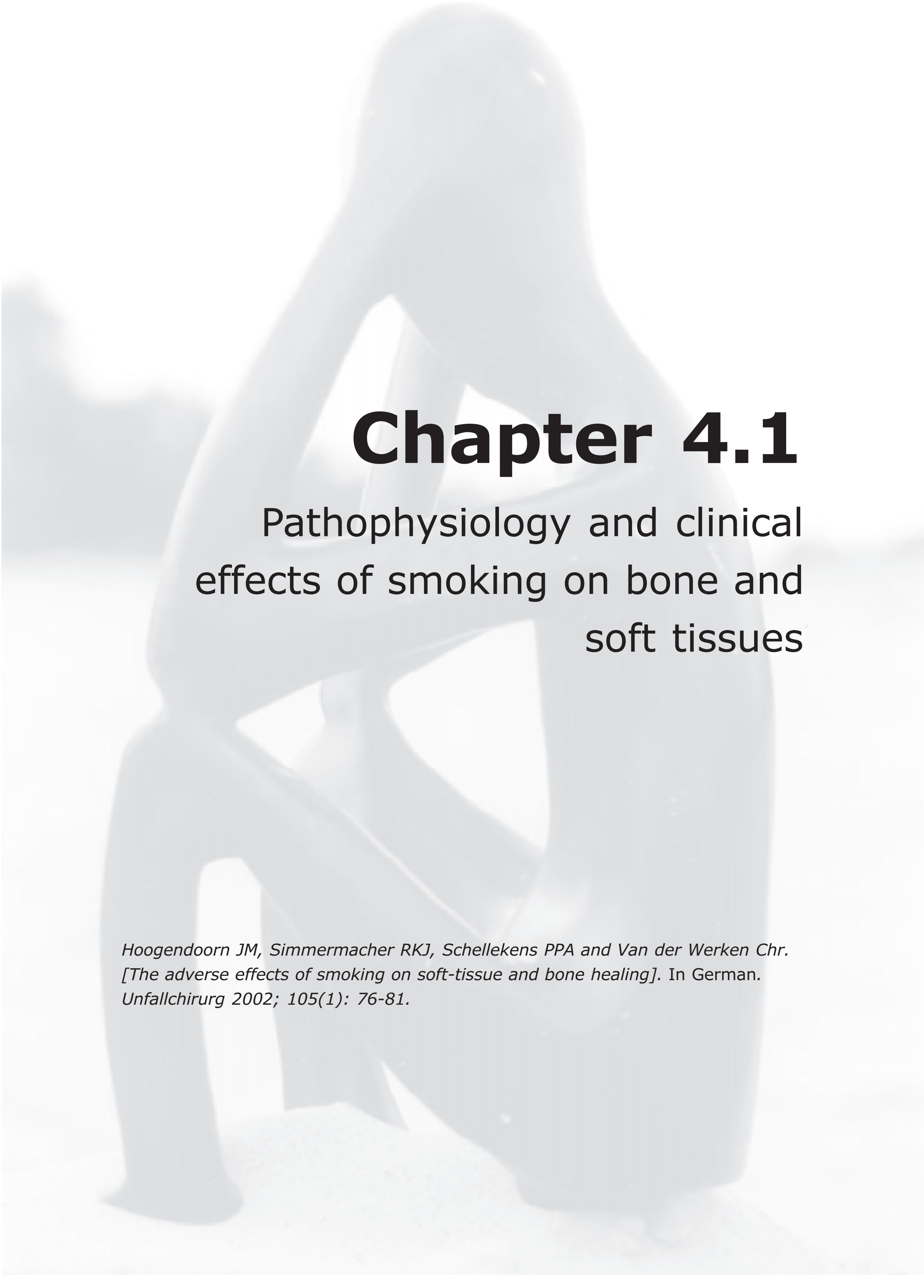
Type	Characteristics	Injuries	Points
Skeletal / soft-tissue	Low energy	Stab wounds, simple closed fractures, small-caliber gunshot wounds	1
	Medium energy	Open or multiple-level fractures, dislocations, moderate crush injuries	2
	High energy	Shotgun blast (close range), high velocity gunshot wounds	3
	Massive crush	Logging, railroad, oil rig accident	4
Shock	Normotensive hemodynamics	BP stable in field and OR	0
	Transiently hypotensive	BP unstable in field, but responsive to intravenous fluids	1
	Prolonged hypotension	Systolic BP less than 90 mmHg in field and responsive to intravenous fluids only in OR	2
Ischemia	None	A pulsatile limb without signs of ischemia	0
	Mild	Diminished pulses without signs of ischemia	1*
	Moderate	No pulse by Doppler, sluggish capillary refill, paresthesia, diminished motor activity	2*
	Advanced	Pulseless, cool, paralysed and numb without capillary refill	3*
Age	<30 years		0
	30-50 years		1
	>50 years		2

* Points x2 if ischemic time exceeds 6h; BP = blood pressure; OR = operating room

Table A6. *Nerve injury, ischemia, soft-tissue injury, skeletal injury, shock, age (NISSSA)*[7]

Type	Characteristics	Description	Points
Nerve injury	Sensitive	No injury of important nerves	0
	Dorsal	Deep or superficial peroneal or femoral nerve injury	1
	Plantar, partial	Tibial nerve injury	2
	Plantar, complete	Sciatic nerve injury	3
Ischemia	None	A pulsatile limb without signs of ischemia	0
	Mild	Diminished pulses without signs of ischemia	1*
	Moderate	No pulse by Doppler, sluggish capillary refill, paresthesia, diminished motor activity	2*
	Advanced	Pulseless, cool, paralysed and numb without capillary refill	3*
Soft-tissue injury	Low	Minimal to no soft-tissue injury, no contamination	0
	Medium	Moderate soft-tissue injury, gunshot wound (low velocity), little contamination, minimal crush	1
	High	Moderate crush, open fracture, gunshot wound (high velocity), heavy contamination	2
	Massive	Massive crush, soft-tissue loss, gross contamination	3
Skeletal injury	Low energy	Spiral fracture, oblique fracture, no to minimal dislocation	0
	Medium energy	Transverse fracture, small-caliber gunshot wounds	1
	High energy	Wedge fracture, moderate dislocation, gunshot wounds (high velocity)	2
	Very high energy	Complex fracture, bone loss	3
Shock	Normotensive hemodynamics	BP stable in field and OR	0
	Transiently hypotensive	BP unstable in field, but responsive to intravenous fluids	1
	Prolonged hypotension	Systolic BP less than 90 mmHg in field and responsive to intravenous fluids only in OR	2
Age	Young	< 30 years	0
	Middle	30-50 years	1
	Old	> 50 years	2

* Points x2 if ischemic time exceeds 6h; BP = blood pressure; OR = operating room



Chapter 4.1

Pathophysiology and clinical effects of smoking on bone and soft tissues

Hoogendoorn JM, Simmermacher RKJ, Schellekens PPA and Van der Werken Chr.
[The adverse effects of smoking on soft-tissue and bone healing]. In German.
Unfallchirurg 2002; 105(1): 76-81.

Abstract

This article reviews the current body of knowledge on the adverse effects of smoking on soft-tissue and bone healing, with emphasis on tibial fractures in combination with severe soft-tissue injury.

The pathophysiological effects are multidimensional, including arteriolar vasoconstriction, cellular hypoxia, demineralisation of bone, and delayed revascularisation. Several animal and clinical studies have been published about the negative effects of smoking on bone metabolism and fracture healing. These studies show that smokers have a significantly longer time to clinical union than non-smokers and a higher incidence of non-union. The negative effects of smoking gained increased interest among plastic and microvascular surgeons, because smokers have been shown to suffer higher rates of flap failure, tissue necrosis, and haematoma formation.

Especially smokers presenting with an open tibial fracture will suffer the negative effects of their smoking behaviour, because these fractures are inextricably bound up with soft-tissue injury. Their fractures will need a significantly longer time to heal than in non-smokers, and will have a higher incidence of non-union. If microvascular surgery is to be performed, persistent smoking significantly increases the rate of postoperative complications, with wound infection, partial flap necrosis, and skin graft loss being more common. Cessation of smoking has both short- and long-term beneficial effects.

Nowadays, there is strong evidence to be very insistent that patients presenting with a (open) tibial fracture should refrain from smoking immediately to promote bone healing and to lower the complication rate. In case of elective reconstructive procedures, patients should refrain from smoking at least 4 weeks before surgery. In both situations, cessation should continue during the full rehabilitation period.

Introduction

Despite known risks and warnings, there are still over one billion smokers worldwide today.[1] Potentially fatal diseases that are positively associated with smoking include malignancies of several organ systems, chronic obstructive pulmonary disease and ischemic heart disease, the last being the most common cause of death in economically developed countries.[2] Medical problems exclusively or largely caused by smoking are peripheral vascular disease, gastric and duodenal ulcers, and osteopenia with an increased fracture risk.[1] In recent years, there has been a growing interest in the possible adverse effects of smoking on soft-tissue and bone healing. In this chapter, the current knowledge on this topic is reviewed, with emphasis on tibial fractures in combination with severe soft-tissue injury.

Pathophysiology

Most surgeons support the opinion that smoking has a profound effect on all types of wound healing, but the exact mechanism of this inhibition is not known. Below, we will summarise the known pathophysiological effects of smoking.

Contents of cigarette smoke

Whole fresh cigarette smoke is composed of both liquid (particulate) and gaseous phases, each containing thousands of constituents. The two constituents most likely to be responsible for the negative effects to be discussed are nicotine (particulate) and carbon monoxide (gaseous).[3]

Vasoconstriction

Already in 1909, Bruce et al. demonstrated that cigarette smoking produced vasoconstriction in the human hand.[4] In 1974, Sarin et al. showed a 42% reduction in the digital flow in human volunteers after they had smoked one cigarette.[5] Nicotine is considered the main causative agent, because it stimulates sympathetic ganglia and the adrenal medullae. Following smoking one single cigarette, an acute increase in both circulating epinephrine and norepinephrine levels is found.[6] These levels peak at the end of smoking and fall to the baseline over the following 10 minutes. Hemodynamic changes in the microcirculation, such as arteriolar vasoconstriction and decreased blood flow, parallel the absorption of nicotine and the secretion of vasoactive hormones. This was proven scientifically by Reus et al., who studied the effects of tobacco smoking on blood flow in the cutaneous microcirculation in the mouse ear. In response to smoke inhalation, an arteriolar vasoconstriction was seen resulting in a 12% decrease in blood flow relative to the baseline.[7] In another study, decreased blood flow was recorded up to 72% of normal flow after intraarterial nicotine infusion in a 1- to 2-mm artery in the dog, a diameter which is in the range of commonly used arteries in microsurgery.[8]

Hypoxia

In the pulmonary capillaries, carbon monoxide combines reversibly with haemoglobin to produce carboxyhaemoglobin, preferentially to oxygen. This results in a decrease in the amount of oxygen carried by the haemoglobin. Furthermore, carbon monoxide is known to effect a shift to the left of the oxyhaemoglobin dissociation curves. This means that the amount of oxygen bound by haemoglobin decreases and that the oxygen carried is not released effectively to be utilised for cellular respiration, with hypoxia or even anoxia as result.[3,9] It has been shown that smoking for 10 minutes causes a reduction in tissue oxygen tension up to one hour.[10] Someone who smokes one pack of cigarettes per day is predicted to be tissue hypoxic almost permanently.[10]

Haemorheological changes and thrombosis

In humans, smoking causes hypercoagulability with increased plasma fibrogen, decreased plasminogen, decreased plasminogen activator, and increased plasma viscosity.[11,12] Experimentally, platelet function has been shown to be extremely sensitive to both nicotine and carbon monoxide.[13] In addition, nicotine stimulates the release of catecholamines - cofactors in the formation of chalones, which are wound hormones known to inhibit epithelialisation.[14] In rats, Pitillo et al. demonstrated histological changes of aortic endothelium following 6 weeks of smoking.[15] Due to the mentioned pathophysiological and histological effects, the risk on thrombosis is increased in smokers.[16]

Decreased collagen production

Collagen production is an important factor in wound repair and has been found to be decreased in patients who smoke.[17] Konno et al. showed a dose dependent adverse effect of nicotine on cell proliferation and protein production in a fibroblast cell line.[18]

Delayed revascularisation

Adverse effects of nicotine on revascularisation (vascular ingrowth which is essential for osteogenesis) have been described as well. Daftari et al. implanted a cancellous bone graft in the anterior chamber of the eyes of 24 rabbits.[19] Half of the animals received placebo and the other 12 received nicotine subcutaneously for 16 to 30 days. It was concluded that nicotine delayed revascularisation within the graft, that the area of revascularisation was smaller, and that grafts were predisposed to necrosis when compared with the control group.[19] Riebel et al. determined the effect of nicotine on the revascularisation and incorporation of autogenous bone grafts implanted in the distal femur of rabbits.[20] They showed that uniform dosages of nicotine in the rabbit model decreased the vascular ingrowth into graft and that this inhibitory effect of nicotine varied between animals - suggesting predisposition in some.

Demineralisation of bone

Cigarette smoke interferes with bone metabolism. Tobacco (smoke) extracts have been reported to induce calcitonin resistance,[21] to increase bone resorption at fracture ends,[22] and to interfere with osteoblastic function.[23] Silcox et al. studied the effects of nicotine on the healing of spinal fusions in rabbits.[24] They found a trend towards less strength and stiffness in the fusion masses of rabbits in which systemic nicotine was administered and suggested that bone formed in the face of systemic nicotine may have inferior biomechanic properties.[24] Similar findings are reported on tibial fracture healing in rabbits.[25] In the earlier-described study by Riebel et al. on the effect of nicotine on incorporation of cancellous bone graft in rabbits, a trend was evident for delayed bone formation in nicotine-exposed animals.[20] Moreover, trabecular thinning and overall diminished trabecular volume was found in those animals exposed to nicotine, indicating more bony resorption. In addition to these studies, Ueng et al. investigated the effect of cigarette smoking on the mineralisation process during distraction osteogenesis in a rabbit.[26] They concluded that smoking delays the mineralisation bone healing process during distraction and, thus, decreases the mechanical strength of regenerating bone. They suspect that this phenomenon is attributable to an inhibitory effect of cigarette smoke on the revascularisation of the distraction zone.

Clinical effects of smoking on bone

The mentioned pathophysiological mechanisms implicate that smoking must adversely affect bone metabolism and fracture healing. We will discuss the effects of cigarette smoke on osteoporosis, on outcome after orthopaedic procedures, and on fracture healing.

Osteoporosis and related fractures

A lower bone mineral density in smokers was already described 25 years ago.[27] Since then, many epidemiological studies showed a convincing evidence of a higher incidence of osteoporotic fractures in smokers. Most recently, Cornuz et al. published the results of a study among 116,226 female nurses, who were followed for 12 years.[28] They found an age-adjusted relative risk of hip fracture of current smokers versus women who never smoked of 1.3. This risk increased with greater cigarette consumption. The benefit of cessation was not observed until after 10 years.[28] In men, similar effects of smoking on bone density and fracture risk have been described.[29,30] In total, one out of eight hip fractures in women is attributable to smoking.[31]

Orthopaedic procedures

In addition to the publications about the detrimental effects of smoking on osteoporosis-related fractures, more recently associations between cigarette smoke and problems following various orthopaedic operations have been reported.[32-35]

Spinal fusion. Most clinical studies in literature confirming the adverse effects of smoking on bone healing focus on spinal fusion. Jenkins et al. retrospectively studied 234 patients who underwent 260 spinal fusions for degenerative disease and found a relative risk for poor outcome (failure of fusion and/or no symptomatic relief) associated with smoking of 2.9.[33] Brown et al. compared the relationship of smoking with the pseudarthrosis rate in 50 smokers and 50 non-smokers, who all had had a two-level laminectomy and posterior fusion. One to 2 years after surgery, they found a 40% pseudarthrosis rate in patients who smoked, versus 8% in non-smokers.[34] Smoking has also been identified as a possible risk factor for the development of infection after spinal fusion.[35]

Joint replacement. Patients who smoke and undergo joint replacement of the hip and knee are found to need statistically longer operating times, and higher charges adjusted for age, procedure, and surgeon than patients who do not smoke.[32]

Fracture healing

Based on the earlier-mentioned studies, it speaks for itself that smoking affects fracture healing as well. The most convincing experimental study suggesting that systemic hypoxia (and thus smoking) may be associated with poor fracture healing was performed by Heppenstall et al. Using a surgical right to left shunt in dogs, the authors showed that systemic hypoxia delayed fibular fracture healing in dogs and altered the healing bone in terms of radiographic, histologic, and mechanic testing criteria.[36] However, up to now clinical studies on fracture healing in smokers are rare. In this paragraph, we will focus specifically on the tibial fractures, because those are the most common long bone fractures in man. Besides, these fractures are usually caused by a high-energy trauma, with subsequent damage of the delicate surrounding soft tissues as well, making them the most troublesome of all fractures. Three clinical studies on the effects of smoking in tibial fractures have been published.[37-39]

Closed and open tibial fractures with limited soft-tissue injury. Kyro et al. retrospectively studied 135 patients with an isolated closed (86%) or (Gustilo)[40] Grade I/II open tibial shaft fracture undergoing conservative treatment.[38] They found smokers to have a significantly longer time to clinical union than non-smokers (mean, 166 versus 134 days), and a higher incidence of delayed union. They also showed that the time to clinical union of the tibial shaft fracture was longer with increasing number of cigarettes smoked, higher age of the patient, and more severe comminution of the fracture. Schmitz et al. reported the effects of smoking on the clinical and radiographic healing of 74 closed and 27 Grade I open fractures.[39] This study confirmed that the mean time to healing was significantly longer in smokers than in non-smokers (clinical: 269 versus 136 days; radiographic: 244 versus 144 days).

Open tibial fractures with severe soft-tissue injury. Whereas both the studies by

Kyro et al. and by Schmitz et al. excluded fractures with severe tissue-loss because of possible confounding variables, Adams et al. specifically focussed on this type of fracture in their recently published study.[37] In particular, they evaluated retrospectively whether cigarette smoking gives a higher risk of free flap failure, infection and non-union following open tibial fractures. Their study group consisted of 72 Gustilo Grade I injuries, 64 Grade II injuries, 74 Grade IIIA injuries, 57 Grade IIIB injuries and six grade IIIC injuries. There were 140 smokers and 133 non-smokers. Both groups were evenly matched demographically and in terms of primary fracture treatment. They found a significant difference in time to union (mean, 32 weeks for smokers versus 28 weeks for non-smokers). This delay in union was most outspoken in Grade IIIA open fractures. Besides, smokers stayed longer in hospital, had more soft tissue covering failures, and had more wound infections than non-smokers, although these differences were not significant.

Clinical effects of smoking on soft tissues

The negative effects of smoking gained increased interest among plastic and microvascular surgeons, because smokers have been shown to suffer higher rates of flap failure, tissue necrosis, and haematoma formation.[41]

Pedicled flaps / skin grafts

The relation between cigarette smoking and necrosis of skin flaps and full-thickness grafts was analysed in several retrospective clinical studies.[42-45] A review by Goldminz et al. revealed that patients smoking actively at a high level (≥1 pack of cigarettes per day) undergoing skin flap or full-thickness skin graft procedures develop necrosis approximately three times more frequently than never smokers, low-level smokers (<1 pack of cigarettes per day), or former smokers.[42] Former smokers and low-level smokers are at a negligible increased risk for necrosis, however, not significantly different from never smokers. However, a weak point of this study is that no differentiation is made by type and size of flaps or full-thickness skin grafts, which resulted in a comparison of unequal groups.[42]

Similar effects are seen after face-lift surgery and muscle transpositions.[44,45] Rees et al. showed that a smoker after a face lift has more than 12 times the risk of experiencing skin slough than a non-smoker.[44] Lovich et al. reported on the effects of smoke on muscle transposition in 300 patients.[45] They suggested that active smoking around the operation significantly increases the postoperative complications rate, with partial muscle necrosis and skin graft loss being the most common.[45] Other investigators confirmed these findings in a variety of animal models.[46] In an animal study, Van Adrichem et al. showed a lesser survival of at random vascularised flaps when rats were smoked pre-operatively.[47] The survival of axial pattern vascularised flaps was not influenced by smoking. Postoperative wound contraction was more evident in "smoked" axial flaps, which indicates the detrimental effects of cigarette smoking on wound healing even when no necrosis occurs. [3,48,49]

Free flaps

The relation between tabacco smoking and pedicled flap complications does not necessarily apply to free-tissue transfer. In pedicled flaps the main concern is distal flap necrosis, whereas in free-tissue transfer the anastomotic patency becomes the focus. However, the results of studies on the relation of smoking and results of free tissue transfers are inconclusive. Some studies found no histological changes or patency-rate differences between animals exposed to tabacco smoke and controls.[8,50] Other animal studies, however, have reported a higher incidence of microvascular thrombosis and free flap necrosis in smokers than in non-smokers.[47,51] Clinical data regarding the effects of smoking on free tissue transfers are limited. In a retrospective analysis of 75 consecutive patients with a free flap transfer, smoking was not found to be significantly associated with early vascular complications or flap failure.[52] Many other factors often blamed for free flap failure such as age, high body mass, a history of cardiovascular disease, or previous irradiation of the recipient site, were neither found significantly associated with failure in this study. Only preoperative infection of the receptor area and prolonged operation time correlated with flap failure, while the use of a vein graft and long peroperative ischaemia correlated with immediate vascular complications.[52] These findings were confirmed by Reus et al., who assessed the risk for complications after an elective free-tissue transfer in 93 smokers and 51 non-smokers.[53] They concluded that cigarette smokers are at increased risk for complications after free-tissue transfer – however, not at the site of the anastomosis, but rather at the flap's interface with the wound edges or overlying skin graft. This can be explained by lack of autonomous innervation at the site of the anastomosis due to stripping of the adventitia, imitating a local sympatectomy.[54] Chang et al. draw the same conclusions in their publication concerning free transverse rectus abdominus myocutaneous (TRAM) flaps for breast reconstruction.[55] Pollak et al. studied the rate of short-term complications associated with both rotational and free flaps for coverage of traumatic soft-tissue defects of the lower leg.[56] Out of 601 patients, prospectively enrolled in a multicenter study of high-energy trauma of the lower extremity (the so-called LEAP-study), 190 patients (195 limbs) requiring flap coverage had at least six months of follow-up. Smokers were not found to be more likely to suffer from wound complications requiring operative treatment than non-smokers (odds ratio, ≥10 cigarettes a day versus non-smokers or <10 cigarettes a day: 0.95). Complications not requiring operative intervention were not reported in this study.

Replantation

Van Adrichem et al. studied the acute effects of smoking on the microcirculation of the skin of the thumb in healthy volunteers (22 smokers and 10 non-smokers).[54] Blood flow was assessed by means of laser Doppler flowmetry. During smoking of their first and second cigarette, respectively a mean decrease in laser Doppler flow of 24% and 29% was seen. Ten minutes after smoking this fall was recovered by half.[54] The investigators repeated this study in patients who had undergone digital replantation or revascularisation several (range, 6-48) months before.[57] During smoking of a first and second cigarette, a mean decrease in laser Doppler flow of respectively 8% and 19% was found in smokers, whereas in non-smokers no major variations were shown. In contrast to the earlier-described "healthy" digits,[54] in the replanted digits almost no recovery could be detected after 10 minutes.[57] The vasoconstricting effect was demonstrated to be more pronounced when the replantation had taken place more recently. It was not possible to investigate the effect of smoking immediately after surgery, because all patients had been strongly advised to stop smoking after replantation and had done so.[57] Two reports have been published, presenting cases in which cigarette smoking in the early postoperative period following digital replantation led to vasospasm with compromise of the microvascular anastomoses.[51,58] These publications confirm that patients should be strongly advised to refrain from smoking after replantation surgery to guarantee optimal circulation.

Cessation of smoking

Although some authors suggest that the microvascular system of habitual smokers becomes inured to smoke[59] and some changes (e.g., macroangiopathy) are hardly reversible[47], it is clear that cessation of smoking has beneficial effects on both short- and long-term.

Several physiological effects of cessation have been described. Kambaum and Chen studied the effects of smoking on the carboxyhaemoglobin levels in volunteers.[46,60] They found that carbon monoxide is cleared rapidly from the blood already 12 hours after smoking.[46,60] Haemorheological changes that take place in the days immediately following tobacco withdrawal from smokers are studied as well.[12] Due to a fall in packet cell volume (PCV) and reductions in total plasma protein and fibrinogen concentrations, substantial and persistent reductions in blood viscosity occur within 2 days.

In an animal study, it was shown that the adverse effects of nicotine on revascularisation were reversible within 2 weeks of nicotine elimination.[20] In clinical studies, it has been reported that preoperative cessation of smoking decreases flap necrosis in random and pedicled skin flaps.[42,61] A longer preoperative cessation of smoking was correlated with a progressively higher flap survival.[61] In a study on the effect of smoking on complications in patients undergoing free TRAM flap breast reconstruction, former smokers (who stopped at least 4 weeks preoperatively) had a similar rate of complications as non-smokers.[55]

Hard-core smokers presenting with open tibial fractures

Despite all reported benefits of cessation, some smoking patients are very hard to convince. Among them are so called "hard-core" smokers: highly addicted (≥15 cigarettes/day) and no intention to quit smoking at any time.[62] They are less likely than others to agree that smoking is harming their own health and that tobacco is a highly addictive drug. About 5% of all smokers can be classified in this group. In general, they are male and have a below-average education level, a lower income, and a weak social support.[62]

The characterisation of patients with lower extremity trauma shows similarities to that of hard-core smokers. MacKenzie et al. charted the characteristics of 601 patients admitted with high-energy lower extremity trauma.[63] Most patients were male, and had an age between 20-45 years. Compared with the general population, they had less years of education, had lower income, and were slightly more neurotic and less open to new experiences. Furthermore, the percentage of heavy drinkers was more than two times higher than reported nationally in the US.[63] In their study on the effects of smoking on the healing of open tibial fractures, Adams et al. noticed that significantly more patients in the smoking group (30%) had consumed alcohol prior to admission compared with the non-smoking group (13.5%).[37] The usual alcohol consumption of the two groups differed significantly as well (mean, 18.5 units per week for smokers versus 11.9 units for non-smokers).[37]

We may conclude that many patients presenting with open tibial fractures are hard-core smokers, although no specific data have been published on this specific subgroup. They will be reluctant to stop smoking during the course of treatment, despite known risks and warnings. In addition to the direct adverse effects of smoking on soft-tissue and bone healing, low treatment compliance may be another problem in this group.

Conclusions

Clinicians should be aware of the effects of smoking when caring for or advising patients who suffer fractures and/or wounds as the result of trauma or who are about to schedule complex and time-consuming procedures. The explicit negative effects of smoking on soft-tissue healing and bone union are multidimensional, including arteriolar vasoconstriction, cellular hypoxia, demineralisation of bone, and delayed revascularisation.

Open tibial fractures are inextricably bound up with soft-tissue injury. For this reason, especially smokers presenting with an open tibial fracture will suffer the negative effects of their smoking behaviour. Their fractures will need a significantly longer time to heal than in non-smokers, and will have a higher incidence of non-union. If microvascular surgery is to be performed, persistent smoking significantly increases the rate of postoperative complications, with wound infection, partial flap necrosis, and skin graft loss being more common. Cessation of smoking has both short- and long-term beneficial effects.

Nowadays, there is strong evidence to be very insistent that patients presenting with an (open) tibial fracture should refrain from smoking immediately to promote bone healing and to lower the complication rate. In case of elective reconstructive procedures, patients should refrain from smoking at least 4 weeks before surgery. In both situations, cessation should continue during the full rehabilitation period.

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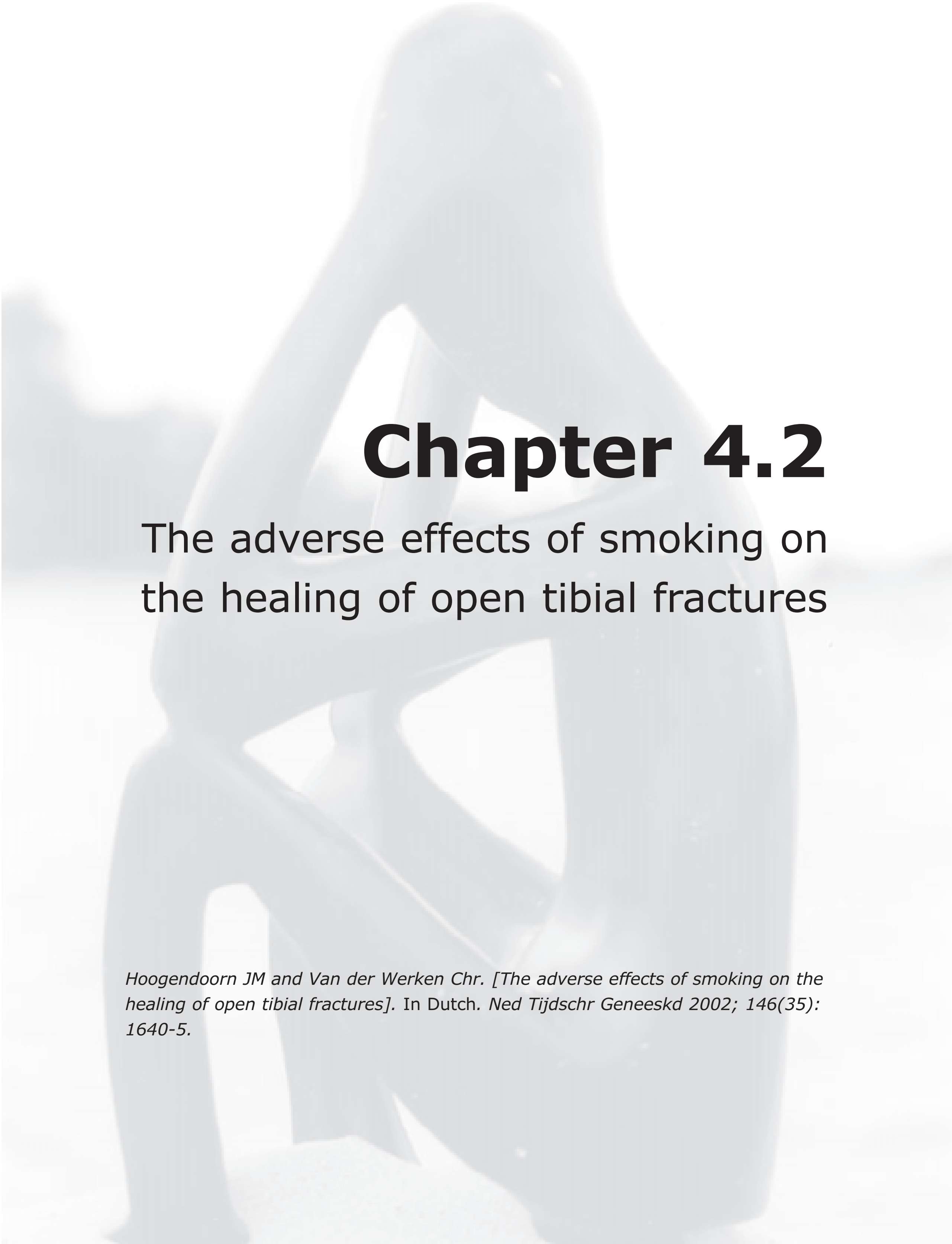

Chapter 4.2

The adverse effects of smoking on the healing of open tibial fractures

Hoogendoorn JM and Van der Werken Chr. [The adverse effects of smoking on the healing of open tibial fractures]. In Dutch. *Ned Tijdschr Geneeskd 2002; 146(35): 1640-5.*

Abstract

Objective
Survey of the influence of smoking on the healing of open tibial fractures.

Design
Retrospective study.

Patients and methods
During the period January 1994 to December 2000, 168 patients were treated at the Department of Surgery (University Medical Centre Utrecht) because of an open tibial fracture. Hundred-eighteen patients with 125 fractures were included in the study. On the basis of their smoking behaviour patients were divided into group I (non-smokers) or group II (smokers). Of all patients complications during treatment were retrieved. On the basis of clinical and radiological criteria it was determined when a fracture was united.

Results
Seventy-two (61%) patients were non-smoker, 46 smoker. The non-smokers had 77 open tibial fractures, the smokers 48. Initial therapy was identical and wound infections occured with similar incidences in both groups. However, there was a significant difference in incidence of osteitis between both groups: 7 (9%) times in group I and 13 (27%) times in group II (p=0.04). The mean time to union was 26 weeks for non-smokers and 33 weeks for smokers (p=0.04). Smokers stayed longer in hospital and underwent more re-operations.

Conclusions
Smoking is negatively associated with the healing of open tibial fractures. Time to union was significantly longer in smoking patients and they suffered more from osteitis. On the basis of the results of our study and data in the literature, we strongly advise smoking patients who present with an open tibial fracture, to stop smoking.

Introduction

Despite broad attention for the adverse effects of smoking, one of three Dutchmen are unable to resist the temptation.[1] Of several disorders, especially of cardiovascular and pulmonary origin, a link with the patient's smoking habit is known for decades.[2,3] In addition, there is ample evidence that osteoporosis and related fractures occur more frequently in smokers.[4-7] In recent years, there has been a growing interest in the possible adverse effects of smoking on soft-tissue and bone healing.[8-13] Moreover, there are strong indications that smoking is associated with a higher risk on postoperative complications, such as wound infections, muscle necrosis, and rejection of tissue transfers.[13-15]

In view of the above-mentioned, it is likely that smoking gives problems in consolidation of fractures as well. However, up to now this is hardly confirmed by clinical studies. In medical practice, these effects can be studied best in patients with an open tibial fracture. On the one hand because those are the most common long bone fractures in man, on the other because in open fractures in general the risk on complications (pseudarthrosis and infection) is substantial. In our hospital, treatment of such injuries is to a large extent protocolised, so study groups are well comparable.

In this chapter, we describe the results of a retrospective study on the effects of smoking on the outcome of treatment in 118 patients with 125 open tibial fractures.

Patients and methods

In the period January 1994 to December 2000, in total 168 patients were treated due to an open tibial fracture at the Department of Surgery (University Medical Centre Utrecht). All fractures were classified according to the Gustilo classification.[16,17] Patients with a Grade I, II, IIIA or IIIB open tibial fracture were eligible for participation in our study. Thirty-four patients with a Grade IIIC fracture - in whom the open fracture was associated with severe soft-tissue damage and relevant arterial injury - were excluded because in this category it would be less clear if eventual complications are caused by severe traumatic injuries or the patient's smoking habit. Furthermore, the data of thirteen patients were not analysed because they had deceased during treatment. Ten died during the initial hospital stay (due to associated injuries), three others in a later stage due to other disorders. Of three patients, the follow-up data were missing. The mean age of the remaining 118 patients was 36 years (range, 15-83) at the time of the accident. Eighty-three were men (70%). Seven patients had bilateral open tibial fractures, making the total number of studied fractures 125.

The patients were divided in two study groups, smokers and non-smokers. Patients were considered to be a smoker if they smoked at least 5 cigarettes per week during treatment (the period from accident to discharge of treatment). Of all patients, the medical charts were reviewed to retrieve their smoking behaviour. If a smoker, the number of cigarettes smoked per day was noted. Moreover, the patients were contacted by telephone to retrieve their smoking behaviour at the time of accident and during treatment. If there was any discrepancy in number of cigarettes smoked, the average number was calculated as basic value for our study. Patients who had smoked in the past (but had stopped smoking before the accident), patients who smoked less than 5 cigarettes per week, and passive smokers were considered as non-smokers.

On the basis of the initial X-rays, the fractures were classified according to the AO Classification. In this generally accepted system, fractures are characterised by localisation and fracture type (type A: simple, type B: wedge, and type C: comminuted).[18] The localisation was that part of the tibia in which the largest part of the fracture was situated (proximal, shaft, distal).

Of all patients, any complications during treatment were retrieved. We paid special attention to wound healing disturbances, (external fixation)-pin tract infections and the presence of deep infections and osteitis. On the basis of clinical and radiological criteria it was determined when a fracture was united. A fracture was considered united clinically if a patient could fully weight bear without pain. The radiological evidence consisted of bridging on minimal three of the four cortices on standard AP and lateral views. Of all fractures in which surgical (re-)intervention was necessary, the course was considered complicated. An exception was made for fractures with traumatic bone and soft-tissue defects, which had to be re-operated (cancellous bone grafts, bone segment transport, skin- or muscle transfers) on within three months after the accident.

We used the chi-square test to compare the characterisation of both study groups. An univariate analysis was performed to compare the two study groups with regard to consolidation time, number of hospital stays, total number of days spent in hospital, and number of operations. We compared the number of complications by logistic regression analysis. All calculations were executed with SPSS for Windows 8.0. A P-value equal or less than 0.05 was considered significant.

Results

Study groups

Seventy-two (61%) patients were non-smoker (group I), the other 46 were smoker (group II). All patients in group II smoked cigarettes or (hand-rolling) tobacco; the mean number of cigarettes smoked per day was 15 (range, 2-30). Non of the patients smoked pipe or cigars. In the smoking group, age was on average lower than in the non-smoking group (significant) and the percentage men was higher (not significant)(table 1). The 72 non-smokers had 77 open tibial fractures, the 46 smokers 48. According to the Gustilo classification, 57 fractures could be considered as

Grade I, 33 as Grade II, 12 as Grade IIIA, and 23 as Grade IIIB. According to the AO classification, 46 fractures were type A, 40 type B, and 39 type C. Smokers had on average more serious fractures: the number of Grade I open fractures was proportionately lower than in the non-smoking group, the number of Grade IIIB open fractures higher (table 1). However, these differences were not significant.

Table 1. *Characteristics of both study groups.*

Variable	Group I (non-smokers)	Group II (smokers)
Number of patients (n)	72	46
Mean age (years)	39.0 (±18.4)*	31.4 (±13.5)*
Men	48 (67%)	35 (76%)
Injury Severity Score (ISS)	19.6 (±12.4)	19.4 (± 12.8)
Number of fractures (n)	77	48
Gustilo		
I	39 (51%)	18 (38%)
II	19 (25%)	14 (29%)
IIIA	7 (9%)	5 (10%)
IIIB	12 (16%)	11 (23%)
AO		
A	26 (34%)	20 (42%)
B	26 (34%)	14 (29%)
C	25 (32%)	14 (29%)

Initial therapy

In group I, the fracture was stabilised 53 times by using internal osteosynthesis (intramedullary nail 42, plate 8, screws 2 and K-wire 1), 22 times by using external fixation and twice by using plaster. Seven times a combination of internal and external fixation was used. The fractures in group II were treated similarly: 38 times internal osteosynthesis (intramedullary nail 27, plate 9, screws 2), 10 times external fixation and once plaster. In the acute phase, 10 fasciotomies were performed. To cover the fracture area, in group I nine split skin graftings, four transpositions of the gastrocnemius muscle, and one free muscle transfer (rectus abdominus muscle) were performed, against respectively seven split skin graftings and six muscle transpositions or transfers (rectus abdominus muscle 1, latissimus dorsi muscle 1, and soleus muscle 4) in group II.

Infection

Healing disturbances of the traumatic wound occurred proportionately in both groups: 17 (22%) times in group I and 10 (20%) times in group II. Pin tract infections of the external fixator occurred eight (25%) times in group I and six (29%) times in group II. Deep infections occurred in similar frequencies in both groups (group I nine (12%) times, group II six (12%) times). In contrast to the wound infections, there was a significant (p=0,04, after correction for differences in fracture Grade, age, and sex) difference in presence of osteitis between both groups. In group I, seven (9%) times osteitis occurred (twice in combination with pseudarthrosis), against 13

(27%) times in group II (in eight cases in combination with pseudarthrosis). Nineteen (25%) fractures in group I and 16 (33%) in group II were re-operated on due to superficial or deep infection. In group I, 11 (14%) times debridement was performed, 12 (16%) times 'infected' implants were removed, four (5%) times a sequestrectomy was performed, and three (4%) times Gentamycin-beads were left in place. In group II, the number of procedures was slightly higher: eight (16%) times debridement, 10 (20%) times removal of 'infected' implants, eight (16%) times sequestrectomy, and six (12%) times inserting of Gentamycin-beads.

Consolidation

At the time of the study, in group I 74 of 77 (96%) fractures were healed, in group II 45 of 48 (94%). The mean time to consolidation was 26 weeks for non-smokers and 33 weeks for smokers (table 2). This difference was significant – even after correction for differences between both groups in fracture Grade, age, and sex. Split up by Gustilo and AO classifications, these differences were found to the prejudice of smokers in almost every subgroup.

Table 2. *Mean time to consolidation for non-smokers and smokers (weeks): total study groups and divided by Gustilo and AO Classifications.*

	Group I (non-smokers)	**Group II (smokers)**
Number of healed fractures	74	45
Total	26.3 *	33.4 *
Gustilo		
I	24.5 (±14.1)	30.8 (±11.1)
II	24.5 (±11.4)	31.9 (±19.1)
IIIA	23.4 (± 9.2)	43.4 (±20.8)
IIIB	37.4 (±21.5)	35.1 (±15.0)
AO		
A	23.6 (±15.9)	27.7 (±12.3)
B	28.0 (±16.8)	35.1 (±15.3)
C	27.2 (±12.2)	36.1 (±17.6)

* significant difference (after correction for differences between both groups in fracture Grade, age, and sex

Twenty-seven (35%) fractures in group I and 24 (49%) fractures in group II were re-operated on due to delayed union. In group I, in 17 (22%) cases cancellous bone graftings were performed to promote bone union, against in 12 (24%) cases in group II. Of all fractures initially stabilised with intramedullary nailing, the screws were removed four times and the nail was exchanged eight times in group I, against respectively eight and two times in group II. A fibula osteotomy was performed six times in both groups. All differences were not significant.

Amputations

In group I, three times a below-knee amputation was performed, one in a high-aged (83 years) polytrauma patient with a persisting infection after intramedullary nailing and two in patients with life-threatening associated injuries ('life before limb'). In group II, amputation was performed three times as well, all in association with infected pseudarthrosis with insufficient reconstruction possibilities.

Hospital stays

Non-smokers stayed on average 33 days in hospital during 2.0 admissions, versus respectively 36 days and 2.7 admissions for smokers. The number of operative procedures differed between both study groups as well (2.5 for non-smokers and 3.4 for smokers). All differences were significant, after correction for differences in fracture Grade, age, and sex.

Discussion

The results of our study confirm that smoking is negatively associated with the healing of open tibial fractures. In smoking patients, consolidation time was significantly longer and they suffered more from osteitis, had more hospital admissions and underwent more operations.

Clinical studies on the influence of smoking on open tibial fracture healing are rare. Kyro et al. published the results of a retrospective study in 135 patients with an isolated closed (86%) or Grade I/II open tibial shaft fracture undergoing conservative treatment.[19] They found smokers to have a significantly longer time to clinical union than non-smokers (mean, 166 versus 134 days). They also showed that the time to union was longer with increasing number of cigarettes smoked, higher age of the patients, and more severe comminution of the fracture.[19] Similar conclusions were drawn from a study by Schmitz et al. on the consolidation time of 74 closed and 27 Grade I open tibial fractures (on average 269 versus 136 days for, respectively, smokers and non-smokers).[20] In the above-mentioned studies most of the fractures were closed, in which pseudarthrosis and infectious complications are rare. For this reason, Adams et al. recently published the results of a study on the effects op smoking on the healing of open tibial fractures.[21] In 140 smoking and 133 non-smoking patients presenting with an open tibial fracture, they studied the rate of pseudarthrosis, the risk on infection and on the rejection of free skin and bone transfers. The study group consisted of 72 Grade I, 64 Grade II, 74 Grade IIIA, 57 Grade IIIB, and 6 Grade IIIC open tibial fractures. These authors again found a significant difference in time to union (mean, 32 weeks for smokers versus 28 weeks for non-smokers), most outspoken in Grade IIIA open fractures. Besides, smokers stayed longer in hospital, had more soft-tissue covering failures, and had more wound infections than non-smokers, although these differences were not significant. However, a disadvantage of this study is the fact that 229 of the original 502 patients had to be excluded, because the smoking behaviour of a large amount of patients could not be retrieved in the medical charts and patients smoking now and then were not included.

In our study, superficial wound healing disturbances occurred with similar frequencies in both smoking and non-smoking groups. This corresponds to the results of a study by Pollak et al. on the presence of wound complications associated with both rotational and free muscle flaps for coverage of traumatic soft-tissue defects of the lower leg.[22] Therefore, they studied 190 patients undergoing 88 rotational and 107 free muscle flaps. Smokers (≥ 10 cigarettes a day) did not have more wound complications requiring operative treatment than non-smokers. However, several other authors concluded that smokers undergoing elective skin grafting and/or muscle transpositions had more postoperative complications than non-smokers.[12,14,23] The discrepancy in these conclusions might be explained by the difference between elective and acute procedures. In the latter, the risk on superficial wound infections is highly determined by other factors, such as contamination, the severity of soft-tissue injuries, and the quality of operative fracture treatment.

In our study, osteitis occurred significantly more often in smokers. In the earlier mentioned study by Schmitz et al. the authors were unable to pronounce upon this difference because of the low incidence of osteitis in the (mainly closed) studied fractures and in the study by Adams et al. the difference was not outspoken.[20,21]

Many smokers are hardly motivating to stop smoking during the treatment of their injuries. However, several studies - mainly performed by plastic surgeons - have demonstrated the positive effects of cessation. Clinically it is proven that cessation of smoking preceding elective procedures diminishes the risk of necrosis of skin graftings.[23] In a study on the effects of smoking in patients undergoing mamma reconstruction, the complication risk in patients who stopped at least four weeks before the operation was similar to non-smokers and significantly lower than in smokers.[24] Recently, the results of a randomised clinical trial on the effect of preoperative smoking intervention on the frequency of complications in patients undergoing hip and knee replacement were published.[15] Hundred-twenty patients were randomly assigned 6-8 weeks before scheduled surgery to either the control (n=60) or smoking intervention group. Smoking intervention was counselling and nicotine replacement therapy, and either smoking cessation or at least 50% smoking reduction. The overall complication rate was 18% in the smoking intervention group and 52% in the controls (p=0.0003). The most significant effects of intervention were seen for wound-related complications (5% versus 31%), cardiovascular complications (0% versus 10%), and secundary surgery (4% versus 15%).[15] It is likely that such advantages can be found in smoking patients treated for an open tibial fracture, who stopped smoking after the accident and persisted during the full rehabilitation course, too. However, this has not been proven by means of a study yet.

Conclusions

The results of our study confirm that smoking is negatively associated with fracture healing. Especially smokers presenting with open tibial fractures will encounter the negative effects of their smoking behaviour. Time to union was significantly longer in smoking patients and they suffered more from osteitis, resulting in a significantly higher number of hospital admissions and secondary procedures. On the basis of the results of our study and data in the literature, we strongly advise smoking patients presenting with an open tibial fracture, to stop smoking immediately and continue this during the full rehabilitation course.

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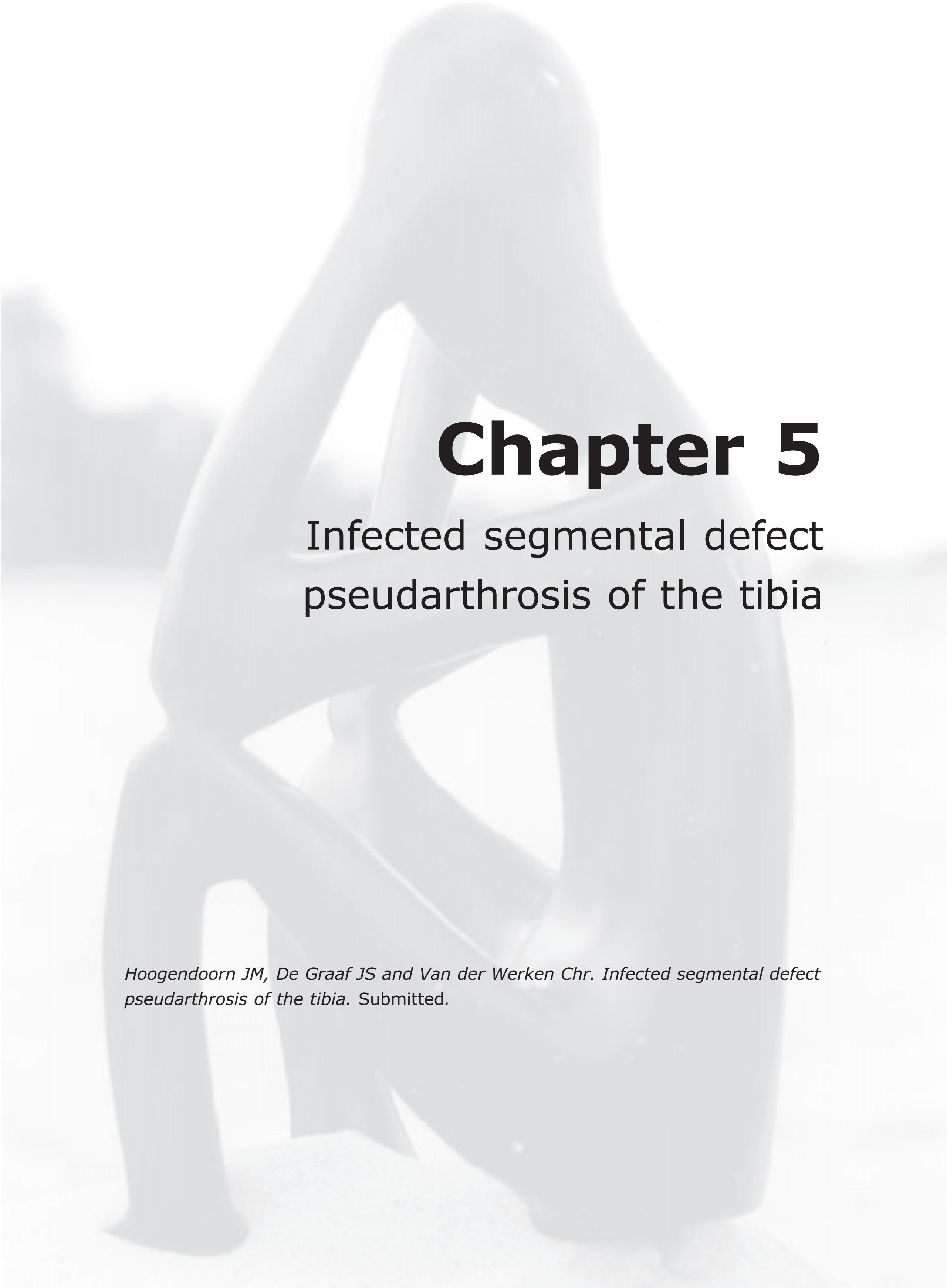


Chapter 5

Infected segmental defect pseudarthrosis of the tibia

Hoogendoorn JM, De Graaf JS and Van der Werken Chr. Infected segmental defect pseudarthrosis of the tibia. Submitted.

Abstract

Objective
The purpose of this study was to evaluate a consequent and protocolised approach of infected segmental defect pseudarthrosis of the tibia.

Patients and methods
In the period 1993-2000, we treated 18 patients for a infected tibial pseudarthrosis with an additional segmental bone loss. Based on the size of the segmental defect, and other factors such as condition of the soft tissues and the patient's age, the method of bone reconstruction was chosen.

Results
In five patients, of whom two were highly aged and one had an irreversible equinus foot, primary shortening was opted. Nine patients underwent one or more cancellous bone grafting procedures to bridge the skeletal defect, three patients (with a bone defect of 11-18 cm) underwent bone segment transport according to Ilizarov, and in the last patient (with an 18-cm tibial defect) our plastic surgeons performed a free vascularised transplantation of the contralateral fibula. The number of complications, operative procedures and hospital admissions differed between the four patients groups with different bone defect reconstructions, however not significant.

In 12 patients limb salvage was successful. Only two of five (40%) patients in the 'primary shortening'-group had successful salvage, against six of nine (67%) in the 'bone grafting'-group, three of three in the 'Ilizarov'-group, and one of one in the 'fibula transfer'-group. Most patients with successful salvage had no or little limitations in daily life and were back to work. The mean lower extremity impairment score (according to the American Medical Association) was 13% (range, 0-43%). Six patients underwent amputation, due to various reasons.

Conclusions
The problem of infected tibial pseudarthrosis with segmental bone loss remains significant - despite advances in diagnostics and management. If limb salvage is successful, the ultimate functional outcome will be good in the majority of cases. In selected cases amputation is still indicated.

Introduction

Managing a patient with an infected segmental defect pseudarthrosis of the tibia is a challenging problem for (orthopaedic) surgeons. In fact, it is a quadruple problem. Due to the delicate surrounding soft tissues of the lower leg, tibial fractures itself are very troublesome - with a high risk on complications. Pseudarthrosis is one of these complications and if infected it forms a great clinical problem. However, infected pseudarthrosis with an additional segmental bone defect (i.e. a complete interruption of the continuity and without contact between the bone ends) is a real challenge. The involved patients need multiple and long hospitalisations and must undergo several operative procedures to eradicate the infection and to achieve healing. Despite recent advances in diagnostics, modern antibiotics, and improved surgical techniques including bone and soft-tissue reconstructions, some patients are still better of with amputation. In this article, we describe our experiences with a consequent and protocolised therapeutic approach of this difficult problem in 18 cases.

Patients

Characteristics

In the period 1993-2000, we treated 18 patients for an infected tibial pseudarthrosis with an additional segmental bone loss. Seven patients had been treated at our department since the time of accident, the others were referred from other hospitals. The mean time between accident and referral was 30 weeks (range, 1-82 weeks). There were 15 males and three females, with ages ranging from 18 to 78 years (average, 46 years). The mechanism of injury had been a traffic accident in 13 cases, an accident at work in three and a fall from height in two. The fracture was originally located in the proximal third of the tibia in one, the middle third in nine, and distally in eight cases. Two fractures had been closed, the other (open) fractures were characterised according to the Gustilo classification[1,2] as Grade I in four, Grade II in three, Grade IIIA in two, Grade IIIB in three, and Grade IIIC in four patients (table 1).

Preceding fracture treatment

The initial treatment had been operatively in all patients (table 1): seven fractures had been treated with internal fixation (intramedullary nail 4, plate 3), seven with external fixation, and four with a combination of both methods (plate and external fixation). Three patients had early soft-tissue reconstruction with a free vascularised muscle flap (rectus abdominus m. 2, latissimus dorsi m. 1) and two others had undergone a pedicled muscle flap (gastrocnemius m.). In eight patients, nine split skin graftings had been performed. Nine patients presented with a segmental defect smaller than 4 cm, five with a defect of 4-10 cm in size, and in four the defect was over 10 cm (table 1). All together, the 18 patients had 103 cm of segmental tibial bone loss (average 6 (1-18) cm) and more or less infected soft-tissue defects.

Table 1. *Patient and fracture characteristics, preceding fracture treatment, and facts about the infected segmental tibial defect pseudarthrosis.*

Patient and fracture characteristics			**Preceding fracture treatment**				**Infected segmental defect pseudarthrosis**	
Patient number	*Age,Sex*	*Gustilo Grade*	*Initial treatment*	*Early soft-tissue reconstruction*	*Ops. (nr)*	*Interval (months)*	*Segmental bone defect (cm)*	*Soft-tissues*
Primary shortening								
1	73,M	I	Plate		1	9	2	Active draining fistula
2	57,M	0	FxX		5	7	2	Sufficient soft-tissue cover
3	52,M	I	Plate	Gastrocnemius m., SSG	6	3	3	Defect (4x4 cm), peroneal n. lesion
4	78,M	II	Nail	Adipofascial transpos. flap, SSG	2	2	4	Soft-tissue defect (5x10 cm)
5	47,M	IIIA	Plate		4	14	2	Active draining fistula
Bone grafting								
6	22,M	IIIC	FxX	SSG	4	3	1	Defect (5x10 cm), comp. syndrome
7	58,F	I	Nail		5	14	2	Sufficient soft-tissue cover
8	55,M	II	Nail		1	10	2	Exposed tibia and plate
9	53,M	IIIA	FxX	Gastrocnemius m.	4	12	3	Atrophia and equinus foot
10	42,M	I	FxX + plate	SSG (2x)	5	12	3	Multiple abscesses
11	33,M	II	Nail		4	2	4	Marginal vitality surrounding muscles
12	18,F	IIIC	FxX		4	2	4	Circumferential defect, peroneal n. lesion
13	46,M	IIIB	FxX	Rectus abdominus m., SSG	1	0	6	Defect (8x15 cm) distal third leg
14	34,M	IIIA	FxX		3	19	6	Sufficient soft-tissue cover
Ilizarov								
15	54,M	IIIC	FxX	Latissimus dorsi m., SSG	3	2	11	Soft-tissue defect, exposed tibia
16	50,M	0	FxX + plate		2	1	12	Soft-tissue defect
17	40,M	IIIB	FxX + plate	Rectus abdominus m., SSG	3	1	18	Active draining fistula, abscesses
Fibula								
18	21,F	IIIB	Plate	SSG	6	0	18	Soft-tissue defect, exposed tibia

FxX = external fixation; SSG = split skin grafting; ops. = operations; comp. syndrome = compartment syndrome

Methods

Management of this complex problem needs a step-by-step approach with the following goals.

1. Healing of infection. Treatment starts with removal of all implants that do not provide stability and debridement of all necrotic and poorly vascularised bone and soft tissues. Gentamycin beads can be locally applied for infection treatment and as spacer. Systemic antibiotics are not included in our therapeutic regimen.

2. Skeletal stabilisation. This is needed to restore length and axis, to correct any rotation, and to provide stability for the healing of infection and to create an optimal situation for soft-tissue and bone reconstruction. Stabilisation can be done with internal or external fixation techniques. In general, external fixation is more appropriate than internal fixation, because of the higher risk of persistent infection with implantation of a large foreign body.

3. Adequate soft-tissue coverage. Sufficient surrounding soft tissues are essential for the healing of an infected pseudarthrosis, because it augments vascularisation at the defect site and helps overcome infection. Loco-regional or free muscle transfer must be performed when indicated.

4. Skeletal reconstruction. Several options exist for reconstructing bone defects after thorough debridement. In general, repeated cancellous bone grafting is suitable for segmental defects up to 6 cm, bone segment transport (the Ilizarov procedure) for defects larger than 4 cm, and free vascularised fibula transplantation for exceptional cases with extreme defects. In some patients, especially in case of an ‘irriversible’ equinus foot or stiff ankle, shortening of 1-2cm is accepted.

A retrospective analysis of the medical records and X-rays of all 18 patients was performed to gather data on number and type of operations and complications, number of days spent in hospital, time to bone union, and clinical outcome. Bone healing was assessed on the basis of clinical and radiographical criteria. A pseudarthrosis was considered to be healed when the patient could fully weight bear and walk without pain in the former defect area and when there was radiological evidence of bridging of three of the four cortices on standard antero-posterior and lateral views. Recently, all patients have been clinically examined, with emphasis on gait, range of motion of the knee and ankle, the sensibility of the leg and foot (sole) and evidence of persistent infection. Based on these findings, we calculated the lower extremity impairment by using the ‘Guides to the Evaluation of Permanent Impairment’ of the American Medical Association.[3] These ‘Guides’, one of the most widely used systems for rating impairments, expresses the degree of loss of function in a percentage of permanent impairment.[4-6]

Table 2. *Treatment for the infected segmental defect pseudarthrosis.*

Patient number	Skeletal stabilisation	Soft-tissue reconstruction	Bone graftings (nr)	Surgery for complications	Complications treated non-surgically	Ops. (nr)
Primary shortening						
1	Nail	-	-	-	-	3
2	FxX	-	-	-	Wound infection	1
3	FxX	Lat. dorsi. m.	-	Revision FxX	-	5
4	FxX	-	-	-	Partial flap necrosis	2
5	FxX	Gracilis m.	1	Absc. drainage (2x)	Wound infection	6
Bone grafting						
6	FxX	Gastrocnemius m.	2	Sequestr. (3x), corrective osteotomy	-	6
7	FxX + plate	Rectus abd. m., gracilis m.	4	-	-	2
8	FxX	Rectus abd. m., SSG	1	Revision FxX (3x), absc. drainage	Flap necrosis	9
9	FxX	-	1	Revision FxX	Pin track infection	4
10	FxX	-	2	Sequestr. (2x), absc. drainage	-	2
11	FxX	SSG	1	Absc. drainage, revision FxX (2x), sequestr.	-	5
12	FxX + plate	SSG	2	Revision FxX (3x), absc. drainage	-	8
13	FxX	-	2	Revision FxX	Osteitis	3
14	Plate	-	1		-	1
Ilizarov						
15	FxX + plate	-	2	FxX due to re-fracture and plate infection	Partial flap necrosis	4
16	FxX + plate	Gracilis m., rectus abd. m., SSG (2x)	1	Muscle transfer, revision FxX (5x), sequestr.(2x)	-	12
17	FxX	-	1	Absc. drainage, revision Ilizarov, fistulectomy	-	3
Fibula						
18	FxX + screws	Lat. dorsi m., SSG (2x)	1	Evacuation hematoma, SSG for skin necrosis	-	4

FxX = external fixation; ops. = operations; sequestr. = sequestrectomy; absc. drainage = abscess drainage

Results

Treatment

As first step, all patients underwent an extensive debridement of bone and soft tissues. Implants were removed in nine patients, and external fixation was revised in eight. Renewed fixation modalities included external fixation (11 patients), internal fixation (IM nail 1, plate 1) and a combination of both methods (external and plate 4, external and screws 1). Gentamycin-beads were used in nine patients. Seven patients underwent nine muscle transfers for treatment of the infected pseudarthrosis. Eight free muscle transfers (rectus abdominus m. 3, gracilis m. 3, latissimus dorsi m. 2), and one local pedicled flap (gastrocnemius m.) were performed by our plastic surgeons to obtain sufficient soft-tissue coverage (table 2). In five patients, seven split skin graftings were done.

Based on the size of the segmental defect, and other factors such as condition of the soft tissues and the patient's age, the method of bone defect reconstruction was chosen. In five patients, of whom two were highly aged and one had an irreversible equinus foot, primary shorting was opted (table 2, patients 1-5). Nine patients, with a segmental bone defect of 1-6cm in size, underwent one or more cancellous bone grafting procedures to bridge the skeletal defect (patients 6-14). Three patients underwent bone segment transport according to Ilizarov with additional bone graftings - they had a segmental bone defect of 11-18cm (patients 15-17). In the last patient, with an 18-cm tibial defect, our plastic surgeons performed a free vascularised transplantation of the contralateral fibula (patient 18).

Almost every patient sustained one or more complications during pseudarthrosis treatment (table 2). Revision of external fixation (16 times in seven patients), additional sequesterectomies (eight in four patients), and abscess drainage (seven times in six patients) were the most common operations for complications. One patient in the 'Ilizarov-group' sustained a re-fracture during treatment, which was stabilised with external fixation (patient 15). In another patient in the 'Ilizarov-group', the transfered gracilis muscle became necrotic, and a (second) free muscle transfer had to be performed (patient 16). The patients underwent on average four operative procedures and they spent on average 44 days in hospital (range, 6-138) during four admissions (range, 1-9) for infected pseudarthrosis treatment (range, 1-12). The numbers of operative procedures and hospital admissions differed between the four patient groups with different bone defect reconstructions, however not significant (table 3).

Outcome

Successful limb salvage. In 12 patients limb salvage was successful and six patients underwent amputation (tables 4 and 5). In the limb salvage group, the mean time to healing was 17 months (range, 4-30) since our start of pseudarthrosis treatment. Personal examination of patients with a salvaged limb revealed good clinical results

Table 3. *Hospital admissions, number of operative procedures for treating infected pseudarthrosis and percentage of successful salvage in the four patient groups with different methods of bone defect reconstruction.*

Group	Admissions (number)	Admissions (days)	Operations (number)	Successful salvage
Primary shortening	3.0 (2-5)	46 (11-76)	3.4 (1-6)	2 (40%)
Bone grafting	4.0 (1-7)	49 (6-138)	4.4 (1-9)	6 (67%)
Ilizarov	5.0 (2-9)	30 (11-54)	6.3 (3-12)	3 (100%)
Fibula transfer	4.0	37	4.0	1 (100%)
Total	*3.9 (1-9)*	*44 (6-138)*	*4.4 (1-12)*	*12 (67%)*

in all. One patient in the ‘primary shortening’-group indeed had a limb length discrepancy of 2 cm, but was fully ambulant with an orthopaedic shoe (table 4, patient 2). Another patient, in the ‘primary shortening’-group as well, was referred with an equinus foot and a shortening of 4 cm (patient 5). He deliberately ended up with a limb length discrepancy of 5 cm, and was fully ambulant with an orthopaedic shoe. One patient, in the ‘bone grafting’-group, refused additional bone grafting procedures and ended up with a limb length discrepancy of 2 cm (patient 14). Malunion at the defect site occurred in three patients (patients 5, 6 and 17) and ankle motion was limited in ten (patients 2, 5, 6, 7, 10, 11, 13, 15, 16 and 18). Of these latter, six had an orthopaedic shoe. Movements of the knee joints were not restricted in any of the patients. In all patients, skin and soft tissues had been healed and there were no signs of infection. Most patients had no or little limitations in daily life and were back to work. The mean lower extremity impairment score was 13% (range, 0-43%).

Amputation. Six of 18 (33%) patients required amputation due to various reasons. Two patients suffered too much pain, being the main reason for amputation (table 5, patients 3 and 9). In two other patients, being respectively 78 and 73 years old, continuing complications and pain combined with age-related factors (such as co-morbidity and inactivity) led to the decision for below-knee amputation. One of them presented with sepsis due to osteitis and underwent amputation as a life-saving procedure (patient 1). Another patient initially presented with a Grade IIIC open tibial fracture, which was treated by vascular reconstruction and external fixation (patient 12). However, she had recurrent infections - despite multiple sequesterectomies, abscess drainages, and the application of Gentamycin-beads. Fifty weeks and 12 operative procedures later, there was not enough clinical progression and the decision was made to perform a below-knee amputation as yet. The last patient requiring amputation was in a poor general health condition (patient 8). He had overweight (Quetelet index 30 kg/m^2), was an alcohol addict, and continued to smoke 40 cigarettes per day. To obtain sufficient soft-tissue coverage, a local adipofascial transfer was performed, but this flap became necrotic. The following free muscle transfer was compromised by abscesses. Considering the poor state of the sur-

Table 4. *Clinical and functional outcome of patients with a successful attempt at salvage.*

Patient number	Consol time (months)	Clinical outcome							Functional outcome	Impairment score
		ROM knee	*ROM ankle*	*Malunion*	*LLD (cm)*	*Sensibility foot sole*	*Signs of infection*	*Skin/soft tissues*		
Primary shortening										
2	5	normal	limited	no	2	normal	no	no defect	orth. shoe, no complaints	11%
5	8	normal	eq foot	recurvation	5	normal	no	no defect	ambulant with orth. shoe	43%
Bone grafting										
6	23	normal	limited	no	-	normal	no	no defect	walks 1500m, back to work	12%
7	4	normal	limited	exorotation 10°	-	normal	no	no defect	orth. shoe, retired	15%
10	23	normal	arthrod.	no	-	normal	no	no defect	orth. shoe, back to work	10%
11	17	normal	limited	no	-	normal	no	no defect	no complaints, former job	7%
13	10	normal	limited	no	-	reduced	no	no defect	no limitations, reactive edema	13%
14	25	normal	normal	no	2	normal	no	no defect	jobless (alcohol abuse)	5%
Ilizarov										
15	20	normal	limited	no	1.5	normal	no	no defect	ambulant with orth. shoe	7%
16	30	normal	arthrod.	no	-	normal	no	no defect	ambulant with orth. shoe	10%
17	15	normal	normal	angulation 5°	-	normal	no	no defect	no limitations, back to work	0%
Fibula										
18	12	normal	limited	no	-	normal	no	scaring	no limitations, back to work	15%

Consol time = consolidation time; ROM = range of motion; arthrod. = arthrodesis; LLD = limb length discrepancy; eq foot = equinus foot; orth. shoe = orthopaedic shoe; impairment score = lower extremity impairment score according to the American Medical Association[3]

Table 5. *Reason for amputation and functional outcome of pseudarthrosis treatment in amputees.*

Patient number	Amp time (months)	Remarks	Functional outcome	Impairment score (amp.)
Primary shortening				
1	7	High-aged, sepsis ('life before limb')	Dead at time of study (after discharge)	70%
3	2	Pain	Retired, walks with prosthesis	80%
4	1	High-aged, persisting infection despite irrigation	Walks with prosthesis, almost no restrictions, retired	70%
Bone grafting				
8	6	Disturbed fracture healing, marginal soft-tissue coverage	Persisting wound at stump, no prosthesis possible	70%
9	8	Pain, persisting infection, marginal soft-tissue coverage	Walks with prosthesis, restricted in daily life, retired	70%
12	10	Non-union and persisting infection	Has job, no major restrictions in daily life	70%

Impairment score = lower extremity impairment score according to the American Medical Association[3] rounding soft tissues and the disturbed fracture healing, amputation was performed 70 weeks after the accident and 26 weeks after we took over treatment.

Illustrative cases

Bone grafting (patient 13, figure 1)

A 46-year old labourer was struck by a forklift truck and sustained a grade IIIB open fracture of the tibia with a traumatic bone defect of 6 cm (figure 1). In the initial operation (which was performed in another institution) external fixation was applied. Five days later, the patient was referred to the University Medical Centre Utrecht for definite therapy. After debridement, removal of remaining dead bone and revision of the external fixator, the remaining soft-tissue defect was reconstructed by our plastic surgeons (rectus abdominus m.). The segmental bone defect was treated with two subsequent cancellous bone-grafting procedures. Four months after trauma, the patient presented with osteitis which was treated conservatively. Another four months later, the bone defect was solidly bridged. Clinical examination more than three years post-trauma revealed a restricted ankle motion (10-0-20°) and a reduced sensibility of the foot sole. He is fully ambulant with a normal shoe, but the lower leg shows tissue swelling after exertion. There are no limitations in social life and he is back to work. The mean lower extremity impairment score was 13% (table 4).

Ilizarov (patient 16, figure 2)

A 50-year old electrician fell from 4m-height, which resulted in a closed, strongly comminuted tibial pilon fracture with severely soft-tissue contusion and an open contralateral calcaneous fracture. Initially, the pilon fracture was immobilised with a plaster cast to slim the swollen tissues. Two weeks after admission, the tibia fracture was treated by both external and internal fixation (plate). Unfortunately, healing was disturbed by a deep necrotising infection, so that the plates and many dead bone fragments had to be removed - with a 12 cm-defect as result. This defect was bridged by external fixation and filled up with Gentamycin-beads. The plastic surgeons performed a gracilis muscle-transfer. Because this flap became necrotic, a second free muscle transfer (rectus abdominus m.) had to be performed one day later. Six weeks later, bone segment transport (according to Ilizarov) was started to bridge the large bone defect. Clinical course was complicated with several pin tract and deep infections. Eighteen months post-trauma, in the docking station an arthrodesis of the tibio-talar joint was performed with a combination of plate fixation, screws and cancellous bone grafting. Eventually, a pseudarthrosis remained and the fistula persisted, but finally union was achieved and infection disappeared - almost three years post-trauma and 12 hospital admissions later. Recently, the patient had no pain at the former defect area and was ambulant with an orthopaedic shoe (table 4). The mean lower extremity impairment score was 10%.

Figures 1a to 1g. Case 'bone grafting'. *a) X-ray of the left lower leg of a 46-year-old male with a grade IIIB open fracture of the tibia. b) External fixation was applied after initial debridement. c and d) The remaining soft-tissue defect was reconstructed by free muscle transfer. e) The segmental bone defect was bridged with two subsequent cancellous bone grafts. f to h) The ultimate clinical and radiological aspects, 8 months after trauma and five surgical procedures later.*

Figure 1a

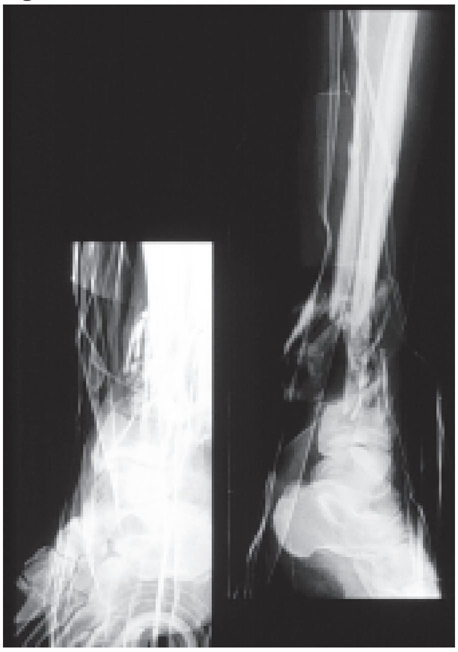


Figure 1b

Figure 1c

Figure 1d

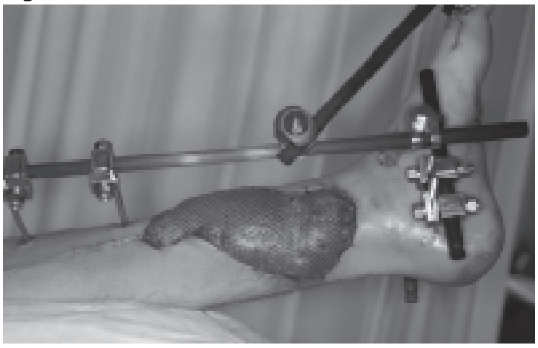


Figure 1e

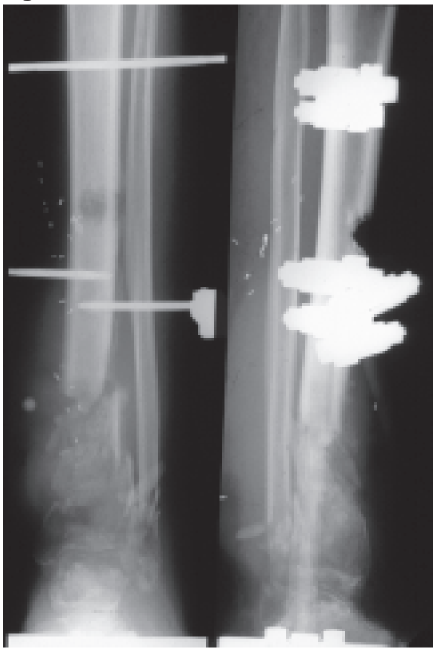
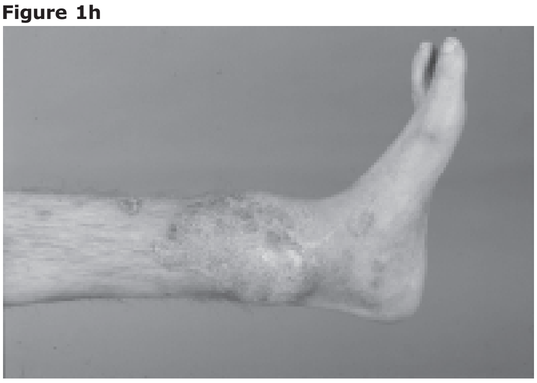


Figure 1f

Figure 1g

Figure 1h



Figures 2a to 2h. *Case 'Ilizarov'. a to c) X-ray and CT-scan of the right distal lower leg of a 50-year old male with a strongly comminuted tibial pilon fracture. d) Initially, the fracture was treated by both plate and external fixation. e) A 12 cm-bone defect was the result of deep infection. f and g) Free muscle transfer and bone segment transport according to Ilizarov were performed. h) Almost three years post-trauma the bone defect was bridged and the tibio-talar arthrodesis was healed.*

Figure 2a

Figure 2b

Figure 2c

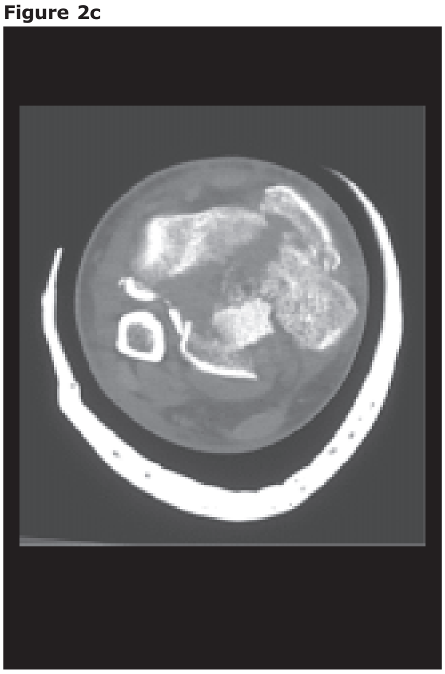


Figure 2d

Figure 2e

Figure 2f

Figure 2g

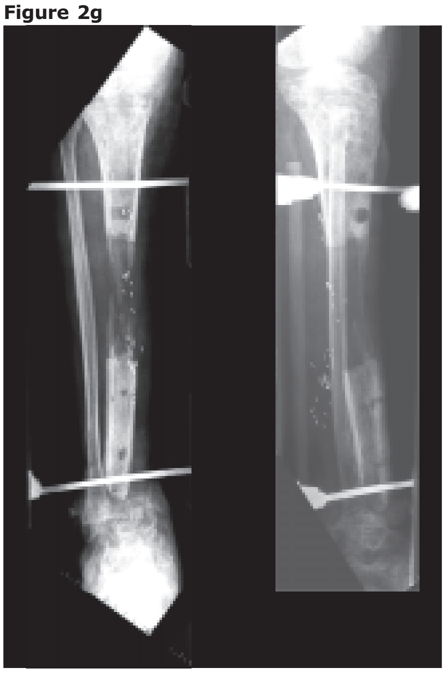
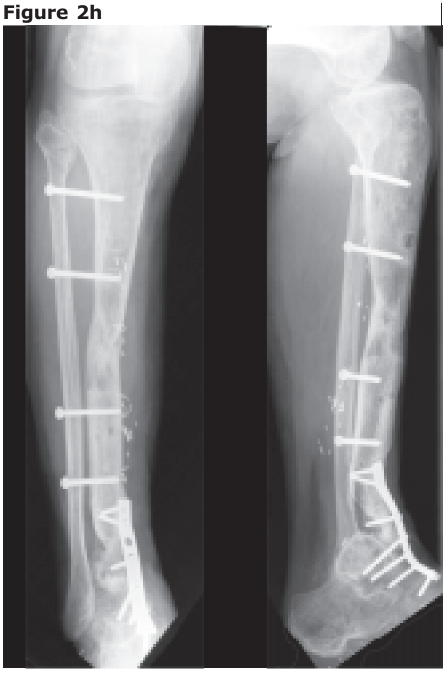


Figure 2h



Figures 3a to 3h. Case 'fibula transfer'. *a and b) X-ray and soft-tissue picture of the left lower leg with an isolated grade IIIB open tibial/fibula shaft fracture with large bone defect in a 21-year old woman. c and d) Initially, the bone ends were fixed with a plate. e and f) Almost three months post-trauma, the defect was reconstructed with a free muscle transfer, two months later followed by a free fibula transfer. g and h) The ultimate radiological and clinical outcome of the involved lower leg.*

Figure 3a

Figure 3b

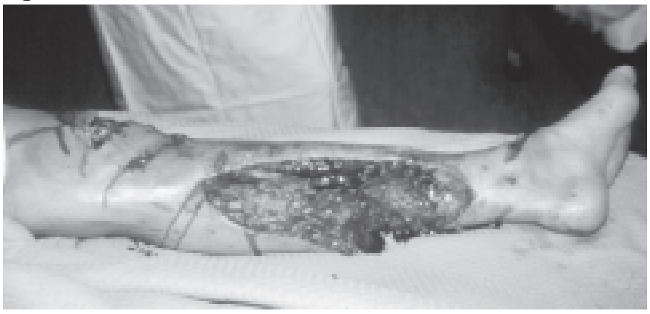


Figure 3c

Figure 3d

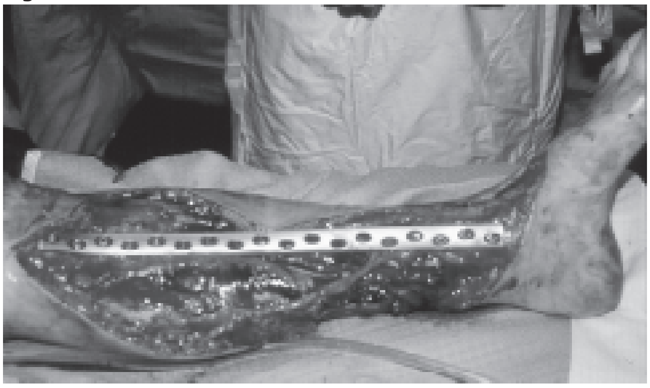


Figure 3e

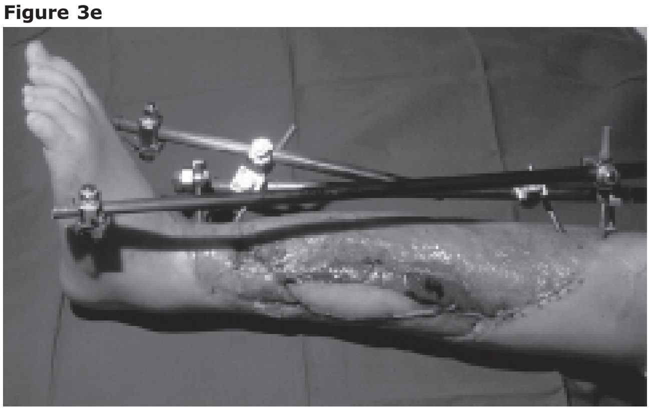


Figure 3f

Figure 3g

Figure 3h

Fibula transfer (patient 18, figure 3)

A 21-year old woman, involved in a motorcycle accident, presented with an isolated grade IIIB open tibial/fibular shaft fracture with 14 cm-bone defect as result. In another hospital the bone ends had been fixed with a plate. Due to persistent infection, three debridements and sequestrectomies had been performed. This patient was referred to us 10 weeks after trauma. An extensive debridement of bone and soft tissue was performed and the plate was replaced by an external fixator. Our plastic surgeons performed a free muscle transfer (latissimus dorsi m.) to obtain sufficient soft-tissue coverage and three months later the large bone defect (18 cm) was reconstructed by free vascularised fibula transfer. More than one year after trauma and 10 surgical procedures later, consolidation was reached. Six months later, this young lady was back to work and had no limitations in social life. Follow-up examination revealed a stiff ankle in plantigrade position, which was functionally acceptable with use of a normal shoe. Inspection of the lower leg showed a large area of scarring tissue, but normal sensibility and no signs of infection. The mean lower extremity impairment score was 15% (table 4).

Discussion

Infected segmental defect pseudarthroses of the tibia are complex problems, which demand enormous efforts from both patient and surgeon. In the literature different success rates are reported, varying from 62 to 97%.[7-15] The decision to proceed the limb salvage process whether to opt for amputation should be made consciously - regarding the clinical situation, the presence of co-morbidity, and the patient's age[16], expectations and compliance. Systemic disorders such as diabetes, renal failure, liver failure, chronic obstructive pulmonary disease, alcohol or tobacco abuse, and overweight will all impact prognosis.[16] These conditions share a common effect on host immune response and local vascularity. The impact of smoking on fracture union and soft-tissue reconstructions has been well documented.[17-24]

If decided to attempt limb salvage, a stepwise approach with scheduled (re-) operations is mandatory. The precursors to a successful outcome are infection control, skeletal stabilisation, sufficient soft-tissue coverage, and bone reconstruction. Chronic infection ultimately always results in impaired vitality of bone and surrounding soft tissues due to the jeopardised vascularisation. This is the combined result of the original trauma, multiple operations, and last but not least the infection itself. Implants not providing stability are to be removed and an adequate debridement of poorly vascularised and necrotic tissue is mandatory. These vigorous steps are essential to eradicate osteitis and to lay the framework for a successful outcome. When no septic complications occur post-operatively and an adequate debridement has been performed in combination with sufficient stabilisation, systemic antibiotics are not indicated.[25] Gentamycin beads can be used as local antibiotics and as spacer. These applications lead to high local tissue levels of the antibiotics, without the risk of systemic side effects.

Sufficient surrounding soft tissues are essential for healing of any fracture. Several local pedicled muscle and myocutaneous transfers, including gastrocnemius and soleus flaps, may provide coverage in the lower leg.[26] Free muscle flaps, including the latissimus dorsi, rectus abdominus, and gracilis muscles have been the most reliable means of coverage for the distal tibia.[15] They allow large areas of bone and soft tissue defects to be covered and eliminate dead space, while vascular anastomoses are remote from the site of infection. This leads to a higher resistance to infection and improves osteogenesis. Our plastic surgeons prefer the latissimus dorsi muscle for larger defects and the rectus abdominus and gracilis muscles for smaller reconstructions. The importance of soft-tissue coverage in treating osteitis and infected tibial pseudarthrosis has been reported in numerous articles.[14,15,26-32]

Several options exist for reconstructing segmental skeletal defects. Methods reported in the literature include cancellous bone grafts, distraction osteogenesis or segmental bone transport (the Ilizarov procedure), and free vascularised (fibula) grafts. The various options have inherent advantages and disadvantages, each with a specific indication. Repeated cancellous bone grafting is most suitable for smaller defects up to 6 cm. It is a relatively easy procedure with a low complication risk.[12,14,15,33,34] Bone segment transport according to Ilizarov offers many possibilities for reconstructing larger skeletal defects in the lower leg.[8,9,12,14,35] However, the transporting frame must be worn for a long period, which is cumbersome and resource intensive.[14] Free vascularised transplantation of the contralateral fibula may be the best option in case of extremely large segmental defects. In our series, 9 patients underwent cancellous bone graftings to reconstruct skeletal defects (table 2, patients 6-14), in three patients bone segment transport according Ilizarov was applied (patients 15-17), and one patient was treated with fibula transplantation (patient 18). In four patients with relatively small defects and one patient with an irreverible equinus foot, primary shortening was chosen (patients 1-5). As shown in tables 3 and 4, there were differences between these four groups regarding hospital stay, number of operative procedures, and outcome. Only two of five (40%) patients in the 'primary shortening'-group had successful limb salvage, against six of 9 (67%) in the 'bone grafting'-group, three of three (100%) in the 'Ilizarov'-group and one of one in the 'fibula transfer'-group. This may be explained by the fact that two of the patients in the first group were at high age, with major associated somatic problems.

The patients in our study paid a high price for the attempts at salvage. On average, they were already treated for six months and had been operated on four times, before presenting with an infected segmental defect pseudarthrosis of the tibia. From that moment, they stayed another 42 days in hospital during four admissions, sustained many complications and underwent multiple complex surgical procedures. Because of the huge physical, psychological and economical impact, and the unremitting suspense about outcome in some cases, proceeding of the limb salvage process has to be questioned repeatedly. By consequent use of the described step-by-step approach, limb salvage can be achieved in the majority of patients. However, in selected cases amputation is still indicated. In our study, six amputations (33%) had to be performed as yet due to various reasons (table 5). Ultimately, most patients had a good clinical and functional outcome with no or little limitations in daily life, and were back to work (table 4).

In conclusion, the problem of infected tibial pseudarthrosis with segmental bone loss remains significant - despite advances in diagnostics and management. The decision either to attempt salvage or to amputate should be made consciously and repeatedly on an individual base - regarding the clinical situation, the presence of co-morbidity, and the patient's age, expectations and compliance. A stepwise approach with scheduled (re-)operations is mandatory, aiming at control of the infection, stabilisation of the pseudarthrosis, adequate soft-tissue coverage, and skeletal reconstruction. If successful, the ultimate functional outcome will be good in the majority of cases. In selected cases amputation is still indicated.

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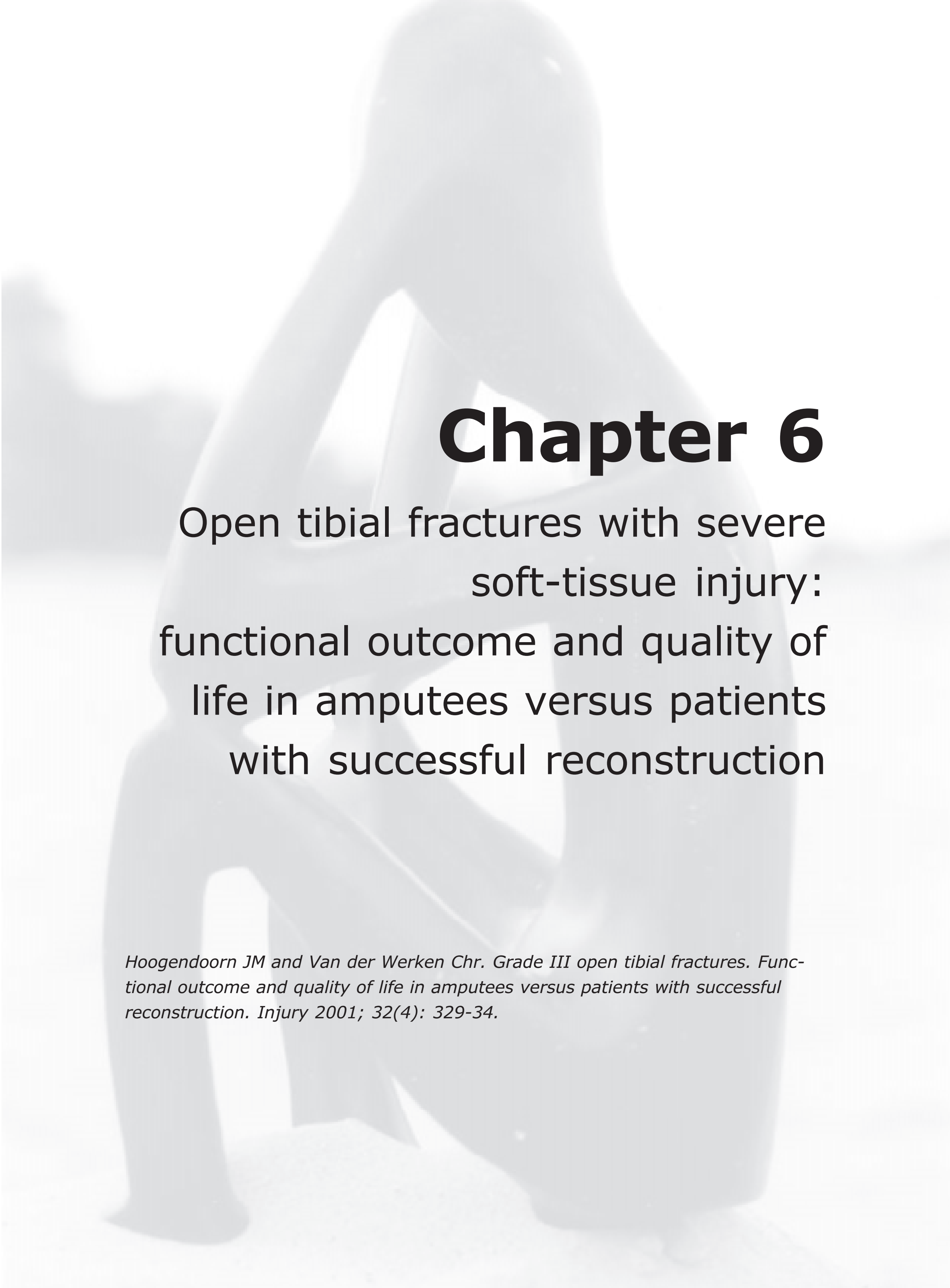


Chapter 6

Open tibial fractures with severe soft-tissue injury: functional outcome and quality of life in amputees versus patients with successful reconstruction

Hoogendoorn JM and Van der Werken Chr. Grade III open tibial fractures. Functional outcome and quality of life in amputees versus patients with successful reconstruction. Injury 2001; 32(4): 329-34.

Abstract

Objective

The purpose of this study was to assess the long-term functional outcome and the quality of life of patients who were treated for a (Gustilo) Grade III open tibial fracture.

Patients and methods

We included 43 patients with successful limb salvage (group A) and 21 amputees (group B). The groups are similar with regard to age, sex, and ISS. The functional outcome was scored using the AMA-Guides. To compare the quality of life we used the Nottingham Health Profile (NHP), the SF-36, and a questionnaire especially designed for this study.

Results

The mean lower extremity impairment (AMA) of patients in group A was 17,6%, compared with 73,5% for patients in group B. The results on both NHP and SF-36 show that patients in both groups have more problems in most categories than a healthy reference group. On the NHP, the difference in score was largest for the categories pain, mobility, energy and sleep. The SF-36 scores correlated well with the NHP scores. No significant difference was found between the two groups.

Conclusions

This type of injury has an enormous impact on each aspect of life - irrespective of the chosen treatment. A significant difference in lower extremity impairment is found between patients with a successful reconstruction and amputees. However, the quality of life is equal.

Introduction

The management of severe lower limb injury remains one of the more controversial subjects in trauma surgery. The objective of therapy in patients presenting with this injury is to achieve the best overall function for the patient. During the last decades, with the improvements in reconstructive techniques, the salvage rate increased.[1-4] However, limb salvage usually involves multiple surgical procedures, a prolonged hospital stay and a long rehabilitation process and may be physically, psychologically, and financially devastating to the patient. On the other hand, early amputation allows a rapid functional recovery.[5-7]

This study was undertaken to get an impression of the long-term function of patients who were treated for an open tibial fracture with severe soft tissue injury (Grade III according to Gustilo[1]). We therefore compared the long-term outcome and the quality of life between patients with a successful reconstruction of the lower limb and amputees.

Materials and Methods

Study groups

In the period 1992-1997, 72 adults were treated for a Grade III open tibial fracture in the University Medical Centre Utrecht, the major trauma center for the area. Six patients were excluded because they died during their first stay in hospital due to associated injuries. One patient was excluded because he underwent bilateral amputation.

A retrospective analysis of the patients' notes was performed to gather data on patient gender and age, mechanism of injury, fracture location and Gustilo grade, treatment, complications, and final outcome. The Injury Severity Score (ISS)[8] was retrieved as a measure of the severity of injury. The patients were divided by final outcome: the 43 patients who had a successful limb salvage constituted group A, group B comprised the 21 patients who underwent an amputation (table 1).

Table 1. *Comparison of patients with a successful reconstruction versus primary and secondary amputees*[a]

	Successful reconstruction (group A)	Primary amputation (group B1)	Secondary amputation (group B2)
Patients (fractures)	43 (44)	14 (14)	7 (8)
Age (years)	39.9 (±16.2)	39.4 (15.9)	50.6 (±20.5)
ISS	29.3 (±12.4)	29.4 (±9.5)	28.5 (±12.2)
Fracture grade (Gustilo)			
IIIA	15 (34%)	0	1 (13%)
IIIB	23 (52%)	2 (14%)	2 (25%)
IIIC	6 (14%)	12 (86%)	5 (63%)
Hospital days	67.1 (±38.3)	38.4 (±12.1)	71.4 (±24.0)
Operations (n)	5.3 (±2.9)	3.8 (±2.0)	5.0 (±1.9)
Complications (n)*	1.8 (±1.6)	0.6 (±0.6)	1.9 (±1.5)

[a] standard deviations in parentheses; * average number of complications for all patients

The mean age of the 43 patients with 44 Grade III open tibial fractures undergoing reconstruction was 39.9 years at the moment of presentation. Thirty-three patients (77%) were male; the mean ISS was 29.3. Most of the open fractures were caused by high-energy accidents. Fifteen of the fractures were classified as Grade IIIA (34%), 23 as Grade IIIB (53%), and 6 had associated major vascular injury and were thus classified as Grade IIIC (14%).

Twenty-one patients with a mean age of 44.6 years underwent an amputation of the leg. One patient had bilateral amputation for Grade III open tibial fractures. The group consisted of 16 male patients (76%). The mean ISS was 28.9. Traffic accidents caused most of the fractures. One fracture was classified as Grade IIIA (5%), 4 as Grade IIIB (19%), and 17 as Grade IIIC (76%). The amputees have been grouped by time to amputation into a primary (less than 1 week from injury, group B1) and a secondary (more than 1 week from injury, group B2) group. Group B1 comprised 14 primary amputees, group B2 7 secondary amputees. The average time to secondary amputation was 8 months (range: 9 days to 29 months). The ISS was equal for both subgroups (respectively 29.4 and 28.5); on average, the secondary amputees were older (50.6 versus 39.4 years).

Functional outcome

The patients with successful limb salvage were invited for a personal examination. In 33 patients, we examined the gait, the range of motion of the knee and ankle, the sensibility of the leg, foot (sole), and evidence of persistent infection. The lower extremity impairment was measured by using the *Guides to the Evaluation of Permanent Impairment* of the American Medical Association.[9] These *Guides*, one of the most widely used systems for rating impairments,[10] provide a standard framework to evaluate the impairment of any human organ system. The degree of loss of function is expressed in a percentage of permanent impairment, also for amputations at different levels: the lower extremity impairment due to a below knee amputation is estimated at 70% and due to an above knee amputation at 80%. On the basis of these standard percentages, it was possible to compare the lower extremity impairment scores of patients with limb salvage with the impairment scores of amputees.

Quality of life

We used a quality-of-life assessment regarding satisfaction with life and perceived disability. It included the Nottingham Health Profile (NHP)[11], the SF-36[12] and an especially for this study designed questionnaire. The NHP is a two-part health-status questionnaire which is used to indicate physical, emotional, and social health problems. Part I measures subjective health status in 6 categories (mobility, energy level, pain, sleep, emotional reaction and social isolation). For each category, 0 points represents no limitations and 100 points represents maximum disability.[13] Part II consists of 7 yes-or-no statements. These assess limitations due to health problems in paid employment (job), housework, family life, social life, sexual function, recreation, and enjoyment of holidays. The SF-36 measures 8 health attributes: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, pain, vitality, and general health perception. The higher the score, the better the health rating with 100 points as the maximum for each concept.[14] Both the NHP and the SF-36 have been tested extensively and found to be reliable and valid in assessing he general health status of large samples of respondents into a variety of medical conditions, including musculoskeletal conditions.[5,15-18] A third questionnaire specifically designed for this study consisted of specific questions related to pain, daily functioning, psychological factors, and handicap with working.

Thirty-eight (88%) patients in group A completed the quality-of-life assessment. Of the remaining 5 patients, 3 died in the meantime, one moved abroad, and one didn't respond. In group B, 18 (86%) of the 21 patients filled in the questionnaires; 2 patients have died and one patient moved abroad.

Analysis of the data

In addition to standard descriptive statistics, we used the Mann-Whitney U test to analyse continuous variables. Most of these variables have highly skewed distributions that would have affected the performance of the Student t test. We used the chi-square goodness-of-fit test to compare qualitative nominal variables. All calculations are executed with SPSS for Windows 8.0. A p-value equal or less than 0.05 was considered significant.

Results

Treatment and complications

Successful reconstruction (group A). Only hospital days relating to treatment of the concerning leg were taken into account. The average overall length of stay in hospital of the patients with a successful limb reconstruction was 67.1 days over an average of 3.8 periods. The patients underwent an average of 5.3 operations on the injured leg; mostly osteosynthesis, tissue transplantation and operative procedures for secondary reconstruction or due to complications. Thirty-four (79%) patients sustained a total of 82 complications, with osteitis (19 patients, 44%), superficial infection (14 patients, 33%), and pseudarthrosis (11 patients, 26%) as the most common complications.

Amputation (group B). We subdivided the variables of treatment for primary and secondary amputation. Fourteen patients underwent a primary amputation; 11 of these were performed below-knee, 2 through-knee because of poor vascularity of the leg, and 1 patient underwent an above-knee amputation due to an associated large femoral bone defect. Seven patients had a secondary below-knee amputation, due to severe complications after attempted salvage. The average overall hospital stay for primary amputees was 38.4 days during 1.4 periods, compared with 71.4

days during 2.6 periods for secondary amputees. Nine (64%) of the 14 primary amputees had complications, with a superficial infection as the most common (6 patients). Two of these patients, in whom initially a below-knee amputation was performed, had to undergo an above-knee amputation due to stump necrosis. Chronic osteitis led to a through-knee amputation in another patient.

Functional outcome

Six patients had a shortening of the lower leg of more than 2 centimeters. The sensibility of the foot sole was normal in 15 (56%) patients, reduced in 7 (26%), increased in 4 (15%), and absent in one (4%) patient. Half of the patients wore normal shoes, the others needed special shoes. The mean lower extremity impairment, according to the *Guides*, was 17.6 (±18.2)%. No significant difference in lower extremity impairment was seen between patients who presented with a Grade IIIA (21.7±23.7%), IIIB (10.7±8.9%), or IIIC (21.8±11.0%) open tibial fracture. The lower extremity impairment for amputees, calculated on the basis of standard values for amputations (as given in the *Guides*), was 70% for below knee amputations and 80% for transgenual and above knee amputations (average 73.5±4.9%).

Quality of life

Successful reconstruction (group A). The results on the Nottingham Health Profile (NHP) showed that the scores of most categories in both parts are considerably higher than the scores of a healthy, age-matched reference group (Figures 1 and 2).[19] In part I, the difference in score was the largest for the categories 'pain', 'mobility', 'energy', and 'sleep', which indicate specific problems in these aspects of life. In part II of the profile, 52% of the patients said that their state of health interfered

Figure 1. *The mean scores for part I of the NHP of the patients who had a successful reconstruction (group A), those who underwent an amputation (group B), and a healthy, age-matched reference group[19]. The numbers indicate weighted responses in each category, with 0 representing no limitations and 100 representing maximum disability.*

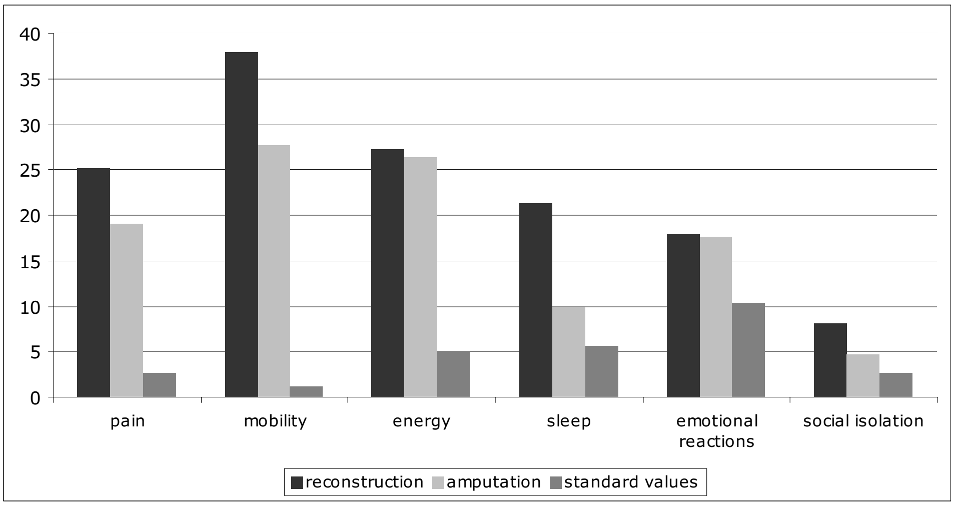
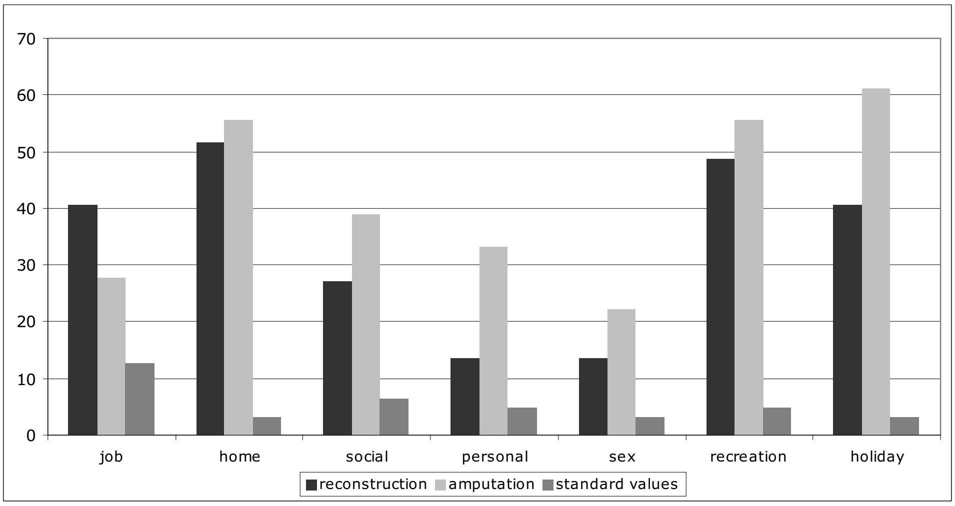
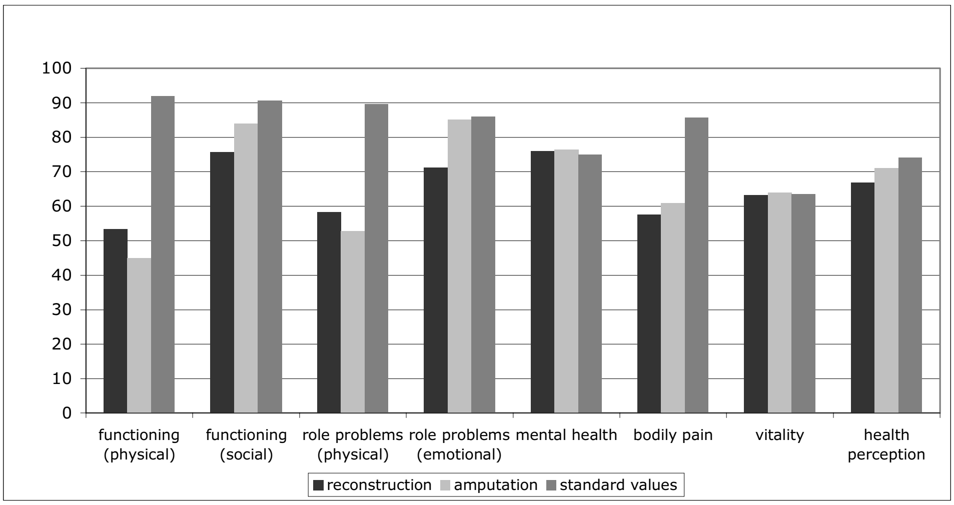


Figure 2. *The percentages of the individuals who had a health-related problem in the areas of the NHP (part II) in group A (successful reconstruction), group B (amputation), and a healthy reference group[19].*



with their ability to do the housework, and 49% of the patients indicated it interfered with their recreational activities. Forty percent of the patients had problems with work; the others had no problems or were jobless. The SF-36 scores correlated well with the NHP scores, and were particularly low for the dimensions relating to the physical consequences of the patients' disability (Figure 3). The scores were lowest for the dimensions 'physical functioning', 'role limitations due to physical problems', and 'bodily pain' (respectively 53, 58 and 58 points, on a scale with a maximum of 100 points). It is worthy of note that the scores for both vitality and general health

Figure 3. *The mean SF-36 scores of the patients who had a successful reconstruction (group A), those who underwent an amputation (group B), and a healthy reference group[26]. The numbers indicate the mean weighted scores for each category, with a scale varying from 0 (worst health status) to 100 (best health status).*



perception corresponded with the normative data. The results on our specific questionnaire showed that 24 (65%) of the patients have problems with walking (they have to stop within a walking distance of 5 kilometers, table 2). The reasons for stopping are mainly fatigue, pain, and shortness of breath. Fifteen (41%) of the patients never have pain in the leg, 17 (46%) patients experience pain occasionally, and in 5 (14%) patients pain was permanent. Thirty-two (86%) patients were satisfied with their treatment. The reasons for being less satisfied are mainly pain and problems with the cosmetic aspect. Eighteen (48%) patients feel disabled, because they cannot do everything they used to do before their accident. Seventeen (45%) patients reported having problems with working.

Amputation (group B). In both parts of the NHP, the scores of most of the categories turned out higher than the scores of the healthy reference group (Figures 1 and 2).[19] In part I, the largest differences are seen for the categories 'pain', 'mobility', and 'energy'. The scores of part II are comparable with those of the patients with a successful reconstruction; many patients reported that they have problems in running the household (56%) and that their health interferes with hobbies (56%) and holidays (61%). Twenty-eight percent of the patients indicated that their state of health interfered with their job; the other patients were jobless or had no problems. The scores on the SF-36 were particularly decreased for the dimensions that reflect the consequences of the perceived injuries (Figure 3). In comparison with the reference group, the largest difference is in the dimensions 'physical functioning', 'role limitations due to physical problems', and 'bodily pain'. The scores for 'general health perception' and 'vitality' were equal to the values of the reference group. The results of the specific questionnaire showed that 13 (72%) patients could not walk over 5 kilometers (table 2). The reasons for stopping in most cases are stump-related pain and fatigue. Fifty percent of the patients never had stump-related pain, 39% had occasionally pain, and 11% of the patients had continuously pain in the stump. Fifteen (83%) patients were satisfied with the result of treatment. Nine (50%) pa-

Table 2. *Results of our specific questionnaire.*

	Successful reconstruction (group A)	Amputation (group B)
Response (n)	38 (88%)	18 (86%)
Walking distance >5 km 100m-5 km < 100 m	 14 (35%) 21 (57%) 3 (8%)	 5 (28%) 8 (44%) 5 (28%)
Pain never occasionally continuously	 16 (42%) 17 (45%) 5 (13%)	 9 (50%) 7 (39%) 2 (11%)
Satisfaction with treatment	32 (86%)	15 (83%)
Problems with profession	17 (45%)	11 (61%)
Feeling of being disabled	18 (48%)	9 (50%)

tients felt disabled and 11 (61%) patients had problems in practicing their previous profession. In none of the outcomes there was a significant difference between below knee and above knee amputees.

Discussion

Surgeons faced with open tibial fractures with severe tissue-damage have to make a principle choice: an attempt at salvage or primary amputation. The ultimate goal of reconstruction is salvage of a viable and functional extremity. If primary amputation is prevented, there are reported disadvantages of reconstructive surgery in these cases as well. Attempted salvage often brings more operations and complications, a longer stay in hospital and a longer rehabilitation.[5,6] Furthermore, patients often still complain of oedema, pain and a diminished sensibility in the leg or foot, while the treatment can be physically, psychologically and financially exhausting.[6,20] There is little reported research on an important aspect of treatment - the long-term outcome and the quality of life of the patients with these injuries.

In this study we compared the various treatments, the complications and the end stage function of patients who had had successful limb salvage with those who underwent primary or secondary amputation. Both groups were equal with regard to age, gender, aetiology of the injury and ISS. The objective difference between the two groups was the severity of the tibial fracture, especially the higher number of vascular injuries in the limbs that were treated with amputation (77% versus 17%). In total, 43 patients had a successful reconstruction, 14 patients underwent primary amputation and 8 patients underwent secondary amputation. In previous publications similar ratios can be found.[3,4,7]

The patients achieving successful limb reconstruction experienced significantly more complications, requiring more operative interventions than the patients treated with a primary amputation. The complications in the first group were mainly related to problems in bone healing; superficial infection caused most of the problems in the second group. Eight patients had a delayed below-knee amputation after failed attempted limb salvage, due to severe complications as ongoing infection with osteitis and poor soft tissues. These patients had twice the average length of stay in hospital as the primary amputation group.

The literature is divided over whether the long-term outcome of a salvaged leg is better or worse than an amputation. Numerous reports have documented the range of short-term complications and impairment following severe open tibial fractures, but few studies have examined the extent to which these impairments translate into long-term functional limitations and disability, including the inability to resume activities such as work and keeping house.[4,7,21,22] Georgiadis et al. concluded in their study that patients with Grade IIIB and IIIC injuries who had had limb salvage did worse than those with an early below-knee amputation.[5] On the other hand, Dagum et al. reported that patients in the amputation group had lower physical functional outcome scores than patients in the successful salvage group. Mental and pain outcome scores were similar in both groups.[23] Puno et al. found no difference in function and pain between primary amputation and limb salvage.[24] In our study, we used a quality-of-life assessment consisting of the SF-36, the Nottingham Health Profile (NHP), and a non-validated questionnaire. Both patient groups had more problems in most of the NHP and SF-36 categories than a healthy reference group (Figures 1, 2 and 3). The results of both groups on the SF-36 scale were especially worse for the scales 'physical functioning', 'role limitations due to physical problems' and 'bodily pain'. No significant difference was found between the 2 groups. In both groups, half of the patients considered themselves disabled. Forty percent of the patients with a successful reconstruction and 60 percent of the amputees had problems in practicing a profession. Despite low scores on the quality-of-life questionnaires, patient satisfaction was very high in both groups. This may be related to low preoperative expectations or satisfaction with care received.[25] The long-term physical disability as measured by these questionnaires was greater than previously thought, regardless of whether the leg was preserved or amputated.

Of particular interest is the correlation between these patient-perceived measures of disability and clinical measures of physical impairment. We therefore examined the patients with a successful reconstruction personally and calculated a lower extremity impairment by using the *Guides to the Evaluation of Permanent Impairment*. The mean lower extremity impairment score for these patients (17,6%) turned out to be significantly lower than for amputees (73,5%), calculated on the basis of standard values as provided by the *Guides*. Unlike the results of the quality-of-life questionnaires these (objective) data show that patients with a successful reconstruction are presumed to achieve a higher level of function than amputees.

In conclusion, in patients presenting with severe lower limb injury, it will always be difficult to choose between primary amputation or an attempt at salvage. The decision to amputate is an emotional one, for both patient and surgeon. The aspirations for both are a normal functioning limb, which can rarely be achieved. Despite advances in reconstructive surgery, primary amputation will be the best treatment in selected cases. Generally, this reliable solution leads to a quick recovery. The results of our study show that patients who underwent a primary amputation had a shorter stay in hospital, underwent fewer operations, and suffered fewer complications than patients who had successful limb salvage. Even if limb salvage eventually seems successful, in a significant number of patients it leads to persisting complications, which may result in secondary amputation. This is exhausting for both patient and doctor, and should be avoided. The results of the quality-of-life questionnaires show that this type of injury has a major impact on each aspect of life, irrespective of the chosen treatment. We therefore advocate amputation as a serious treatment option in patients presenting with a fractured tibia with major soft-tissue injury.

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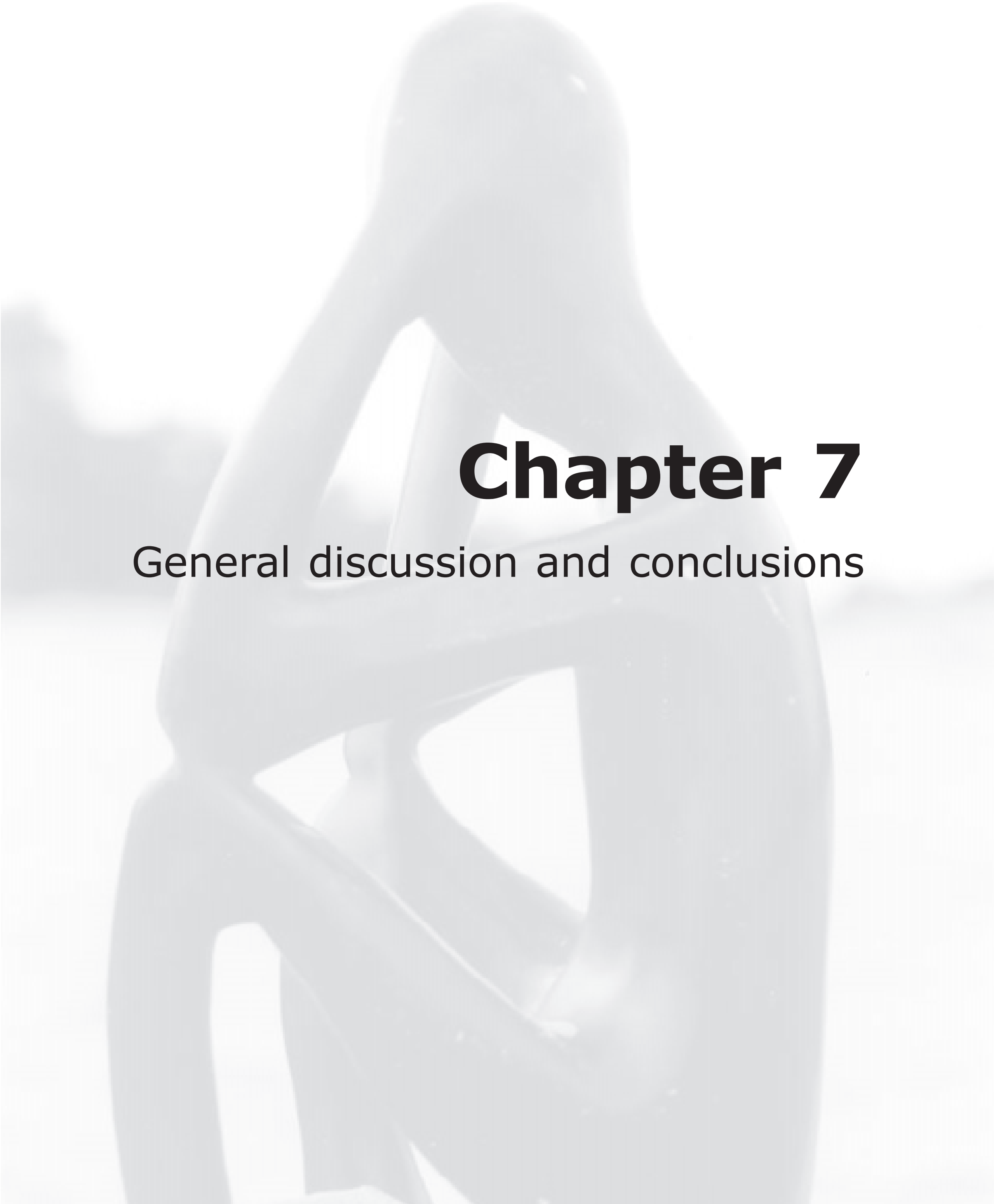

Chapter 7

General discussion and conclusions

GENERAL DISCUSSION

Due to the delicate soft tissues of the lower leg, open tibial fractures are at risk for infection and disturbed healing. Recent improvements in therapy - including better antibiotics, new fracture fixation techniques and microvascular reconstructions - created possibilities previously unavailable to the surgeon. Multidisciplinary approach led to some remarkable successes in term of limb salvage and have improved the outlook for patients with a mangled extremity. Nevertheless, some patients are still better off with amputation. The decision whether to reconstruct or to amputate a severely injured leg remains the subject of extensive debate in the literature, resulting in wide variations in practice across hospitals and individual surgeons. In this thesis, we tried to clarify several aspects of this difficult clinical problem by answering the following questions:

1. Is it possible to predict outcome in individual patients with a mangled lower leg?
2. What are the short-term consequences of the chosen treatment?
3. How is the long-term outcome of successful salvage and amputation?
4. What are the influences of smoking on the healing of open tibial fractures?
5. How are the results of treatment of infected segmental defect pseudarthrosis of the tibia?

In this general discussion, we pass these questions in separate revue.

1. Is it possible to predict outcome in individual patients with a mangled lower leg?

The objective of therapy in patients with severe injury to an extremity is the salvage of a functional limb. When this goal is not obtainable, early amputation can avoid costly attempts at salvage and save the patient significant morbidity and even mortality. Currently, the determination of viability of the injured lower leg is based on subjective criteria including the extend of tissue loss, the presence of vascular and/or nerve injury and the grade of contamination. The use of these subjective criteria alone has led to a high incidence of delayed amputation and in the last two decades attempts have been made to establish objective criteria, which could be useful for early discriminating between limbs requiring amputation and those likely to be salvaged successfully. Based on these criteria, predictive scoring systems have been developed. By graduating the factors composing these systems, subscores can be given. It is stated that if the total score exceeds the threshold, amputation should be strongly considered. The most widely described scoring systems are the Mangled Extremity Syndrome Index (MESI)[1], the Predictive Salvage Index (PSI)[2], the Hannover Fracture Scale (HFS)[3], the Limb Salvage Index (LSI)[4], the Mangled Extremity Severity Score (MESS)[5], and the Nerve injury, Ischemia, Soft-tissue injury, Skeletal injury, Shock and Age of patient (NISSSA) Score[6]. The originators of the various scoring systems validated these by demonstrating high rates of sensitivity (i.e., with almost all limbs with total scores below the cut-off point salvaged) and specificity (i.e., with almost all limbs with total scores above the cut-off point amputated). However, most scores were based on retrospective studies, with small sample sizes, and were affected by the clinical bias of the index developers.

Our independent study could not confirm successes as reported in the original articles (Chapter 3.2). We retrospectively analysed the medical charts and X-rays of 57 patients who were treated at our department for a Gustilo Grade III open tibial fracture, to gather data on type of injury, clinical and operative findings and final outcome. With these data the total scores for each of the above-mentioned systems were calculated, so their predictions could be compared with the observed clinical outcome (successful salvage versus amputation). The Limb Salvage Index had the highest sensitivity and specificity (respectively, 0.67 and 0.95), but even this scoring system predicted wrongly in 14% of the patients. A greater number of variables did not create a more reliable scoring system. Other independent studies showed similar results.[7-9] Therefore, we may conclude that scoring systems have limited clinical value and cannot be used as a reliable criterion for decision-making in patients with a mangled leg.

2. What are the short-term consequences of the chosen treatment?

When confronted with a mangled lower leg, it is the natural inclination of both surgeon and patient to opt for attempt at salvage. However, reconstructive surgery may have several disadvantages: numerous reports have documented the differences in number and complexity of performed operations, in duration of hospitalisation, and in number and type of complications in patients with successful limb salvage on the one hand and those undergoing primary or secondary amputations on the other.[9,10,12-16]

Operations

Patients with attempted limb salvage require significantly more and more complex operations than primary amputees.[9,10,14-16] In a study on the outcome of treatment of 72 Grade III open tibial fractures, we found that patients with a (successfully) salvaged limb underwent 5.3 operations on average, versus 3.8 (generally minor surgery) for early (within one week after admission) amputees and 5.0 for secondary amputees (Chapter 6). This difference is quite logical: patients in whom salvage is attempted undergo more major reconstructive procedures (e.g. fracture fixation, vascular reconstructions and/or (micro)vascular tissue transplantations). In their comparison of the consequences of primary versus secondary amputation, Bondurant et al. showed that a delay in amputation was associated with an even more dramatic increase in number of operations (1.6 for primary and 6.9 for delayed amputations).[12]

Hospital days

The number of days spent in hospital is strongly correlated with the number of operations. Compared with primary amputees, patients with a successful reconstruction spend on average almost twice as many days in hospital, (in our study, respectively 38.4 and 67.1 days (Chapter 6)).[9,10,16]

Complications

Patients undergoing limb salvage procedures suffer significantly more and other complications than primary amputees (Chapter 6).[1,10,16] In the first group infection with osteitis, partial or complete free flap loss, and pseudarthrosis are the most common complications.[10,16] These complications can be so severe and persisting that they ultimately result in a secondary amputation. Simple wound healing disturbances are the most common complications after amputation.[10,16]

3. How is the long-term outcome of successful salvage and amputation?

The ultimate measure of the result of treatment of a mangled lower leg is the ability to perform daily activities and to enjoy a good quality of life on the long term. Historically, outcome of treatment of mangled lower legs was just defined as either 'successful salvage' or 'amputation', but in recent years the functional consequences have received increased attention. To date, few studies examined the extent to which the earlier-mentioned complications translate into long-term physical impairment and disability in both patients with a salvaged leg or amputees.[8,10,14,16-18]

Impairment

This is a measure of function, at the level of an organ or body system. It is generally assessed by clinicians and based on physical findings, X-rays and laboratory tests.[19] The American Medical Association (AMA) developed a standard framework to evaluate the impairment of any human organ system.[20] These *Guides to the Evaluation of Permanent Impairment*, are nowadays one of the most widely used systems for rating impairment.[21-23] The degree of function loss is expressed in a percentage of permanent impairment, also for amputations at different levels. Based on these percentages, it is possible to compare the lower extremity impairment of patients with limb salvage versus amputees. In 1993, Kemp et al. retrospectively objectified the results of 17 patients with successfully salvaged Gustilo grade III open fractured tibiae by using the *AMA Guides*.[18] They found that the impairment score of salvaged tibiae for each group, grades IIIA, IIIB and IIIC, was lower than that after a through- or below-knee amputation. We performed a study in 18 amputees and 38 patients with a salvaged limb (Chapter 6). All patients were personally examined and the lower extremity impairment was measured by using the *AMA Guides*. The mean lower extremity impairment in reconstructed patients was 17.6% compared to 73.5% for amputees. This is a large difference, but it should be mentioned that the lower extremity impairment for amputees was calculated on the basis for standard values for amputation (as given in the *Guides*) - 70% for below-knee amputations and 80% for transgenual and above-knee amputations.[20]

Disability

This is defined as the possibility of performing everyday activities within a defined physical and social environment. Disability is a measure of outcome from the patient's perspective and represents the influence on the quality of life. It is typically measured by standardized quality-of-life questionnaires and assesses outcome across several domains of function, including physical health, psychosocial well-being, and role function. The literature is divided over whether the long-term disability of a salvaged leg is better or worse than an amputation. On the basis of their study, Georgiadis et al. concluded that patients who had had limb salvage did worse than those with an early below-knee amputation.[10] Significantly more patients who had limb salvage considered themselves severely disabled and had more problems with the performance of occupational and recreational activities. A weak point of this study was that 35 percent of the (attempted) salvage group was lost to follow-up. Similar conclusions were drawn from studies by Dagum et al. and Herthel et al.[8,14] Fairhurst showed that early amputees had higher scores for limb function and quality of life than patients with a salvaged leg and he suggested that amputation should be strongly considered when confronted with a borderline salvageable lower limb.[17] Return to work was accomplished by six months in the early amputee group, late amputees required 36 months to return to work and salvaged tibiae patients 18 months.[17] Limitations of this study are, however, the small group (12 amputees and 12 patients with successful salvage) and the use of a non-validated questionnaire.

In our study, we found no significant differences regarding disability in 18 amputees and 38 patients with a salvaged limb (Chapter 6). We used two validated questionnaires (the Nottingham Health Profile (NHP)[24] and the SF-36[25]) and a specially for this study designed questionnaire. Both patient groups had more problems in most of the NHP and SF-36 categories than a healthy reference group. The results were especially worse for the scales 'physical functioning', 'mobility', and 'pain'. Forty percent of the patients with a successful attempt at salvage and 60 percent of the amputees had problems in practicing a profession. In conclusion, the results of the quality-of-life questionnaires show that this type of injury has a major impact on each aspect of life, irrespective of the chosen treatment.

4. What are the influences of smoking on the healing of open tibial fractures?

Many factors are involved in the healing of lower extremity fractures with associated soft-tissue injury. Of these, the patient's smoking behaviour is one of the most underestimated. In the past decades, it has been shown that smoking is positively associated with malignancies of several organ systems, chronic obstructive pulmonary disease and ischemic heart disease. Experimental and clinical studies showed that nicotine and carbon monoxide, the most harmful constituents of tobacco, influence important physiological mechanisms - varying from acute effects such as vasoconstriction and hypoxia, to more chronic effects such as a delayed revascularisation and demineralisation of bone (Chapter 4.1). These pathophysiological effects implicate that smoking must adversely affect bone and soft-tissue healing as well. In recent years, there has been a growing interest in the effects of smoking on the results of (elective) plastic and orthopaedic surgery. However, up to now clinical studies on fracture healing in smokers are rare.

We therefore performed a (retrospective) study on the effects of smoking on the outcome of treatment in 118 patients with 125 open tibial fractures (Chapter 4.2). In smoking patients consolidation time was significantly longer (33 versus 26 weeks) and they suffered more from osteitis (27% versus 9%) than non-smoking patients. This resulted in more (re-)operations (on average, 3.4 versus 2.5) and more hospital admissions (on average, 2.7 versus 2.0). Several studies have demonstrated the positive effects of smoking cessation preceding elective surgery,[26-28] and - although not proven yet in trauma surgery - it seems plausible that immediate cessation benefits patients with an open tibial fracture as well. On the basis of the results of our study and data in the literature, we strongly advise smoking patients presenting with an open tibial fracture, to stop smoking immediately and continue this during the full rehabilitation course.

5. How are the results of treatment of infected segmental defect pseudarthrosis of the tibia?

The majority of open tibial fractures will heal without major problems, unfortunately some patients will face severe complications. One of these complications is a combination of segmental defect pseudarthrosis (i.e., a complete interruption of the continuity and without contact between the bone ends) and osteitis of the tibia. Due to the delicate surrounding soft-tissues of the lower leg, it is a real challenge to achieve union and to overcome infection. In the past decades, new reconstructive techniques such as free tissue flap transfers, bone segment transport according to Ilizarov and free vascularised fibula transplantation have become increasingly popular. Nowadays in the literature success rates are reported varying from 62% to 97%.[29-37]

We retrospectively evaluated a consequent and protocolised approach of infected segmental defect pseudarthrosis of the tibia in 18 patients (Chapter 5). A stepwise approach with scheduled (re-)operations was practised in all patients, aiming at control of the infection, stabilisation of the pseudarthrosis, adequate soft-tissue coverage, and skeletal reconstruction. Based on the size of the segmental defect, and other factors such as condition of the soft tissues and the patient's age, the method of skeletal reconstruction was determined. In general, repeated cancellous bone grafting was considered suitable for defects up to 6 cm, bone segment transport for defects larger than 4 cm, and free vascularised fibula transplantation for exceptional cases with extreme bone loss. In some patients, especially in case of an 'irreversible' equinus foot or stiff ankle, some shortening was accepted. Following this regimen, limb salvage was achieved in 12 (67%) cases. Our patients paid a high price for the attempts at salvage. On average, they had already been treated for six months and had been operated on four times, before presenting with an infected segmental defect pseudarthrosis of the tibia. From that moment, they stayed another 42 days in hospital during four admissions, sustained many complications and underwent multiple complex surgical procedures. Because of the huge physical, psychological and economical impact, and the unremitting suspense about outcome in some cases, proceeding of the limb salvage process has to be questioned repeatedly by doctor and patient. The decision either to attempt salvage or to amputate should be made consciously on an individual base - regarding the clinical situation, the presence of co-morbidity, and the patient's age, expectations and compliance. By consequent use of the described step-by-step approach, limb salvage can be achieved in the majority of patients presenting with an infected segmental defect pseudarthrosis of the tibia. In selected cases amputation is still an excellent and simple alternative.

CONCLUSIONS

When confronted with a patient with a severest lower leg injury, it is difficult to decide between primary amputation or an attempt at salvage. The management of these injuries can only be successful if tailored to the individual needs and specific circumstances. A consequent step-by-step approach is imperative, starting with proper fracture classification followed by the planning of several subsequent procedures. Explicit determination of fracture type and soft-tissue injury will aid the discussion and facilitates prediction of outcome. Several scoring systems have been developed to assist the surgeon in decision-making and, in that way, to prevent delayed amputation. However, all these systems fail and cannot be used with confidence in clinical practice. Therefore, the decision is to be based on a mixture of clinical impressions - regarding patient-related factors (age, co-morbidity, and smoking behaviour), local trauma-related factors (mechanism of injury, fracture pattern, soft-tissue injury, vascular injury, neurological injury, ipsilateral injury, and contamination), and general trauma-related factors (injury severity, shock, and hypothermia). In doubt, the decision how to handle should be postponed after acute fracture stabilisation, immediate vascular repair, extensive debridement, and complete fasciotomies. Thereafter a ‘second look’ procedure 24 to 48 hours later is to be planned. In attempts at salvage four cornerstones are essential: 1) vigorous and repeated debridement; 2) immediate fracture stabilisation using different methods depending on the fracture type and site, the soft-tissue condition and contamination, the condition of the patient, and personal preference; 3) early soft-tissue reconstruction, and; 4) secondary surgery to promote fracture healing and/or to reconstruct skeletal defects if needed.

Despite all advances in reconstructive surgery, there is still a distinct place for primary amputation in selected cases: 14 (21%) in our study group of 64 Gustilo grade III open fractures. The decision to amputate is an emotional one, both for the patient and for the surgeon. It is the natural inclination of the surgeon and strong wish of the patient and relatives to preserve the limb whenever possible. However, patients going for limb salvage will undergo more (on average, 5.3 versus 3.8) and more complex operations, they will stay longer in hospital (on average, 68 versus 38 days), and will suffer more complications (on average, 1.8 versus 0.6) than primary amputees. Delayed amputation , sometimes after many months or even years, is extremely disappointing for both patient and doctor and should be avoided if possible.

Most studies on the long-term outcome of mangled legs report higher impairments for amputees than after successful reconstruction. However, the quality of life is generally equal in both groups, though considerably less than in a healthy population. Most patients suffer from physical problems and pain on a regular base. More than half of them has problems with walking due to pain or fatigue, and their state of health interferes with recreational activities and the ability to do the household, showing the enormous impact on daily life. Fifty percent of patients in both groups feel disabled, because they cannot do what they used to do before the accident.

In conclusion, open tibial fractures with severe soft-tissue injury remain challenging problems. The wish for both surgeon and patient - a normally functioning limb - can rarely be met. By following a stepwise protocol, salvage can be achieved in most cases. However, in some patients primary amputation is the best treatment. It is nevertheless important to realise that both successful limb salvage and early amputation rarely return the patient to a normal, pain-free life.

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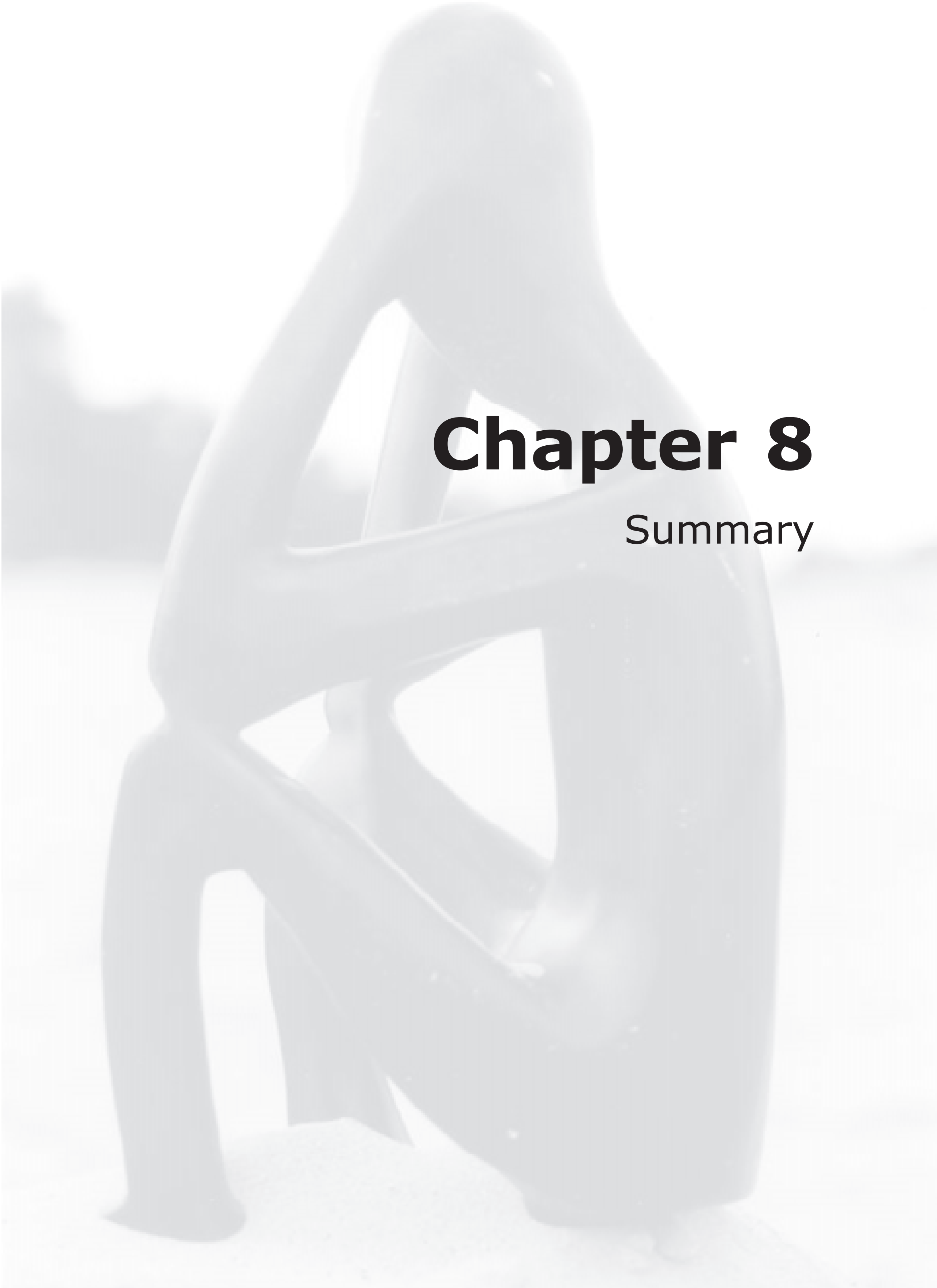


Chapter 8

Summary

A surgeon faced with a patient presenting with an open tibial/fibular fracture in combination with severe damage of the surrounding soft tissues, has to make the difficult decision whether to attempt salvage or to perform an immediate amputation of the leg.

Nowadays, attempt at salvage is frequently chosen, because due to modern reconstructive techniques this is successful in the majority of cases. However, in some patients - for example due to persisting ischemia of the lower leg or to concomitant life-threatening injuries - it is obvious that immediate (primary) amputation is the option of choice. Unfortunately, in some of these cases nevertheless salvage is attempted - mainly due to a combination of wrong clinical judgement and optimistically thinking of the surgeon. Although these attempts seem successful eventually, after a long period of untreatable infections and other complications (secondary) amputation has to be performed as yet. These patients generally undergo more and more complex operations, and suffer more from complications than patients with a primary amputation. It is clear that it should be avoided that a patient will end up in such a situation. In this thesis we highlight the treatment, complications, and long-term consequences of severe open tibial fractures.

The treatment of these fractures can only be successful if it is tailored to the individual needs and specific circumstances. A consequent step-by-step approach is imperative, starting with proper classification of the injuries, followed by the planning of necessary procedures. In **Chapter 2**, the most commonly used classification systems for (open) fractures are discussed; the AO Comprehensive Classification of Fractures of Long Bones, the Tscherne Oestern Classification of closed fractures with concomitant soft-tissue injury, and the Gustilo Classification of open fractures. Subsequently, the present treatment options of open tibial fractures are discussed. Four cornerstones are essential: 1) vigorous and repeated debridement; 2) immediate fracture stabilisation using different methods depending on the fracture type and site, the soft-tissue condition and contamination, the condition of the patient, and personal preference; 3) early soft-tissue reconstruction and; 4) secondary surgery to promote fracture healing and/or to reconstruct skeletal defects if needed.

The major decision in treating mangled lower legs is not whether one *can*, but whether one *should* attempt salvage. The decision is often clearly mandated by the nature and extent of the lower extremity injury, and the patient as a whole. In **Chapter 3.1**, the factors playing a decisive role in the choice between attempt at salvage and primary amputation are discussed successively. These factors can be divided in three categories: patient-related (age, co-morbidity, and smoking behaviour), local trauma-related (mechanism of injury, fracture pattern, soft-tissue injury, vascular injury, neurological injury, ipsilateral injury, and contamination), and general trauma-related (injury severity, shock, and hypothermia).

Based on the mentioned variables several predictive scoring systems have been developed to objectify the regional injury severity of the limb in order to assist the surgeon in decision-making. Ideally, by early discriminating between limbs requiring amputation and those likely to be salvaged successfully, delayed amputations are prevented. However, for clinical use it is imperative that the respective scoring system predicts correctly with absolute certainty. In **Chapter 3.2**, the results of a retrospective evaluation of the utility of six of the most described scoring systems in 57 patients with a (Gustilo grade III) open tibial fracture are reported. Based on our data, the scoring systems predicted outcome correctly in about 80% of the cases. Although this percentage seems high on the first sight, it must be emphasised that in one of five patients a false prediction would have been produced. If the decision was solely based on the result of the scoring system, too many patients would undergo primary amputation, and too often salvage would be attempted unrealistically - with all consequences. We conclude that the present scoring systems have limited clinical value and cannot be used as a reliable criterion for decision-making in patients with a mangled lower leg. Until a more rigid protocol is developed, decision-making must rely upon a flexible approach that considers the array of the previously discussed local and general variables.

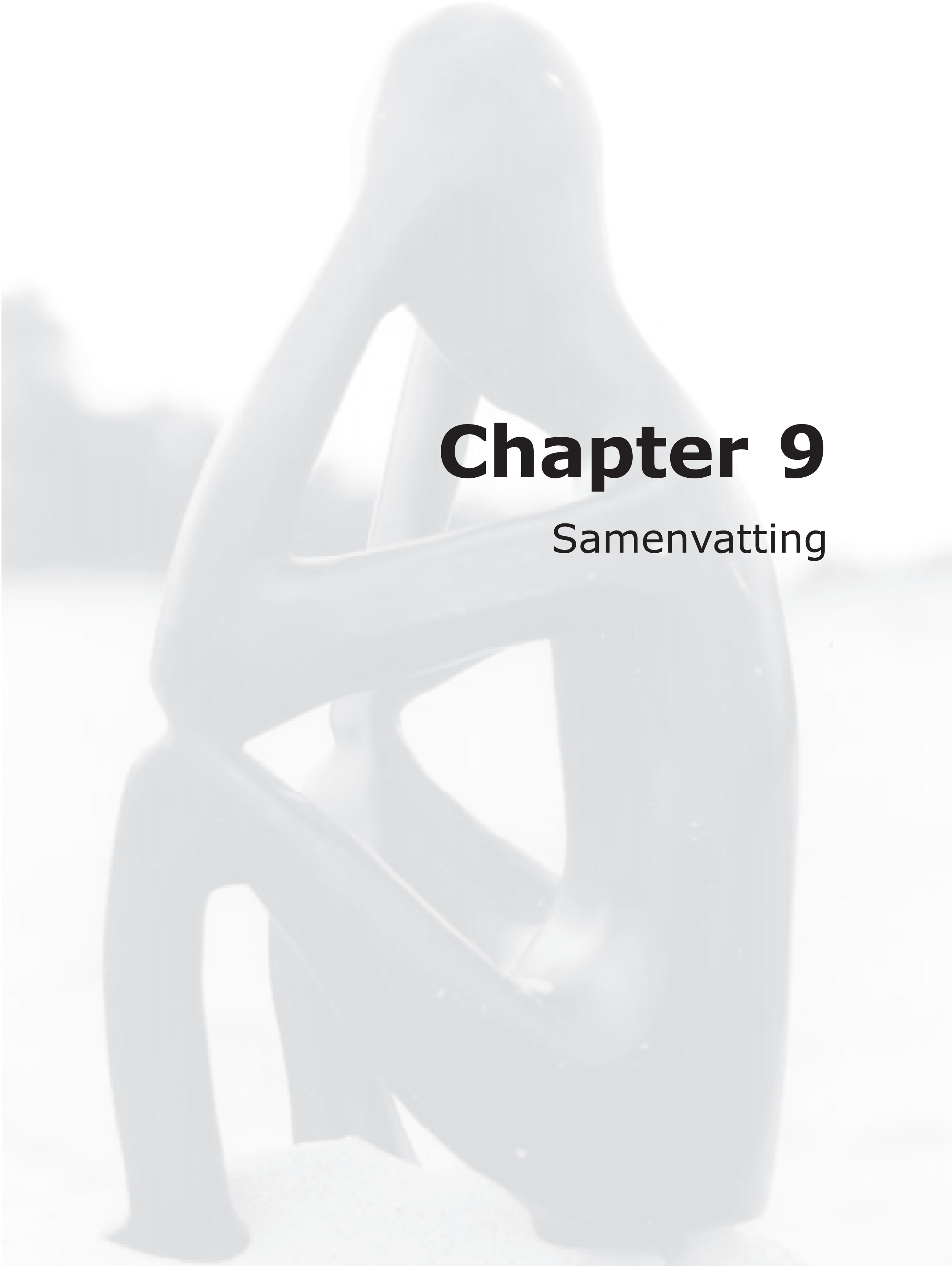
Of several disorders – especially of cardiovascular and pulmonary origin - the adverse effects of and the association with smoking is already known for decades. In recent years, there has been a growing interest in the possible adverse effects of smoking on soft-tissue and bone healing. In **Chapter 4.1**, the current knowledge on the pathophysiology of smoking and its clinical effects on bone and soft tissues in general, and on the healing of injuries in particular, are discussed.

There are strong indications that smoking gives problems in the consolidation of fractures as well, although up to now this is hardly confirmed by clinical studies. In **Chapter 4.2**, we describe the results of a retrospective study on the effects of smoking on the outcome of fracture treatment. We included 118 patients with 125 open tibial fractures, whom were treated at the UMC Utrecht in the period January 1994 till December 2000. The study group consisted of 48 (33%) fractures of smokers and 77 of non-smokers. At the time of the study, 45 of 48 (94%) fractures in the smoking group were healed, compared with 74 of 77 (96%) in the non-smoking group. The mean time to consolidation was 33 weeks for smokers and 26 weeks for non-smokers (significant difference). Twenty-four (49%) fractures in the smoking group and 27 (35%) in the non-smoking group were re-operated on due to delayed union. Healing disturbances of the traumatic wound occurred proportionately in both groups. However, there was a significant difference in the presence of osteitis to the prejudice of smokers. Moreover, they stayed longer in hospital and underwent more operations. The results of our study confirm that smoking is negatively associated with fracture healing. On the basis of data in the literature and the results of our study, we strongly advise smoking patients presenting with an open tibial fracture, to stop smoking immediately and to continue this during the full rehabilitation course.

Despite major advances in diagnostics and treatment of mangled lower legs, each attempt at salvage may lead to severe complications. One of the most dramatic problems is an infected segmental defect pseudarthrosis of the tibia. In these cases, there is a complete interruption of the continuity of the tibia associated with infection of the bone ends and surrounding soft tissues. A stepwise approach with scheduled (re-)operations is mandatory, aiming at control of the infection, stabilisation of the pseudarthrosis, adequate soft-tissue coverage, and skeletal reconstruction. In **Chapter 5**, we describe our experiences with a consequent and protocolised therapeutic approach of this difficult problem in 18 patients. In 12 (67%) patients limb salvage was successful. In this group, the mean time to healing was 17 (4-30) months since our start of pseudarthrosis treatment. Personal examination of patients with a salvaged limb revealed good clinical results in all. Most patients had no or little limitations in daily life and were back to work. Six (33%) patients required (secondary) amputation, after on average six (1-10) months. The main reason for amputation was continuous pain in two patients, healing disturbances in two other (high-aged) patients, lack of clinical progression despite multiple operations in another, and a disturbed healing due to a poor general health condition in the last. Because of the huge physical, psychological and economical impact, and the unremitting suspense about outcome in some cases, proceeding of the limb salvage process has to be questioned repeatedly. This decision should be made consciously - regarding the clinical situation, the presence of co-morbidity, and the patient's age, expectations and compliance. If successful, the ultimate functional outcome will be good in the majority of cases.

The objective of therapy of patients with severe lower limb injury is to achieve the best overall function for the patient. There is little reported research on the long-term outcome and the quality of life of these patients. We retrospectively compared the various treatments, the complications and the end stage function. - including the quality of life - of patients who had had successful limb salvage with those who underwent amputation (**Chapter 6**). In the period 1992-1997, 64 patients presented with 66 Gustilo grade III open tibial fractures. In 44 cases the limb could be salvaged (group A), in the other 22 amputation had to be performed (group B); 14 times this was primary (less than 1 week from injury), eight times secondary. Patients who underwent a primary amputation had a shorter stay in hospital, underwent fewer operations, and suffered fewer complications than patients who had successful limb salvage. On the contrary, patients with a secondary amputation stayed much longer in hospital and underwent more operations. Clinical outcome was measured by using the *Guides to the Evaluation of Permanent Impairment* of the American Medical Association. The lower extremity impairment was 17.6% for patients in group A and 73.5% for patients in group B. The quality of life was assessed with three questionnaires - the Nottingham Health Profile (NHP), the SF-36, and an especially for this study designed questionnaire. The results on both NHP and SF-36 showed that both patients groups had more problems in most of the categories than a healthy reference group. In the NHP, the difference in score was the largest for the categories ‘pain’, ‘mobility’, ‘energy’, and ‘sleep’. In group A, 52% of the patients indicated that their state of health interfered with the ability to do the household, and 49% of the patients indicated it interfered with their recreational activities. These percentages were, respectively, 56% and 56% for the patients in group B, and 4% and 5% for the (healthy) reference group. The SF-36 scores correlated well with the NHP scores. It has to be emphasized that no significant differences regarding disability were found between both study groups.

Open tibial fractures with severe damage of the surrounding soft tissues remain challenging problems. The aspirations for both surgeon and patient are a normally functioning limb - which can rarely be achieved. By choosing a consequent and stepwise approach most of these limbs can be salvaged, although primary amputation will stay the best option in selected cases. It is nevertheless important to realise that both successful limb salvage and early amputation rarely return the patient to a normal, pain-free life.



Chapter 9

Samenvatting

Een chirurg die wordt geconfronteerd met een patiënt met een gecompliceerde onderbeenfractuur (een botbreuk van het onderbeen met een open verbinding naar de buitenwereld) in combinatie met ernstige beschadiging van de omgevende weke delen, staat voor de moeilijke beslissing om een poging tot behoud te ondernemen of om onmiddellijk over te gaan tot amputatie van het been.

Tegenwoordig wordt vaak gekozen voor een poging tot behoud, omdat het dankzij moderne reconstructieve technieken mogelijk is om de meerderheid van dergelijke onderbenen te “redden”. Er zijn echter ook patiënten - bijvoorbeeld die met een te langdurige onderbreking van de bloedvoorziening van het onderbeen of met levensbedreigende letsels elders in het lichaam - bij wie vanaf het eerste moment duidelijk is dat primaire (onmiddellijke) amputatie is aangewezen. Helaas wordt soms - meestal door de combinatie van een onjuiste inschatting en een te optimistische kijkvan het behandelend team - ten onrechte getracht zo’n onderbeen toch te redden. Hoewel deze pogingen dan aanvankelijk lijken te slagen, blijkt na een periode van onbehandelbare infecties en andere complicaties dat alsnog moet worden overgegaan tot een (secundaire) amputatie. Voor het zover is worden deze patiënten in het algemeen zeer lang (klinisch) behandeld, ondergaan ze meer en complexere chirurgische ingrepen en lopen ze vaker complicaties op dan patiënten met een primaire amputatie. Het is duidelijk dat getracht moet worden om te voorkomen dat een patiënt in een dergelijke situatie terechtkomt. In dit proefschrift staan de behandeling, complicaties en lange-termijngevolgen van patiënten met een extreem gecompliceerde onderbeenfractuur centraal.

De behandeling van dergelijke fracturen kan alleen dán succesvol zijn als die wordt toegespitst op individuele behoeften en specifieke omstandigheden. Een consequente en stapsgewijze benadering is daartoe essentieel, startend met de exacte classificatie van het letsel, gevolgd door planning van de noodzakelijk geachte ingrepen. In **hoofdstuk 2** worden de meest gebruikte classificatie systemen voor fracturen besproken; de AO Comprehensive Classication of Fractures of Long Bones, de Tscherne-Oestern Classification voor weke-delen letsel bij gesloten fracturen en de Gustilo Classification voor gecompliceerde fracturen. Vervolgens komen de huidige, gangbare behandelingen van gecompliceerde onderbeenfracturen aan bod. Die zijn gebaseerd op vier hoekstenen: 1) uitgebreid en herhaald débridement (verwijdering van verontreinigd, slecht doorbloed of dood weefsel); 2) onmiddellijke stabilisatie van de fractuur met gebruik van interne en/of externe fixatiemethoden, dit laatste afhankelijk van type en lokalisatie van de fractuur, letsel van de weke delen, mate van contaminatie, algehele conditie van de patiënt en persoonlijke voorkeur; 3) vroege reconstructie van de weke delen en 4) aanvullende ingrepen om de fractuurgenezing te bevorderen of om eventueel aanwezige botdefecten te reconstrueren.

De belangrijkste vraag bij de behandeling van een onderbeenfracturen met ernstig weke-delenletsel is niet of het *mogelijk* is het onderbeen te behouden, maar of dit *verstandig en zinvol* is. Het besluit is uiteraard vooral afhankelijk van soort en ernst van de letsels en de toestand van de patiënt in het algemeen. In **hoofdstuk 3.1** worden de factoren die van invloed zijn bij de keuze tussen een poging tot behoud of primaire amputatie van het been afzonderlijk besproken. Globaal kunnen deze factoren worden ingedeeld in drie categorieën: patiëntgebonden (leeftijd, onderliggende aandoeningen en rookgedrag), lokaal, ongeval-gerelateerd (ongevalmechanisme, type fractuur, ernst van weke-delen letsel, mate van contaminatie, eventueel vaat- en/of zenuwbeschadiging of overige letsels aan hetzelfde been) en algemeen, ongeval-gerelateerd (ernst van het totaal aan verwondingen, shock en onderkoeling).

Op basis van bovengenoemde factoren zijn verschillende scoresystemen ontwikkeld die de chirurg zouden kunnen helpen bij het nemen van de beslissing om het onderbeen te amputeren dan wel om te pogen het te behouden. Door snel duidelijkheid te krijgen over de "ideale" behandeling voor de betreffende patiënten met specifieke letsels van het onderbeen zou het aantal late amputaties beperkt kunnen worden. Een voorwaarde voor gebruik in de kliniek is wel dat het scoresysteem met een grote zekerheid correct moet kunnen voorspellen of een patiënt inderdaad het best geholpen is met de gekozen behandeling. In **hoofdstuk 3.2** worden de resultaten beschreven van een retrospectief onderzoek dat we uitvoerden - naar de waarde van de zes meest beschreven scoresystemen - bij 57 patiënten met een gecompliceerde tibia fractuur met ernstig weke-delen letsel (Gustilo graad III). Gebaseerd op onze patiëntgegevens bleken alle scoresystemen in ongeveer 80% van de gevallen het eindresultaat correct te voorspellen. Hoewel dit percentage op het eerste gezicht hoog lijkt, moet met nadruk worden vermeld dat dus bij één op de vijf patiënten een verkeerde voorspelling zou zijn gedaan. Als de keuze volledig zou worden gebaseerd op de uitkomst van een scoresysteem zouden te veel patiënten ten onrechte een amputatie primair worden aangedaan, maar tevens zou te vaak een onrealistische poging tot behoud worden ondernomen, met alle gevolgen van dien. We concluderen derhalve dat de bestaande scoresystemen alleen niet betrouwbaar genoeg zijn om in de praktijk het beleid op te baseren. Bij de behandeling van een individuele patiënt met een specifieke gecompliceerde onderbeenfractuur is een genuanceerde aanpak van het probleem noodzakelijk, waarbij de eerder genoemde lokale en algemene factoren een belangrijke rol spelen bij de besluitvorming.

Van diverse aandoeningen - met name op het vlak van de hart-, vaat- en longziekten - is de negatieve invloed van en het verband met roken al tientallen jaren bekend. Pas in de afgelopen jaren is er ook aandacht gekomen voor de gevolgen van roken op de genezing van bot- en weke-delen letsels. In **hoofdstuk 4.1** geven we een overzicht van de pathofysiologie van het roken en de klinische effecten ervan op bot- en weke delenweefsel in het algemeen en op de genezing van verwondingen in het bijzonder.

Hoewel er sterke aanwijzingen zijn dat roken ook problemen geeft bij de genezing van fracturen, is dit fenomeen nauwelijks door klinische studies bevestigd. In **hoofdstuk 4.2** worden de resultaten beschreven van een retrospectief onderzoek naar de invloed van roken op de uitkomsten van fractuur behandeling. Wij voerden dit uit bij 118 patiënten met 125 gecompliceerde tibia fracturen, die in de periode januari 1994 en december 2000 in het UMC Utrecht werden behandeld. De onderzoeksgroep bestond uit 48 (38%) fracturen bij rokers en 77 bij niet-rokers. Ten tijde van het onderzoek waren 45 van de 48 (94%) fracturen in de rokersgroep genezen, tegenover 74 van de 77 (96%) in de niet-rokers groep. De gemiddelde duur tot consolidatie (benige verbinding van de fractuurdelen) was 33 weken voor rokers en 26 voor niet-rokers (een significant verschil). Vierentwintig (49%) fracturen van rokers en 27 (35%) van niet-rokers moesten opnieuw worden geopereerd vanwege vertraagde consolidatie. Wondgenezingsstoornissen traden proportioneel op in beide groepen. Er was echter wel een significant verschil in het voorkomen van posttraumatische osteïtis (botinfectie), ten nadele van rokers. Daarnaast moesten rokers significant vaker en langer worden opgenomen en ondergingen zij meer operaties. Ons onderzoek bevestigt dat er een negatief verband bestaat tussen roken en fractuurgenezing. Op basis van gegevens uit de literatuur en de resultaten van ons onderzoek adviseren wij om rokers die een gecompliceerde tibia fractuur oplopen, op het hart te binden om te stoppen met roken en dit gedurende de gehele behandeling vol te houden.

Ondanks grote vooruitgang in de diagnostiek en behandeling van ernstig gecompliceerde onderbeenfracturen kan elke poging tot behoud soms tot ernstige complicaties leiden. Eén van de meest dramatische problemen is een geïnfecteerde pseudarthrose van de tibia met een segmenteel botdefect. Er is hier dan sprake van een volledige onderbreking van de continuïteit van het scheenbeen met een infectie van de fractuurstukken en de omgevende weke-delen weefsels. In deze gevallen is een stapsgewijze aanpak met geplande (re)operaties noodzakelijk, met als doelen om de infectie te genezen, de pseudarthrose te stabiliseren, een adequate bedekking met weke delen te verkrijgen en het botdefect te reconstrueren. In **hoofdstuk 5** beschrijven we onze ervaring met dit behandelregime bij 18 patiënten met een dergelijk intens complex probleem van het onderbeen. Bij 12 (67%) van hen was de poging tot behoud succesvol. In deze groep duurde het gemiddeld 17 (4-30) maanden na starten van onze behandeling alvorens consolidatie was bereikt. Klinisch onderzoek toonde aan dat bij hen het eindresultaat in het algemeen goed was. De meeste patiënten voelden zich niet sterk beperkt in het dagelijks leven en hadden hun werk weer hervat. In zes gevallen werd in de loop van de behandeling alsnog tot amputatie van het onderbeen overgegaan - gemiddeld na zes (1-10) maanden. Twee maal was onhoudbare pijn ter plaatse van de pseudarthrose de belangrijkste reden, twee maal een slechte genezingstendens bij een hoge leeftijd, één maal onvoldoende vooruitgang ondanks vele ingrepen en één maal een gestoorde wondgenezing bij patiënt in een slechte algehele conditie. Vanwege de enorme fysieke, psychologische en economische consequenties, en de voortdurende onzekerheid over de uitkomst, moet telkens worden afgevraagd of de poging tot behoud mag worden doorgezet. Deze beslissing moet weloverwogen worden genomen, met inachtneming van de klinische toestand, de aanwezigheid van onderliggende aandoeningen én de leeftijd, verwachtingen en medewerking van de patiënt. Indien succesvol, is de klinische eindsituatie in de meeste gevallen goed.

De behandeling van patiënten met een ernstig onderbeenletsel heeft als doel om tot een zo goed mogelijk functioneel eindresultaat te komen. Er is slechts weinig onderzoek verricht naar de lange-termijn gevolgen en kwaliteit van leven van de patiënten. Wij vergeleken retrospectief de verschillende behandelingen, de complicaties en de eindfunctie - inclusief kwaliteit van leven - van patiënten die hun onderbeen behielden dan wel amputatie ondergingen (**hoofdstuk 6**). Van de 64 patiënten die zich in periode 1992-1997 presenteerden met 66 Gustilo graad III-gecompliceerde tibia fracturen, kon in 44 gevallen het onderbeen worden behouden (groep A) en werd 22 maal een amputatie uitgevoerd (groep B); 14 maal was deze primair (binnen 1 week na het ongeval) en acht maal secundair. Patiënten met een primaire amputatie werden gemiddeld korter opgenomen, ondergingen minder operaties en liepen minder complicaties op dan patiënten met een behouden onderbeen. Bij patiënten met een secundaire amputatie was het aantal opnamen en operaties daarentegen aanmerkelijk hoger. De klinische eindfunctie werd gescoord volgens richtlijnen van de American Medical Association (AMA). Hieruit bleek dat de beperking van de onderste extremiteit 17.6% bedroeg voor patiënten in groep A en 73.5% voor patiënten in groep B. De kwaliteit van leven werd gemeten met een drietal vragenlijsten - de Nottingham Health Profile (NHP), de SF-36 en een speciaal voor dit onderzoek ontworpen lijst. De resultaten van zowel NHP als SF-36 lieten zien dat de patiënten in beide onderzoeksgroepen in de meeste categorieën veel meer problemen hebben dan een gezonde referentiegroep. Voor de NHP was het verschil het grootst voor de categorieën pijn, mobiliteit, energie en slaap. In groep A gaf 52% van de patiënten aan dat hun gezondheid hen beperkte in het huishouden en 49% gaf te kennen dat het hen belemmerde in het uitoefenen van hobby's. Deze percentages waren respectievelijk 56% en 56% voor de patiënten in groep B en 4% en 5% voor de (gezonde) referentiegroep. De scores van de SF-36 kwamen goed overeen met die van de NHP. Opvallend was dat er geen significante verschillen werden waargenomen tussen beide groepen.

Een gecompliceerde tibia fractuur in combinatie met een ernstige beschadiging van de omgevende weke delen blijft een uitdaging voor het behandelend team. De wens van zowel de chirurg als de patiënt is een normaal functionerend been - iets wat vaak niet kan worden bereikt. Door te kiezen voor een consequente en stapsgewijze benadering kunnen de meeste onderbenen worden behouden, maar voor enkele patiënten blijft een vroege amputatie echter de beste optie. Het is hoe dan ook belangrijk om te beseffen dat zowel succesvol behoud van het onderbeen als amputatie de patiënt geenszins leidt naar een normaal, pijnvrij bestaan.

Dankwoord
&
Curriculum vitae

DANKWOORD

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CURRICULUM VITAE

The author of this thesis was born on May 29th, 1975, in Gouda, The Netherlands. He attended secondary school at the Dr. F.H. de Bruyne Lyceum in Utrecht and graduated in 1993. The same year he started medical school in Antwerp, Belgium, where he passed his first year's exams. Afterwards, he was admitted to medical school in Utrecht, The Netherlands, and returned to the city where he had grown up.

During his study, he was active in several committees at the Faculty of Medicine and nationally. In 1996, he set up the students' edition of the Dutch Medical Journal (*Nederlands Tijdschrift voor Geneeskunde - Studenteneditie*), of which he was editor-in-chief till 2000. In the academic year 1998-1999, he was the students' advisor of the dean (successively, prof. dr. W.H. Gispen and prof. dr. J.S. Stoof) and president of the national Medical Students Council (Studenten Overleg Geneeskunde). In the same year, he started doing research at the Department of Surgery (University Medical Centre Utrecht), which resulted in this thesis. As an intern, he worked four months at the Trauma Unit of the Groote Schuur Hospital, Cape Town, South-Africa (head: dr. P.C. Bautz), and two months at the Department of Gynaecology of the North-Western Adelaide Health Service, Adelaide, Australia (head: prof. dr. G.A. Dekker).

After graduating from medical school in 2001, he started working as a junior resident in general surgery at the University Medical Centre Utrecht, Utrecht, The Netherlands.