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Patients with femoral and tibial shaft fractures: aspects on epidemiology and pain therapy

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Patients with femoral and tibial shaft fractures: aspects on epidemiology and pain therapy

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To the man who put me on the right track since I was a young child. He showed me all good values a human being could have and taught me the art of respectfully dealing with patients and not only treating them. I dedicate this work to you, my first and best tutor in life, my dear uncle Professor ***Taher Q. Al-Dabbagh***, Mosul, Iraq.

ABSTRACT

Background

Fractures of the tibial and femoral shafts are common injuries with outcomes depending on injury mechanism, fracture pattern, patient-specific data and treatment methods. Nationwide epidemiological data on these often serious injuries are sparse. Information on long-term therapy with opioids in these patients is lacking in the literature. Therefore, the aim of the present thesis was to study the incidence, mechanism of injury and treatment methods of patients with tibial and femoral shaft fractures. Soft tissue reconstructions and amputations after open tibial fractures in Sweden were also analyzed. Moreover, the long-term pattern of opioid prescriptions in patients after tibial and femoral shaft fractures was examined on a nationwide basis.

Patients and methods

Data on all hospital admissions for tibial and femoral shaft fractures during 1998-2004 (study I-II) and for open tibial fractures during 1998-2010 (study III) were extracted from the Swedish National Hospital Discharge Register. Incidence rates (IR) per 100,000 person-years (pyr), mechanisms of injury, surgical interventions and amputation rates were analyzed. The Swedish Prescribed Drug Register was used to extract data on long-term opioid prescriptions for patients sustaining tibial (study IV) and femoral (study V) shaft fractures during 2005-2008. Age- and sex-matched control groups without the index fracture were gathered from the Total Population Register for comparisons.

Results

Study I: 10,627 admissions for tibial shaft fractures corresponding to an annual IR of 17/100,000 pyr were identified. The number of hospital admissions declined by 12% during the study period with more reduction in male incidence. Most admissions were found in the age-groups 10-19 years in males and 50-59 years in females.

Study II: 6,409 admissions for femoral shaft fractures were identified corresponding to an annual IR of 10/100,000 pyr. The total number of hospital admissions remained stable during 1998-2004. Most admissions were generated by females in the 80-89 years age-group and by males under the age of 10 years.

Study III: Of 3,777 patients with open tibial fractures, 9% underwent soft tissue reconstructive surgery. The overall rate of amputation was 3.6%. The risk of amputation according to an adjusted analysis was increased in patients older than 70 years (OR 2.7) and in patients who underwent soft-tissue reconstructions (OR 3.1).

Study IV: A total of 2,571 patients with isolated tibial shaft fractures were identified, of whom 25% filled prescriptions of strong opioids after the fracture. An adjusted analysis revealed that older patients (>=50 years) were more likely to end opioid prescriptions (HR 1.5). At six, 12 and 18 months after the fracture, 21%, 14% and 11% of the patients respectively, were still getting prescribed opioids.

Study V: A total of 1,471 patients with isolated femoral shaft fractures were identified, of whom 61% received prescriptions of opioids (strong and/or weak) during a median follow-up of 20 months. In the age- and sex-matched control cohort without fracture (7,339 individuals), 25% had opioid prescriptions dispensed during the same period.

Conclusions

Nationwide epidemiological data on patients with tibial and femoral shaft fractures can be used by healthcare providers to plan hospital beds, surgical interventions, risk preventions and centralization of more complicated injuries. The amputation rate after open tibial fractures is low. The risk of amputation is increased in older patients and if the reconstruction is delayed beyond 72 hours. A notable proportion of patients continue to receive prescribed opioids several months after femoral and tibial fractures. However, the risk of dose escalations seems to be small.

LIST OF SCIENTIFIC PAPERS

I. Decreasing incidence of tibial shaft fractures between 1998 and 2004: information based on 10,627 Swedish inpatients.

Weiss RJ, Montgomery SM, Ehlin A, **<u>Al Dabbagh Z</u>**, Stark A, Jansson KÅ.
Acta Orthop. 2008 Aug;79(4):526-33.

II. National data of 6409 Swedish inpatients with femoral shaft fractures: stable incidence between 1998 and 2004.

Weiss RJ, Montgomery SM, **<u>Al Dabbagh Z</u>**, Jansson KÅ.
Injury. 2009 Mar;40(3):304-8.

III. Lower extremity soft tissue reconstruction and amputation rates in patients with open tibial fractures in Sweden during 1998-2010.

Tampe U, Weiss RJ, Stark B, Sommar P, **<u>Al Dabbagh Z</u>**, Jansson KÅ.
BMC Surg. 2014 Oct 16;14:80.

IV. No signs of dose escalations of potent opioids prescribed after tibial shaft fractures: a study of Swedish National Registries.

<u>Al Dabbagh Z</u>, Jansson KÅ, Stiller CO, Montgomery S, Weiss RJ.
BMC Anesthesiol. 2014 Jan 13;14:4.

V. Long-term pattern of opioid prescriptions after femoral shaft fractures.

<u>Al Dabbagh Z</u>, Jansson KÅ, Stiller CO, Montgomery S, Weiss RJ.
Acta Anaesthesiol Scand. 2016 May;60(5):634-41.

CONTENTS

LIST OF ABBREVIATIONS

B-value	Regression coefficient
CI	Confidence interval
HR	Hazard ratio
ICD	International classification of diseases
ICD-E	External codes
IQR	Interquartile range
IR	Incidence rate
IRR	Incidence rate ratio
MED	Morphine equivalent dose
NSAIDs	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
PYR	Person-years
SD	Standard deviation
SNHDR	Swedish National Hospital Discharge Register
SPDR	Swedish Prescribed Drug Register
SFR	Swedish Fracture Register
TPR	Total Population Register

1 INTRODUCTION

1.1 Background and motivation

Shaft (diaphyseal) fractures of the tibia and femur are common and often serious injuries that almost always require hospitalization and surgical treatment. Patients sustaining these fractures become often immobilized in bed or unable to walk properly for a considerable period of time. Moreover, these injuries are painful and many patients need strong analgesic drugs during the fracture healing and rehabilitation process. These fractures, their complications and the need for often long rehabilitation and pain therapy, impose a high burden on the patients, the health-care system as well as on the community at large.

The outcome of these injuries depends on several patient- and fracture-related characteristics which influence treatment methods and the risk of complications. Some of these injuries such as open fractures after crush injuries need multidisciplinary management to avoid amputation and life-threatening complications. In clinical practice, the long-term treatment of patients with these fractures with opioid analgesic drugs often raises concerns among physicians and health care providers regarding the risk of dose escalations, addiction and abuse problems.

Previously published studies on a nationwide basis on patients with lower limb injuries are either sparse or lacking in the literature. Most other studies addressing fractures of the lower limbs are limited to case-series from single hospitals or counties. Moreover, there are no previous studies on the long-term prescriptions of opioid analgesics after long bone injuries on a nationwide basis.

1.2 Tibial shaft fractures

The lower leg contains two major long bones, the tibia and the fibula. The tibia is the stronger and the larger of the two bones. The fibula articulates to the tibia by a synovial joint proximally and by a fibrous tissue (syndesmosis) distally as well as a strong inter-osseous membrane in between. The shaft of the tibia is the part of the bone that extends from below the insertion of the patellar tendon at the tuberosity down to about five cm proximal to the ankle joint. The tibia carries about five times the body weight of the axial force during walking [1]. The medial surface of the tibia is subcutaneous making the bone vulnerable to direct injuries with higher risk of acute compartment syndrome as compared with other long bones. Furthermore, a closed fracture of the tibia can easily become an open fracture with higher risk of complications and healing problems.

The annual incidence of tibial shaft fractures has been reported to be 22/100,000 inhabitants [2]. The treatment and prognosis of tibial shaft fractures are influenced by the anatomical location (proximal, middle or distal third) and fracture type (transverse, oblique, spiral or comminuted), as well as by displacement and angulation at the fracture site [3]. For both clinical and research purposes, different classification systems of tibial shaft fractures have been developed both for the fracture and for associated soft tissue injuries [4, 5]. Fractures of the tibial shaft are among the most common of serious skeletal injuries in all age-groups [6]. They are slow to heal and frequently cause permanent morbidity [7]. Nonunion rates of up to 17% have been reported in the literature imposing significant health and economic burdens [8, 9].

Tibial shaft fractures with an intact fibula are common. An intact fibula has been blamed to be a cause of nonunion by some authors [10], while others did not find any significant influence on union rates or functional results even in patients with open fractures [11]. Interlocking reamed intramedullary nailing has become the gold standard for treatment of displaced tibial shaft fractures with an overall postoperative infection rate within one year of 3%

[12, 13]. The majority of all previously published studies on the incidence of tibial shaft fractures were limited to single hospitals or regions and with varying results [14-20].

1.3 Femoral shaft fractures

The femur is the longest, strongest and largest tubular bone in the human body. The shaft (diaphysis) is the portion of the bone between a point five cm distal to the lesser trochanter to eight cm proximal to the adductor tubercle. In contrast to the tibial shaft, no part of the femoral shaft is subcutaneous and both acute compartment syndrome and open fractures are uncommon. Fractures of the femoral shaft are among the most common major injuries that an orthopaedic surgeon is required to treat. They are common in all age-groups and almost always require admission to a hospital and surgical treatment [21, 22]. Intramedullary nailing with various techniques has become the standard treatment of femoral shaft fractures in adults. In children under six years of age, non-surgical treatment has always been the gold standard. External fixation has become more popular in children at school age decreasing inpatient time and improving early mobilization [23, 24].

Despite modern treatment, both tibial and femoral shaft fractures can cause long-term morbidity with residual dysfunction one year after injury and often poor outcome in patients with delayed union or nonunion of the fracture [25]. The clinical outcome varies depending on several patient- and fracture-specific characteristics with greatest morbidity associated with high-velocity trauma [26]. As in tibial shaft fractures, it is commonly assumed that femoral shaft fractures are mainly caused by high-energy trauma in younger patients [27].

In contrast to fractures of the femoral neck and the trochanteric region, little attention has been given to the risk of femoral shaft fractures associated with low-energy trauma in older patients [14, 27-31]. The few previously published studies were retrospective or limited to case-series from single hospitals or regions [2, 15, 27, 32].

1.4 Open fractures

A fracture with communication of the bone with the exterior of the body is classified as an open fracture. The soft tissue injury may range from a small skin penetration by a spike of bone at the fracture site (open from within) in a low-energy trauma to an extensive injury with big lacerations and damage of blood vessels and nerves leading to amputation. In clinical practice, open fractures are commonly graded according to the Gustilo-Anderson classification into types I-III, with subgroups A-C in type III, depending on the size of the skin laceration, the degree of contamination, the extent of soft tissue injury and the fracture configuration [33]. A Gustilo type IIIB injury shows extensive damage with periosteal stripping and bone exposure with inadequate soft tissue coverage. Therefore, these injuries often need some kind of soft tissue reconstruction.

Open fractures are associated with high complication rates regarding soft tissue infection, osteomyelitis, malunion and nonunion of the fracture as well as the risk of amputation [34, 35]. In a prospective observational study, Enninghorst et al. showed that early debridement and stabilization of open tibial fractures (mean eight hours after injury) eliminated the degree of contamination and the time to debridement as predictors of poor outcome [36] . In this study, 67% of the fractures healed at one year, deep infection was seen in 17% and 6% of the patients needed amputation [36]. In another observational study on tibial shaft fractures, open fractures were seen in 22% of the patients showing a higher risk of nonunion compared with closed fractures (OR 2.2) [37]. The incidence rate of open fractures of long bones have been found to be

11.5/100,000 pyr in epidemiological studies, with a large proportion occurring in the tibia [18, 38-40].

In patients with severe Gustilo type III fractures, the choice between re-construction and amputation has been discussed in some studies [33, 35, 41-43]. In a study on patients with leg-threatening injuries, a similar clinical outcome was found after limb salvage compared with primary amputation at two years follow-up [41]. Other studies had shown better cost-utility outcome after reconstruction and a trend towards limb salvage rather than amputation, due to improved reconstruction techniques [35, 44].

Patients sustaining major lower limb injuries often suffer from long-lasting pain following discharge from hospital. In clinical practice, a considerable proportion of these patients need opioid therapy despite concerns about prolonged use and risks for dose escalations or addiction problems. Previous published literature in this field is sparse and nationwide studies with long-term follow-up are lacking [45].

1.5 Sources of epidemiological data

1.5.1 The Swedish National Hospital Discharge Register (SNHDR)

In Sweden with a population of over nine million, inpatient care is publicly funded and available to all inhabitants. Each resident, native or immigrant has a unique 10-digit national identification number which includes date of birth and sex. During every hospitalization, it is obligatory to register dates of admission and discharge, codes for the main diagnosis with up to seven contributory diagnoses including complications, as well as interventions including up to 12 surgical procedure codes. In addition, a code for the mechanism of injury (external codes) and other demographic data are registered.

The SNHDR is a nationwide, government controlled and publicly funded database which was started in 1964 and completed its coverage of all diagnoses including injuries in 1987 [46]. It covers at least 98% of all hospital admissions in Sweden. Validation surveys indicated almost 90% accuracy of diagnosis and surgical procedure codes when compared with medical files [47].

Diagnosis codes are registered according to the International Classification of Diseases (ICD). The old ICD-9 version was replaced by the current ICD-10 version in Sweden during 1997. One county (Skåne), however, continued using the older version throughout 1997 but changed to the current version on January 1st 1998. Codes for surgical procedures and interventions follow the classification by the Swedish Board of Health and Welfare (revised in 2004). Bone- and fracture-specific surgical procedure codes are registered [48]. The SNHDR has all the advantages of a longitudinal register and serves as an administrative database extensively used for medical research.

1.5.2 The Swedish Prescribed Drug Register (SPDR)

Previously called the National Pharmacy Register, the SPNR was completed in July 1st 2005, including all prescriptions dispensed from pharmacies in Sweden [49]. All prescriptions of opioid analgesic drugs are included in this Register. Data obtained from the Register include the brand name of the drug, date of filling the prescription, the strength of the drug, the dose and the total number of pills prescribed. These data make it feasible to perform pharmaco-epidemiological research on a nationwide basis [50]. The Register, as with the SNHDR, is a government-controlled and validated database. The scientific output of this Register one decade after its establishment (2005-2014) included more than 300 publication, 20 of which were validation studies [51].

In a comparative study between the Netherlands and the United States, Lindenhovius et al. found notable national differences in prescribing narcotic pain medications after surgery of lower limb fractures, even when accounting for factors such as age, surgeon and duration of hospital stay [52]. These differences reflected the influence on prescribing practice imposed by national standards for pain control among both physicians and patients [52]. According to the current recommendations of the Swedish Medical Product Agency (www.lakemedelsverket.se) for the use of opioids in non-cancer pain conditions, the extent of prescribing opioids to patients should be based on individual assessment of risks and benefits. Experiences from clinical practice have suggested that strong opioids should only be prescribed in selected cases [53].

Concerns about prolonged opioid use in chronic non-cancer pain conditions, including dose escalations and abuse/addiction problems, have been discussed in the literature, mostly from the United States [54-57]. In a meta-analysis of efficacy and safety of long-term opioid therapy for chronic non-cancer pain, only few patients showed signs of abuse or addiction and many patients could discontinue the use of opioids [58]. Continuous increase in the use of opioids for non-cancer pain was reported from the US during the period 2000-2010 [59]. A cross-sectional survey from 2010 based on the Danish national register showed a 4.5% prevalence of opioid use in the general population [60]. The SPDR provides a reliable source of information to investigate these problems on a national level in long-term follow-up studies.

1.5.3 The Swedish Total Population Register (TPR)

Statistics Sweden (Statistiska Centralbyrån) is an official national institute dealing with all kinds of population registers with 100% coverage [61]. The TPR stores data on life events as birth, death, marital status, residential area and migration within Sweden as well as to and from other countries [62]. In addition, the TPR can be used to extract matched cohorts of control groups from the general population, making it possible to calculate incidence rates and estimates of the population at risk for the entire Swedish population regarding any specific disease or injury found in the SNHDR or in any other relevant health-care register. The relatively stable population volume, the well-organized public health-care system and the comprehensive population registers make Sweden an ideal country to perform epidemiological surveys and quality controls. The Swedish personal identification number acts as linkage between the different health-care registers facilitating epidemiological and clinical studies on a nationwide basis [62].

2 AIMS

The overall aim of this thesis was to describe the epidemiological profile and to investigate the use of opioid prescriptions in patients with common lower limb injuries utilizing validated national registers in Sweden.

The specific aims of this thesis were:

1. To analyze the incidence, admissions, frequency and temporal trends of patients with tibial shaft fractures (paper I).
2. To analyze the incidence, admissions, frequency and temporal trends of patients with femoral shaft fractures (paper II).
3. To describe the soft tissue reconstruction and amputation rates after open tibial fractures (paper III).
4. To study the long-term prescription pattern of strong opioids in opioid naïve patients with tibial shaft fractures (paper IV).
5. To analyze the long-term prescription pattern of all opioid analgesic drugs after femoral shaft fractures in opioid naïve patients (paper V).

3 PATIENTS AND METHODS

3.1 Study I and II

Data on all patients admitted to a hospital in Sweden between January 1st 1998 and December 31st 2004 with a discharge diagnosis of tibial (study I) or femoral (study II) shaft fractures were extracted from the SNHDR database using relevant ICD-10 diagnosis codes. The codes for shaft fractures of the tibia (study I) were: S82.20 (closed), S82.21 (open) and S82.2 (unspecified). The codes for shaft fractures of the femur (study II) were: S72.30 (closed), S72.31 (open) and S72.3 (unspecified). In addition to age and sex of the patients, information on dates of admission and discharge, length of hospital stay, mechanism of injury, methods of treatment (surgical/non-surgical) and type of surgical intervention (method of fracture fixation) were collected.

The following age categories were used: <10, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89 and >=90 years. The length of hospital stay was classified as short (<=2 days), medium (3-7 days) or long (>=8 days) duration. Mechanisms of injury were analyzed according to the ICD E-codes (external codes) and grouped into the following six categories: fall on the same level, fall from height, unspecified fall, transport accident, miscellaneous and not reported cause. Regarding the method of treatment, all patients with surgical procedure codes (NGJ09-NGJ99, TNX35 and TNX40) related to tibial shaft fractures (study I) or codes (NFJ09-NFJ99, TNX30, TNX35 and TNX40) related to femoral shaft fractures (study II) were analyzed. The surgical procedures were grouped in five categories: fixation with intra-medullary nail, fixation with plate and screws, external fixation, closed reduction and casting and other fracture surgery.

Sex- and age-specific fracture incidence rates for the Swedish population were calculated by dividing the number of admissions with relevant fractures by the total number of person-years (pyr) at follow-up. The total person-time was the sum of the number of inhabitants living in Sweden during the study period. We extracted detailed estimates of the population at risk during the study period from the TPR. Thus, incidence rates for the entire Swedish population were calculated. Number of admissions and patients, mechanisms of injury, surgical procedures and length of hospital admissions were analyzed from within the patient population.

3.2 Study III

Data on all patients (>= 15 years of age) admitted to a Swedish hospital between January 1st 1998 and December 31st 2010 with ICD-10 codes of open fractures of the proximal tibia (S82.11), the tibial shaft (S82.21) and the distal tibia (S82.31) were extracted from the SNHDR. No exclusions were made and all readmissions were included. The following data were analyzed: fracture localization in the bone, mechanism of injury, method of fixation, the type of reconstructive soft tissue procedure, timing of free or pedicle flaps, time to amputation or reconstruction after the acute injury, cause of amputation as well as the level of amputation in the extremity. Fracture incidence rates (IR) per 100,000 person-years (pyr) were calculated from the TPR. Mechanisms of injury were retrieved from ICD E-codes and divided into five categories: fall on the same level, fall from height, unspecified fall, motor vehicle accident (MVA) and miscellaneous. Fall from height and MVA were considered as high-energy injuries. Fixation methods were grouped into six categories: intramedullary nailing, plating with screws, closed reduction and casting, external fixation only, combination of external fixation and other methods of definitive fixation and miscellaneous. Reconstructive soft tissue procedures were grouped into three categories: free flap (ZZQ), pedicle flap (ZZS) and skin graft only (ZZA00). Timing of flap surgery was registered in three categories: within three days, between day four and 90 and after 90 days from injury. The level of amputation was analyzed according to the surgical procedure codes as follows: transfemoral (NFQ19), disarticulation of the knee (NGQ09), transtibial (NGQ19) and amputations through the ankle or foot (NHQ). The amputation was defined as either early (within three months) or late (after three months of the initial injury). The following causes for amputation were registered: severe acute injury, deep infection/osteomyelitis, nonunion of the fracture (pseudarthrosis), old age and other/unknown etiology.

3.3 Study IV and V

Data on all patients (>=16 years of age) admitted to a Swedish hospital between July1st 2005 and December 31st 2008 with a diagnosis of tibial (study IV) or femoral (study V) shaft fracture were extracted from the SNHDR. In both studies, a control group consisting of five individuals for each patient was extracted from the TPR. The comparators were matched for age, sex and residential area. None in the control group had been admitted to a hospital for a tibial (study IV) or a femoral (study V) shaft fracture during the study period. In both the study and control groups, persons who died or emigrated during follow-up were identified through the TPR. From the SPDR, data for opioid analgesics prescribed for all individuals included in the study (patients and controls) were extracted and analyzed. The doses obtained were converted to morphine equivalent doses (MED) using available opioid equianalgesic tables [63]. The median MED per day was calculated for each month and categorized as being low (<20 mg), moderate (20-180 mg) or high (>180 mg) [64, 65]. Patients who received opioid prescriptions prior to hospital admission for the fracture where not included in the final study cohort. In study IV, we analyzed prescriptions of strong opioids such as morphine, oxycodone or fentanyl. In study V we studied both strong and weak opioid analgesics such as tramadol and codeine.

3.4 Statistical Methods

The level of significance in all studies was set at $p<0.05$. The following statistical methods were used in the different studies.

Study I and II

Descriptive analysis was used to investigate frequency of admissions, number of patients and operations. Incidence rates and incidence rate ratios with corresponding 95% CI according to sex and age-group were calculated using the population at risk as the denominator. We performed a linear regression analysis with summary variables to record the number of admissions or the incidence rates of the fracture each year as the dependent variable and the year of discharge as the independent variable.

Study III

The Welsh two Sample t-test was used to calculate differences for mechanism of injury, sex and mean age of the amputated compared with the non-amputated patients. Fisher`s exact test was used to calculate amputation rates and rate differences in relation to the timing and the type of soft tissue reconstruction. Logistic regression analysis assessed the risk of amputation within three months after the fracture. Results were adjusted for age, sex, mechanism of injury and surgical procedure.

Study IV and V

Kaplan-Meier analysis was used to calculate the proportion of patients who received opioid prescriptions after the fracture. Opioid therapy was considered to have ceased if no new dispensed prescription was found during three (study IV) or four (study V) consecutive months. Values were expressed as medians with IQRs and 95% CIs. A Cox multiple-regression model was used to study risk factors for prolonged opioid prescriptions expressed as hazard ratios (HR) with corresponding 95% CIs. A HR >1 indicated a lower risk to continue with opioid prescriptions compared with patients in the reference group.

4 RESULTS

4.1 Study I

During the 7-year study period, a total of 10,627 patients were admitted to a hospital with the diagnosis of tibial shaft fracture. The overall median age (SD) was 37 (25) years. Females were fewer (38%) and older (median age 51 years) than males (median age 28 years). The overall number of hospital admissions due to tibial shaft fractures decreased by 12% during the study period. Admissions for males decreased by 11% and for females by 14%.

The crude total IR of tibial shaft fractures was 17 per 100,000 pyr (males 21 and females 13 per 100,000 pyr). The overall incidence rate ratio (IRR) between males and females was 1.6. The total IR decreased during the study period (B=-0.4), as well as for males (B=-0.5) and females (B=-0.3) (Figure 1).

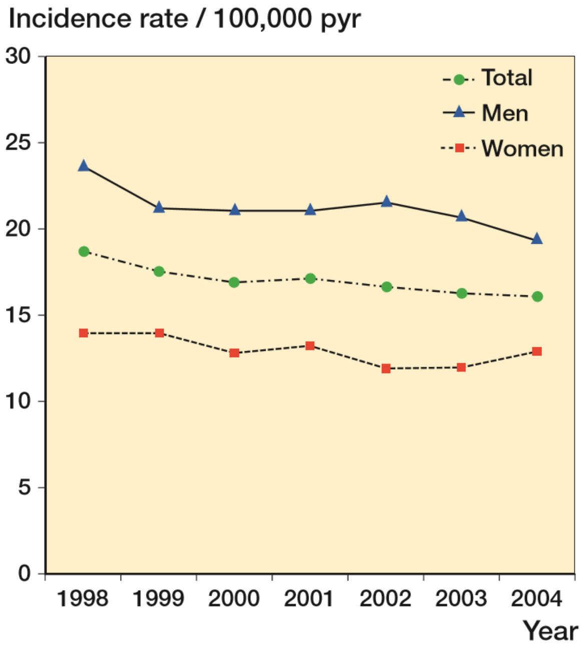

Figure 1: Crude incidence rates per 100,000 pyr of tibial shaft fractures during 1998-2004.

In male individuals, the IR peaked in the age-group 10-19 years with 39 per 100,000 pyr and was lowest with 12 per 100,000 pyr in the age-group 80-89 years. In women, the lowest IR was found in the age-group 20-39 years with six per 100,000 pyr and increased steadily to a peak at 90+ years of age with 36 per 100,000 pyr. The IR was higher in men compared with women up to the age-group 50-59 years. From 70-79 years onwards, women had a higher IR for tibial shaft fractures compared with men (Figure 2).

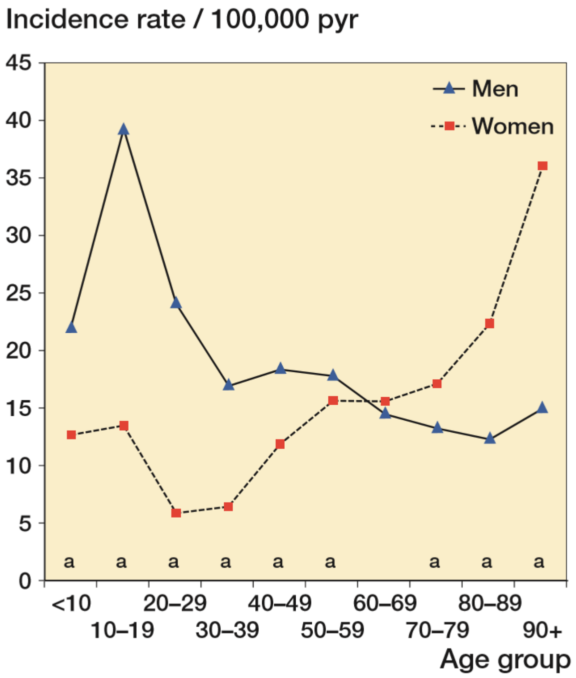

Figure 2: Incidence rates per 100,000 pyr of tibial shaft fractures in Sweden during 1998-2004. [a]p<0.05 indicating statistically significant incidence rate ratio between men and women.

The most common mechanism of injury was fall on the same level (48%), followed by transport accidents (21%). Of all patients, 58% underwent some kind of surgical intervention for the fracture. The most common procedure was fixation with an intramedullary nail (48%), followed by closed reduction and plaster cast (27%), external fixation (12%), fixation by plate and screws (8%) and other methods (5%). Of the fractures, 12% were classified as open with 70% male dominance and with transport accidents as the most common injury mechanism (43%).

4.2 Study II

A total of 6,409 patients with the diagnosis of femoral shaft fractures were admitted to a hospital in Sweden during the study period. The overall median age of the patients was 67 (IQR 19-83) years. There were fewer males (46%) than females and the median age in men was 27 years as compared with 79 years in women. Most admissions were generated by male individuals in the age-group <10 years and by women in the age-group 80-89 years (Figure 3).

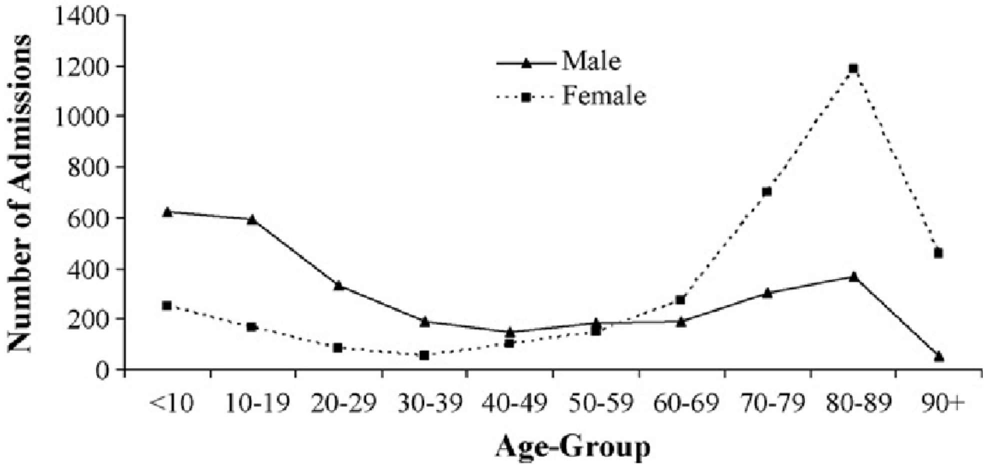

Figure 3: Total number of hospital admissions for femoral shaft fractures stratified by sex and age-group in Sweden during 1998-2004.

The total number of admissions for femoral shaft fractures was stable during the study period (B=-0.2, 95% CI -14.1 to 13.7). The total IR was 10 per 100,000 pyr. In both males and females, the IR declined from childhood up to the middle-ages where the rates began to rise steadily to peak at the age-group 90+ years. The overall IRR between males and females was 0.9 and showed an increase for males up to the age-group 40-49 years. Females showed a higher IR from the age-group 60-69 years and onwards (Figure 4).

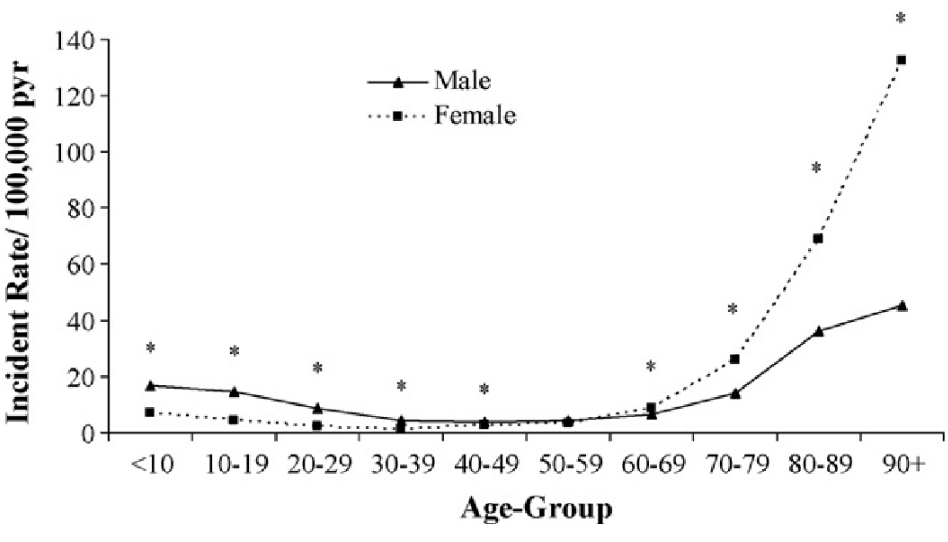

Figure 4: Incidence rates per 100,000 pyr of femoral shaft fractures in Sweden stratified by sex and age-group during 1998-2004.*p<0.05 indicating statistically significant incidence rate ratios between males and females.

Fall on the same level was the most common mechanism of injury in the female population (64%) and transport accidents dominated in the male population (74%). The distribution of surgical procedures was as follows: fixation with intramedullary nails (54%), osteosynthesis with plate and screws (16%), skeletal traction (14%), external fixation (6%) and other fracture surgery (20%).

The fractures were classified as closed (82%), open (2%) and unspecified (16%). Patients with open fractures were younger (median age 27 years) compared with patients with closed fractures (median age 69 years). Males generated 75% of the open fractures compared with 45% of the closed fractures.

4.3 Study III

A total of 3,777 patients with the diagnosis of open tibial fracture were admitted to a hospital in Sweden during 1998 to 2010. The median (SD) age at admission was 47 (20) years. There were more males (67%) and they were younger (mean age 42 years) compared with females (mean age 55 years). The open tibial fracture was bilateral in 2% of the patients. The fracture location was as follows: 60% shaft, 14% proximal end and 26% distal end of the tibia. The age distribution is shown in figure 5.

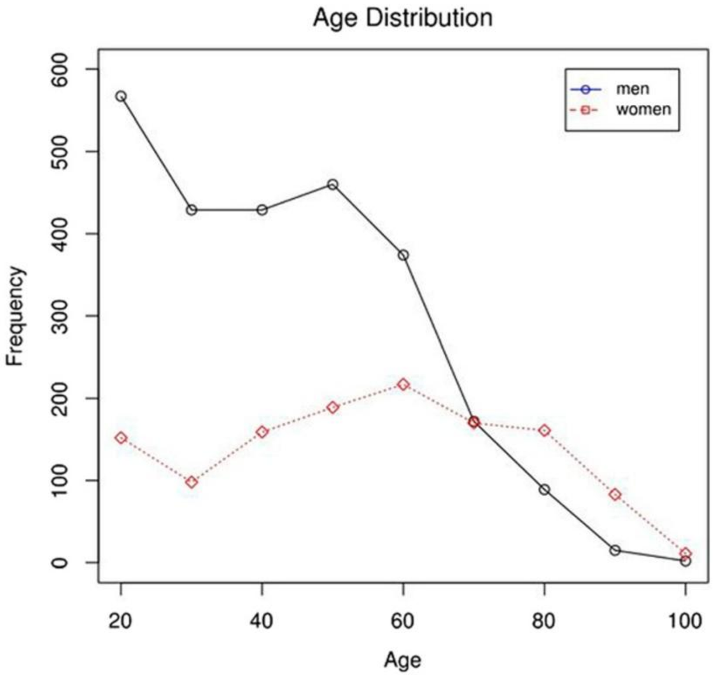

Figure 5: Age distribution of men and women with open tibial fractures in Sweden during 1998-2010.

The IR ranged between 2.8 and 3.4 per 100,000 pyr and it was higher for males compared with females. The IR did not change significantly over time during the study period (Figure 6).

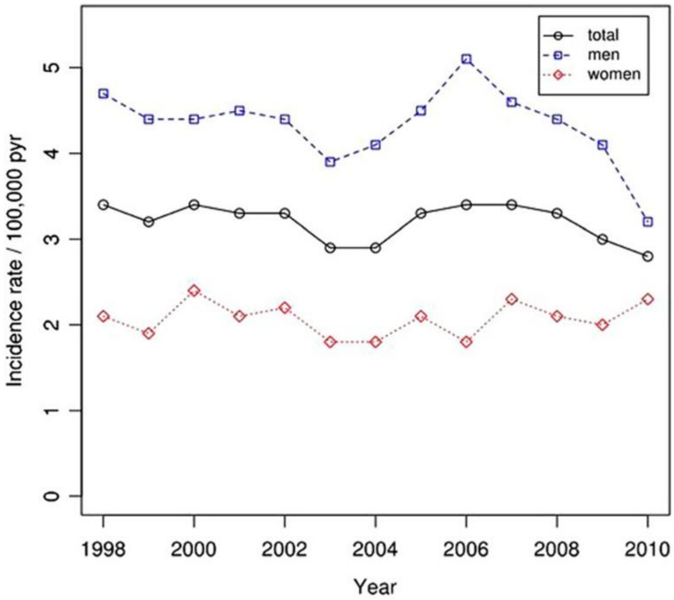

Figure 6: Incidence rate of open tibial fractures per 100,000 pyr.

The most common cause of injury was motor vehicle accident (MVA) (43%), followed by fall on the same level (21%). Most fractures caused by MVA (73%) and fall from height (73%) occurred in males. Fractures caused by fall on the same level were more common in females (55%).

The most common fixation method was with intramedullary nails only (32%), followed by a combination of external fixation and other methods (22%), plate fixation only (9%), external fixation only (8%), closed reduction and casting (4%) and miscellaneous methods (26%).

Soft tissue reconstructions were performed in 9% of the patients (n=342). There were 102 free flaps, 83 pedicle flaps and 166 skin grafts only. About 50% of the flaps were operated within 10 days after the injury. 27 patients were operated with a flap within three days. None of these patients underwent an amputation during the study period. Three of the 24 flaps (13%) performed between day four and seven resulted in an amputation. Of the 97 flap reconstructions performed between day four and 90, 12 patients (12%) went to amputation.

During the study period, 125 amputation procedures were performed in 93 patients. Of the amputations, 59% were transtibial, 24% transfemoral, 14% knee disarticulations and 3% ankle and foot amputations. Early amputations (within 90 days) were performed in 63 patients (67%) and late amputations in 30 patients (33%). The rate of amputation was higher (7%) in patients who underwent soft tissue reconstructions compared with patients without reconstructions (2%). There was no significant difference between the three methods of tissue coverage regarding subsequent amputation.

The risk of amputation within three months after an open tibial fracture was higher in males (HR 2.0), for older patients (>70 years: HR 2.3; >80 years: HR 7.2), after soft tissue reconstructions (HR 3.0) and when the fracture was operated by other methods than intramedullary nailing only (HR 4.4-12.1). Fracture mechanism showed no significant association with the amputation risk.

4.4 Study IV

We identified 3,732 patients with tibial shaft fractures. Of these, 2,571 patients had neither prior opioid use nor associated fractures. 25% (639 patients) of these patients filled opioid prescriptions at some point after the fracture (Figure 7). The median age was 45 years and the majority was males (61%).

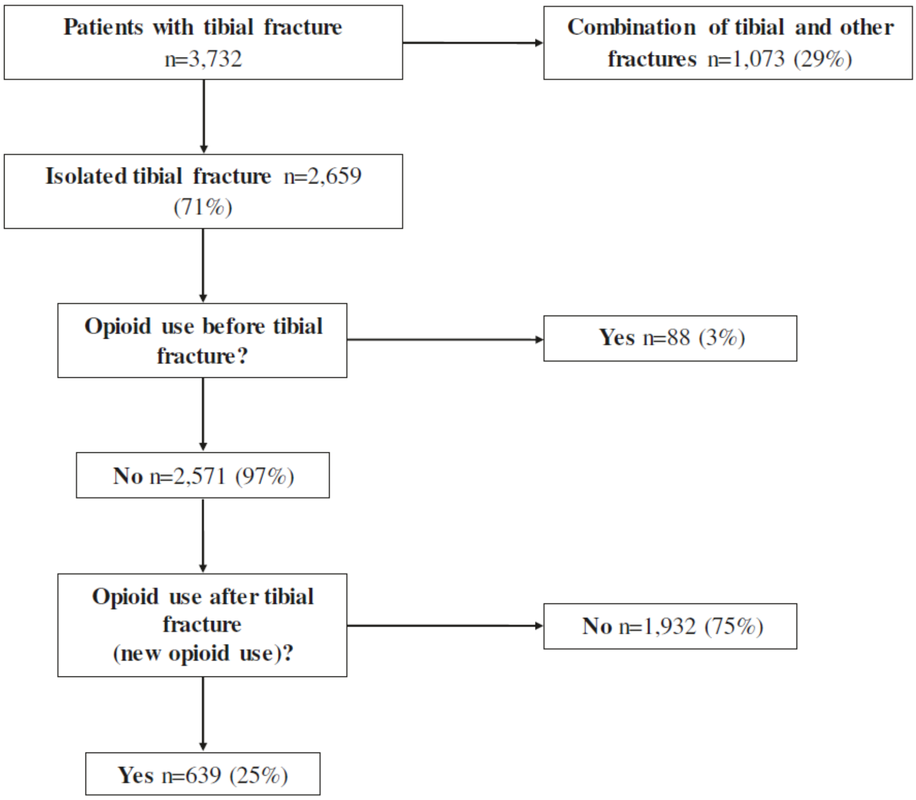

Figure 7: Cohort eligibility and final sample size.

At six, 12 and 18 months after the fracture, 21%, 14% and 11% of the patients were still getting opioid prescriptions (Figure 8). In the corresponding age- and sex-matched control cohort without tibial shaft fractures (n=12,855), 3% of the individuals had opioid prescriptions during the same time period.

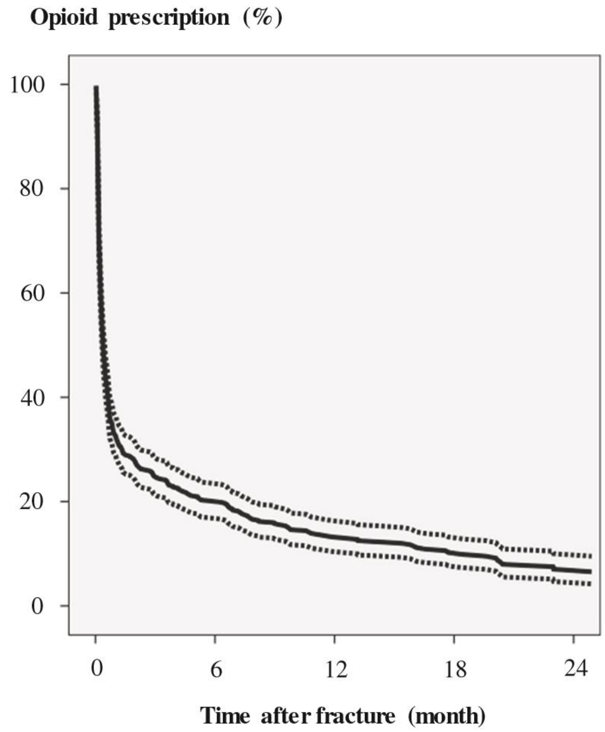

Figure 8: Kaplan-Meier-analysis with 95% CI of the last opioid prescriptions of patients with tibial shaft fractures.

The majority of the patients (86%) dispensed the first opioid prescription within the first month after the fracture and had a median daily MED at 21 (IQR 8-23) mg within the first month (Figure 9).

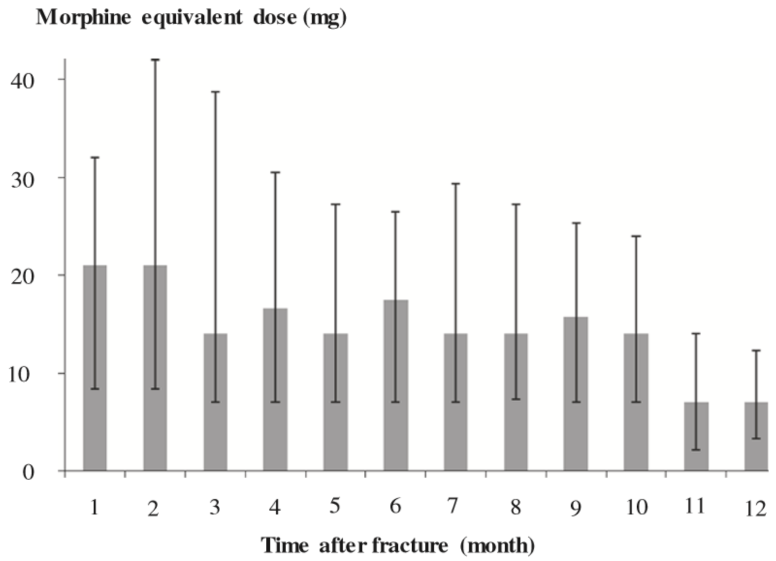

Figure 9: The median (IQR) morphine equivalent dose in mg per day prescribed to patients with tibial shaft fractures in different time periods after injury.

During follow-up, the proportions of patients receiving high and moderate opioid doses decreased and the proportion of patients who stopped dispensing opioids increased over time (Figure 10).

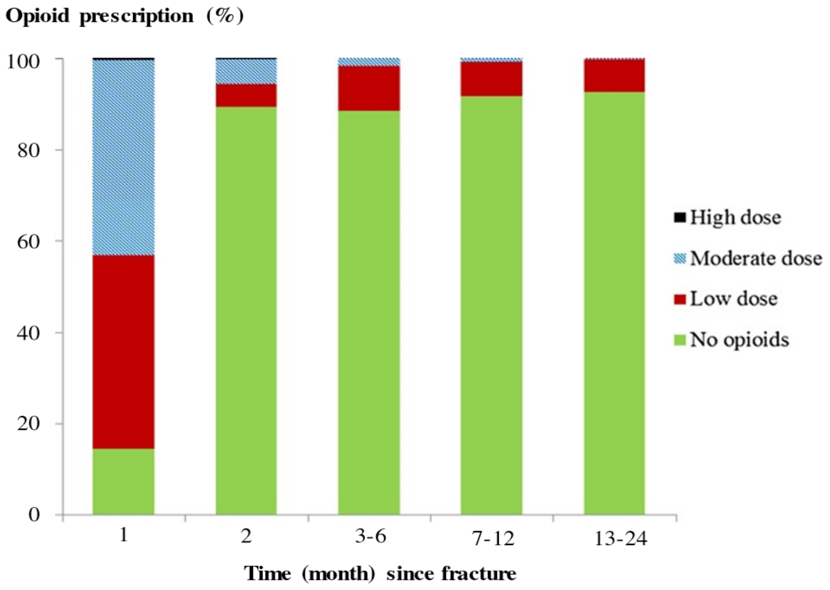

Figure 10: The distribution of opioid prescriptions in 639 patients in different time intervals after tibial shaft fracture (low dose: <20 mg MED per day; moderate: 20=<180 mg; high:>180 mg).

The unadjusted Cox regression analysis showed that patients aged >50 years (HR 1.7), females (HR 1.3) and patients treated non-surgically (HR 1.4) were less likely to continue taking opioid prescriptions. After adjustment for covariates in the multiple Cox analysis, older age remained a statistically significant factor (HR 1.5).

4.5 Study V

Of 2,926 patients who underwent surgery for a femoral shaft fracture, 630 patients (22%) were excluded due to associated fractures and 825 patients (36%) for having opioid prescriptions prior to the admission for the index fracture. Of the remaining 1,471 patients, 891 (61%) had an opioid prescription dispensed at some point during follow-up (the final study cohort) (Figure 11). Of the corresponding age- and sex-matched control group without femoral shaft fracture (n=7,339), 25% dispensed opioid prescriptions during the study period.

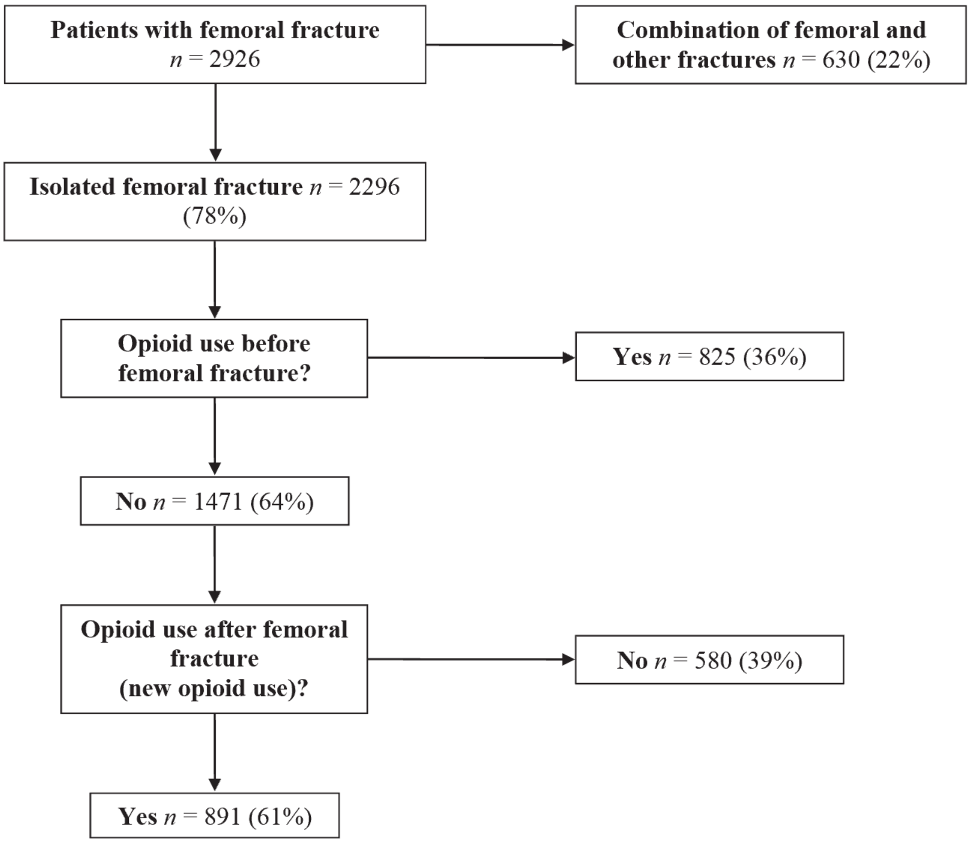

Figure 11: Cohort eligibility and final sample size.

The median age of patients in the final study cohort was 75 (range 16-102) years. The fractures were open in 3% of the patients and were caused by fall on the same level in 48%, followed by transport accidents in 18%. Of the 891 patients, 45%, 36% and 29% dispensed opioid prescriptions at six, 12 and 18 months follow-up, respectively (Figure 12).

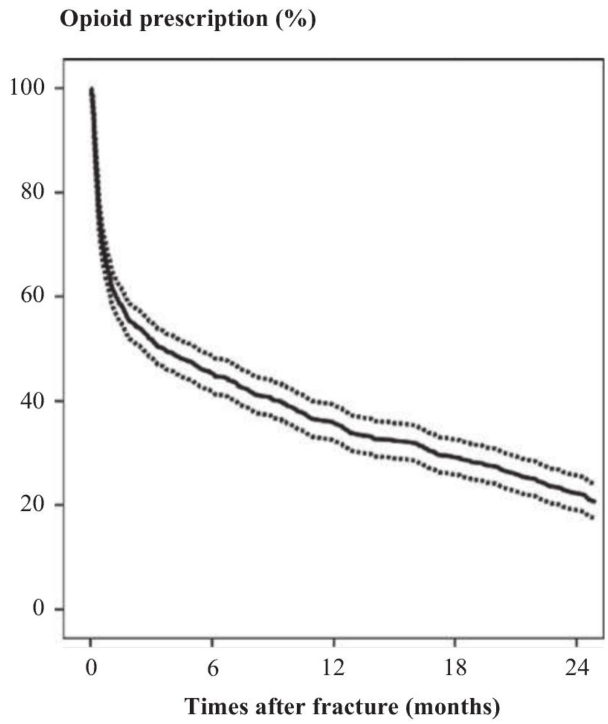

Figure 12: Kaplan-Meier-analysis with 95% CI of the last opioid prescription in patients with femoral shaft fractures.

For patients who started dispensing opioids directly after discharge from hospital, the median daily MED was 17 mg (IQR 10-30) within the first two months, showing a stable pattern within the first year after injury (Figure 13).

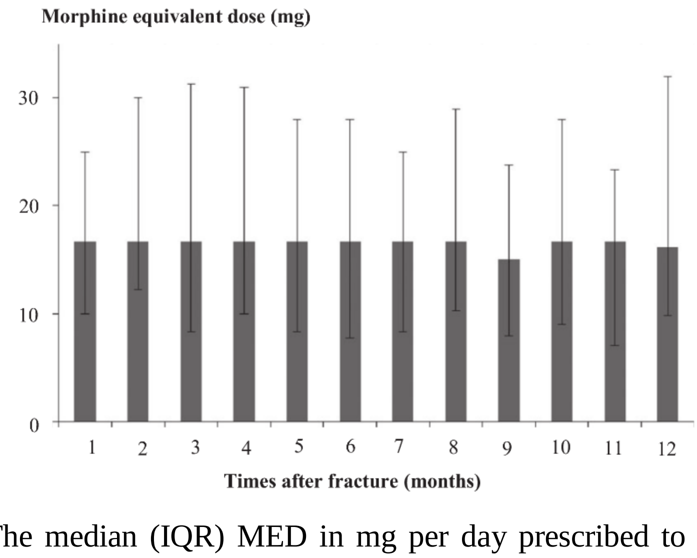

Figure 13: The median (IQR) MED in mg per day prescribed to patients with femoral shaft fractures at different time intervals after injury.

The number of patients with high and moderate doses of opioid prescriptions was falling off during follow-up (Figure 14).

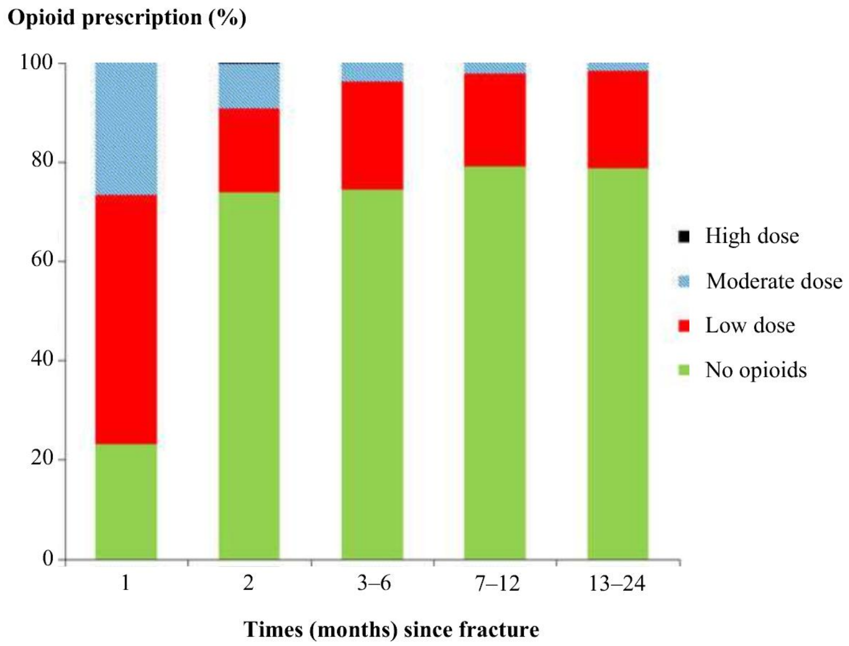

Figure 14: The distribution of opioid prescriptions in 891 patients in different time intervals after femoral shaft fracture (low dose: <20 mg MED per day; moderate: 20=<180 mg; high: >180 mg).

Oxycodone, followed by morphine, was the most commonly dispensed strong opioid, while tramadol was the most often dispensed weak opioid (Figure 15).

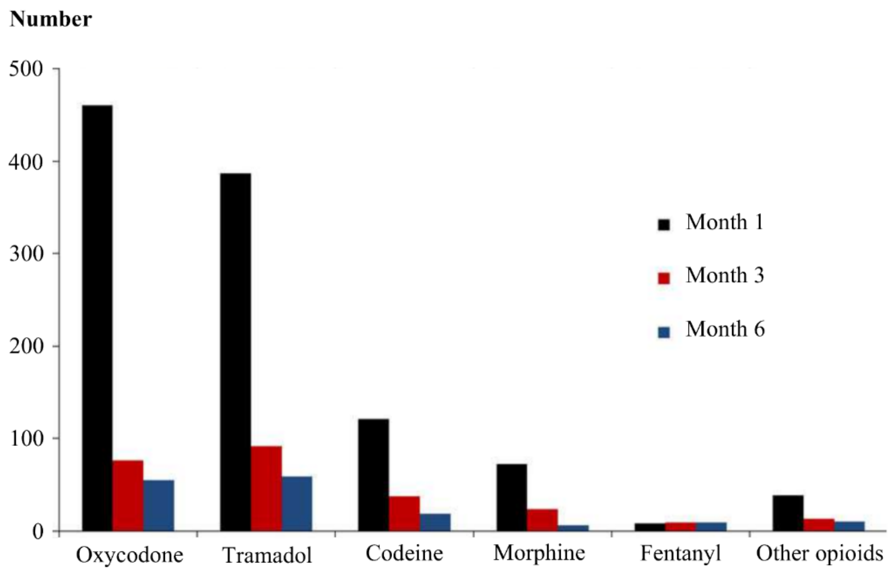

Figure 15: The number of prescriptions of opioids among patients with isolated femoral shaft fractures (one, three and six months after fracture).

5 DISCUSSION

5.1 Study I

The main finding of the study was the decreasing number of admissions for tibial shaft fractures in Sweden during 1998 and 2004. This decline was more pronounced in male compared with female incidence. During the study period, the proportion of cases from transport accidents was stable while admissions due to fall on the same level decreased. This could reflect a true decrease in fracture incidence caused by fall on the same level in males. It could, however, also be caused by a decrease in the severity of the fracture and/or the economically motivated shift from inpatient to more outpatient management of some less serious low-energy injuries, which therefore would not be found in the SNHDR database.

During the study period, the number of vehicles (motorbikes and cars) increased steadily in Sweden, as did the total number of injured people due to road traffic accidents according to the Swedish Institute for Transport and Communications Analysis (www.sika-institute.se). However, in the present study, the number of admissions for tibial shaft fractures caused by these accidents did not increase during the same period. This finding may be explained by improvements in road traffic safety.

Other surveys had shown wide variations in the incidence of tibial shaft fractures [2, 19]. Two Swedish studies comparing the incidence of tibial shaft fractures between two periods in the same region, showed no change in incidence rates between the periods 1950-55 and 1980-83 [15], but a decrease in the incidence rate between the periods 1970-75 and 1986-90 [18]. In the latter study, the decline was almost entirely attributed to the decrease of fractures sustained by young male motorcyclists. However, the overall fracture incidence in both periods was higher than that found in the present study [15, 18].

In accordance with other studies, the distribution of fracture incidence rates showed a homogenous pattern, regarding age and sex of the patients [17, 19, 20, 66, 67]. In the present study, peak incidence rates were observed in young males (10-19 years, IR: 39/100,000 pyr) and in old females (=>90 years, IR: 36/100,000 pyr). In both groups, the most common cause of fracture was fall on the same level (49% and 77% respectively). The steep rise of fracture incidence in older women starting at the age of 70 years may indicate an association with low bone density [66, 67]. However, other factors could also influence this high incidence in older people including increased risk of falls due to balance problems and muscle weakness due to age and high prevalence of cardiovascular and CNS-active drugs [66, 67]. A population-based register study including more than 29,000 fractures in the north of Sweden (Umeå) during 1993-2004 showed that low-energy falls (on the same level or from <1m height) caused 53% of all fractures in patients aged >=50 years and >80% of fractures in those older than 75 years. The authors concluded that most fractures in older patients had a fragility component and that the contribution of osteoporosis-related fractures to the overall incidence was found to be more important than previously thought [68].

5.2 Study II

The main finding of this analysis was the high proportion of femoral shaft fractures caused by low-energy trauma in older patients. The overall annual incidence of 10 per 100,000 pyr was similar to reports from the United Kindom [2], Finland [32] and the United States [69]. In contrast to tibial shaft fractures (study I), a bimodal age distribution was found in both males and females, with one peak in children and the other peak in elderly patients. This pattern of distribution differs from other studies where children were not included [2, 19]. The sex distribution with a higher IR in males up to the age of 50 and a higher IR in females from the age of 60 was also shown in other studies [2, 15, 19]. In contrast to other studies, we found an overall predominant female incidence with an IRR between males and females of 0.9 [15, 22, 27, 29, 32].

In females, the predominant external fracture cause was fall on the same level (low-energy trauma) with a steeply increasing fracture incidence after the age of 60. Thus, osteoporosis-related fractures seem to play also an important role in the femoral shaft and not only in the neck and the trochanteric region of the femur.

The Swedish population, as in other Western European countries, is aging with time [61]. It is therefore notable that the fracture incidence did not increase during the 7-year study period. This may suggest that better preventive measures and treatment modalities for osteoporosis and/or other changes in health care and lifestyle may have prevented an increase in incidence of femoral shaft fractures in Sweden.

Only a small proportion of fractures were classified as open (2%, IR 0.3 per 100,000 pyr). Court-Brown et al. described a similar epidemiological profile of open femoral shaft fracture as in the present study: male dominance (75%) and transport accidents as the major cause (50%) [70]. The overall low numbers of open fractures in Sweden may suggest the need of more centralization and competence concentration for improved multi-disciplinary management and follow-up of patients sustaining these difficult and often complicated injuries [38, 71].

5.3 Study III

This study showed that 9% of the patients with open tibial fractures were operated with a soft tissue flap. The risk of subsequent amputation after open fractures was low ranging between 2-10%. Older age (>70 years) and soft tissue reconstruction were risk factors for amputation within three months after fracture.

These findings are comparable with other studies concerning IRs (2.8-3.4 per 100,000 pyr), male dominance (67%), MVAs as external cause (43%) and intramedullary nailing as only fixation method (32%) [38, 72]. In males, the age distribution showed a uni-modal pattern with a peak incidence around the age of 20, mostly caused by high-energy trauma (MVA and falls from height). In females, a rather bimodal tendency around the ages of 20 and 60 years was observed. The latter could well represent osteoporosis-related fractures caused by low-energy trauma (fall on the same level). Similar tendencies were shown in other studies [38, 68, 72].

In this study, patients operated on with soft tissue flaps were assumed to had sustained trauma with more extensive soft tissue damage classified according to Gustilo and Anderson as type III open fractures [33]. This classification is unfortunately not included in the SNHDR database. Still, our results are in accordance with other studies based on a review of patient records where the Gustilo-Anderson classification was used. In a recently published study from a major trauma unit in the United Kingdom, all patients with a Gustilo IIIB open tibial shaft fracture were promptly treated by combined orthopaedic and plastic surgery, according to newly introduced major trauma guidelines [73]. The results were compared with previously published data from the same unit and the authors found a substantial improvement in the outcome of these severe injuries: 94% limb salvage, 99% successful reconstruction, only 2% deep infections and 7% nonunions [74]. The increased risk of early amputation for older patients in this study may reflect the presence of co-morbidities which negatively affect the outcome after limb salvage procedures. However, further statistical analyses of co-morbidities based on information obtained from the SNHDR were considered unreliable.

The finding of a better outcome, with lower risk of amputation, when the fracture was fixed by an intramedullary nail only, as compared with all other fixation methods, could reflect the clinical practice to use this method as the gold standard for early fixation of open tibial shaft fractures when the soft tissue injuries are not extensive (Gustilo type I-II) and thereby indicating a better outcome.

Other studies had emphasized the importance of early soft tissue coverage (within 72 hours) to obtain high success rates of limb salvage procedures after open tibial fractures[73, 75]. This coincides with the findings in the present study. None of the flap reconstructions performed within three days (n=27) and only three of the 24 reconstructions performed between day four and seven resulted in an amputation. Still, no significant difference in the amputation rate after reconstruction by free flaps as compared with local flaps was found (9% and 10% respectively). Other reports showed varying rates of failure between the two flap types [35, 76]. This highlights the importance of preoperative decision making according to the reconstructive ladder [77].

It is often difficult in the specific patient situation after severe open lower limb injuries to decide whether to initiate limb salvage procedures or to plan directly for an amputation. This decision depends upon a variety of factors related to the injury, the patient and the available medical resources that must be taken into consideration. This may explain reported amputation rates after these injuries varying between 4% and 40% in different studies [35, 42, 76, 78, 79].

5.4 Study IV

In this study, the long-term prescriptions of strong opioids in opioid naïve patients with tibial shaft fractures were analyzed on a nationwide basis in Sweden. An age- and sex-matched control group without tibial fracture was included. The main finding was that 25% of the fracture patients filled a prescription for opioid analgesics at some point after the fracture.

In the present study, the median daily MED was predominantly moderate to low after discharge from hospital. At follow-up, less than 5% of the patients had a high to moderate daily MED at three months. No evidence of major dose escalations of prescribed opioids in the fracture patients was observed during follow-up.

The lower risk of prolonged opioid use in older patients shown in this study may be reassuring, as some reports had raised increasing concerns on the safety of opioids and their possible effect on cognitive function in the elderly [80-82]. The findings of an increased risk to continue opioid therapy in patients younger than 50 years may be explained by the predominance of more extensive and high-energy injuries often caused by road traffic accidents in younger patients as compared with low-energy injuries often caused by falls on the same level in older patients.

5.5 Study V

Long-term prescriptions of both strong and weak opioids after femoral shaft fractures were analyzed. The main findings were that 61% of the patients dispensed at least one opioid prescription at some point after discharge from hospital. 25% of the controls without fracture received opioid prescriptions during the study period. The proportion of patients and controls using opioids were lower in study IV which may be explained by the fact that we only analyzed strong opioids in that study.

As mentioned in the introduction, a major concern in the use of opioids poses the risk of physical dependence and addiction [83]. Continuous use of especially high doses may lead to tolerance indicated by higher prescribed doses [64]. In the present study, 45% of the patients who received opioids after discharge were still receiving opioid prescriptions at six months. Despite that, no indication of major dose escalations in the patient cohort was detected during the study peiod. The median daily MED was between 15-17 mg during the first 12 months. The distribution of opioid prescriptions showed that most patients received low doses. Prescriptions of moderate and high doses of opioids continuously decreased during follow-up.

6 METHODOLOGICAL CONSIDERATIONS AND LIMITATIONS

In study I and II, only the first hospital admission for tibial and femoral shaft fractures was included in the analysis. A new fracture of the same bone (same code) in the same patient during the study period was therefore not included in the analysis. If a patient was transferred from one hospital (first admission) to another hospital or a trauma center for further surgical treatment (second admission), the second hospitalization was not included in the analysis. Therefore, some intervention codes may have been missed in the analysis.

The SNHDR gathers only inpatient data. Fractures in patients who were treated as outpatients were not included in the present thesis. Outpatient data are not well validated and they do not cover the entire country of Sweden [84]. The availability of hospital beds has been increasingly limited allowing hospital admissions to be confined to more serious and complicated cases [85]. This caused a gradual shift from inpatient to outpatient treatment of some skeletal injuries in the lower limbs, which may include uncomplicated tibial fractures in young healthy patients who were treated non-surgically.

High energy trauma is getting increasing attention in clinical practice, as it has often a great impact on both treatment methods and prognosis. Still, high energy trauma is not found as a separate entity in the present national registers which are based on the ICD system with the relevant E (external) codes for the mechanism of injury. The E-codes for fall from height and for transport accidents are used by some authors to indicate high energy trauma [68]. Moreover, some known causes of high energy injuries such as gun-shot and shrapnel injuries, though still uncommon, are increasing in Sweden according to the Swedish National Council for Crime Prevention (www.bra.se). These injuries are currently registered as “miscellaneous” causes of fracture, as they have no specific E-codes in the ICD-system.

The SHDR is securely valid for the primary diagnosis, especially for trauma patients. However, data on co-morbidities are considered not enough validated and secure to allow statistical analysis using the ICD codes for co-morbidities [46]. This issue was discussed in study III, when analyzing the influence of co-morbidities on amputation risk was considered.

Information on the severity of the fracture and soft tissue involvement are lacking in the SNHDR. In clinical practice, the Gustilo-Anderson classification is widely used for grading of open fractures but it is unfortunately not included in the SNHDR [33]. A study from the United Kingdom on open tibial fractures showed a prevalence of up to 20% of severe Gustilo type IIIB injuries that often needed soft tissue coverage and had a high risk of amputation [72].

A new central fracture register was developed in recent years (www.registercentrum.se). The Swedish Fracture Register (SFR) that was launched in 2011 makes it possible to follow patients with uncommon and more complicated limb injuries. The SFR gathers several patient- and fracture-specific variables such as detailed fracture classification systems [90]. The AO/OTA fracture classification in the SFR has a high reliability for tibial fractures [91]. Based on the experience with the national registers in this thesis, data from the SFR may play an important role concerning prognosis, quality control and research for fractures of the lower limbs in the future.

The SPDR used in study IV and V is well validated [48]. No opioid analgesic can be dispensed without prescription and all dispensed opioids are registered in the SPDR database which became complete in July 2004 [49]. However, dispensed drugs are not equal with opioid consumption. This may include a possible overestimation of the actual drug intake of a patient as not all dispensed drugs may be consumed. Some other commonly used analgesic drugs such as paracetamol and NSAIDs can be dispensed without prescriptions and are therefore not included in the Register. The use of these non-opioid pain medications by the patients may influence the use and/or the dosage of the opioids prescribed.

In study IV and V, Patients with concomitant fractures other than the index shaft fracture (study IV 29% and study V 22%) were excluded in order to get a homogenous study group without being confounded by other associated injuries. This exclusion could have resulted in selection of less severely injured patients with less pain resulting in an underestimation of opioid prescriptions.

The exclusion of patients who received opioid prescriptions before admission for the index fracture (study IV and V) was aimed to study patients with "new opioid use" (opioid naïve patients), thereby minimizing the risk of being biased by chronic painful conditions such as fibromyalgia, back pain or arthritis.

7 CONCLUSIONS AND FUTURE PERSPECTIVES

1. Studies based on information retrieved from validated nationwide registers are reliable sources of epidemiological and clinical data which can be used by healthcare providers in planning health-care facilities, hospital beds, surgical interventions and risk preventive measures as well as to decide on centralization of uncommon and more complicated injuries which need highly specialized and multidisciplinary management.
2. The risk of amputation in patients with open tibial fractures increases with age and is higher if the fracture is stabilized by other methods than intramedullary nailing only and if the soft tissue reconstruction is delayed beyond 72 hours from the time of injury.
3. The long-term follow-up of opioid naïve patients receiving prescriptions of opioids after sustaining isolated tibial and femoral shaft fractures did not show significant dose escalations of the prescribed opioids.
4. A notably high proportion of opioid naïve patients with isolated tibial and femoral shaft fractures continue to receive prescriptions of opioids after the injury. This calls for further investigation to study the therapeutic and the adverse effects of prolonged opioid therapy in these patients.
5. There is a need for a nationwide fracture register based on well-established classification systems with documented effects on treatment and prognosis. The relatively new SFR is very promising and seems to fill the requirements for both clinical and research purposes. However, the SFR needs further validation studies and continued expansion to reach full coverage over the entire country.

8 POPULÄRVETENSKAPLIG SAMMANFATTNING

Skaftfrakturer i lårben och underben är vanliga och relativt allvarliga skador. Prognosen varierar beroende på skademekanismer fraktur- och patientspecifika egenskaper samt behandlingsmetoder. Nationstäckande data rörande epidemiologi och långtidsbehandling mot smärta med opiater vid dessa frakturer saknas i stor utsträckning i litteraturen.

Syften

1. Att få fram epidemiologiska data rörande incidenser, skademekanismer samt mönster och behandlingsmetoder av skaftfrakturer i underben och lårben i Sverige.

2. Att analysera nationella data om mjukdelstäckning och extremitetsbevarande ingrepp vid öppna underbensfrakturer samt identifiera möjliga riskfaktorer för amputation.

3. Att på nationell nivå studera långtidsbehandling mot smärta med opiater hos patienter med skaftfrakturer i lårben och underben samt identifiera eventuella dosupptrappningar av förskrivna opiater vid långtidsuppföljning efter frakturen.

Patienter och metoder

1. Information om första slutenvårdstillfälle i Sverige, för alla patienter med skaftfrakturer i underben och lårben under perioden 1998-2004 (studie I-II) och om samtliga slutenvårdstillfällen för öppna underbensfrakturer hos patienter äldre än 15 år under perioden 1998-2010 (studie III), inhämtades från nationella patientregistret. Med hjälp av patienternas personnummer och relevanta diagnos- och ingreppskoder kunde uppgifter rörande patienter, diagnoser, skademekanismer, frakturtyper samt behandlingsmetoder insamlas och analyseras med relevanta statistiska metoder.

2. Information från nationella läkemedelsregistret rörande alla patienter äldre än16 år som under perioden 2005-2008 blev inlagda på sjukhus i Sverige för isolerade skaftfrakturer i underben (studie IV) eller lårben (studie V) och som hade expedierats recept på opiater någon gång efter utskrivningen, insamlades, analyserades och jämfördes med kontroller från den allmänna populationen i Sverige. Upptrappningar av opiatdoser bedömdes genom att räkna ut den dagliga morfin equivalenta dosen (MED) för varje patient och månad under uppföljningstiden som i genomsnitt var 18 månader.

Resultat

Studie I-II: Den årliga incidensen av skaftfrakturer per 100,000 invånare och år (pyr) under perioden 1998-2004 var 17 (n=10,627, män 62%) i underben och 10 (n=6,409, kvinnor 54%) i lårben. Under studieperioden sjönk antalet inläggningar med 12% för underbensfrakturer medan det var stabilt för lårbensfrakturer. I bägge studierna var männen i genomsnitt betydligt yngre än kvinnorna vid skadetillfället. Fall i samma plan var den vanligaste skademekanismen och operation med märgspik var den vanligaste behandlingsmetoden. Öppna frakturer utgjorde 12% av underbens- och 2% av lårbensfrakturerna, med över 70% manlig dominans.

Studie III: Av alla patienter (n=3,777, män 67%) genomgick 342 patienter (9%) någon form av mjukdelsrekonstruktion, varav 185 lambåer (fria eller lokala), under studieperioden med i genomsnitt sex års uppföljning. Amputationsfrekvensen var signifikant högre hos patienter som behövde mjukdelstäckning (7% jämfört med 2% utan), vid försenad rekonstruktion mer än 72 timmar efter skadan, hos män, hos patienter äldre än 70 år, samt om frakturen var fixerad med annan metod än enbart märgspik. Av alla frakturer var 60% skaftfrakturer och 2% var bilaterala.

Studie IV-V: Av de patienter som inte behandlades med opioidanalgetika vid skadetillfället erhöll 25% (n=639, män 61%) med skaftfrakturer i underbenet (studie IV), och 61% (nr= 891, kvinnor 56%) i lårbenet (studie V), expedierade recept på opioidanalgetika under uppföljningstiden, de flesta inom de första två månaderna efter utskrivningen från sjukhuset. Ett år efter skadan sjönk andelen patienter som hämtade ut opioidanalgetika från apoteken till 14% (studie IV) respektive 36% (studie V) och likaså sjönk den genomsnittliga dagliga opiatdosen (MED) med tiden. I båda studierna var hög patientålder en signifikant indikator för att tidigare upphöra med användning av opiater.

Slutsatser och framtidsperspektiv

1. Studier baserade på validerade nationella register utgör en källa för pålitliga epidemiologiska och kliniska data som sjukvårdspolitiker kan använda för att planera sjukvårdsinrättningar, sjukhusplatser, kirurgiska interventioner och riskpreventiva åtgärder samt för att fatta beslut om centralisering av ovanliga och komplicerade skador som kräver högspecialiserad multidisciplinär vård.
2. Risken för amputation vid öppna underbensfrakturer ökar med stigande ålder, vid frakturbehandling med annan metod än märgspik och om rekonstruktion med mjukdelstäckning blir försenad mer än 72 timmar efter skadan.
3. Vid långtidsuppföljning av patienter som inte står på opioidanalgetika innan skadetillfället och som hämtar ut opioidanalgetika på recept efter behandling för isolerade underbens- eller lårbensskaftfrakturer noteras ingen dosökning över tid.
4. En märkligt hög andel av patienter med isolerade lårbensskaftfrakturer fortsätter att få förskrivning av opiater efter skadetillfället. Detta bör studeras närmare avseende terapeutiska effekter och biverkningar vid förlängd användning av opiater samt med ännu längre uppföljningstider.
5. Det finns behov av ett modernt nationellt frakturregister med frakturklassificering byggd på dokumenterad inverkan på behandling och prognos. Det nya svenska frakturregistret verkar lovande och ändamålsenligt men det behövs fler valideringsstudier och fortsatt arbete för att uppnå deltagande från hela landets sjukhus.

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