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THE IMPACT OF SMOKING ON ORTHOPAEDIC PATIENTS

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Cover photo: Matts Jonsson

To my family

ABSTRACT

Smoking has devastating effects on general health, including the outcome after surgery. There were three main objectives in this thesis. Firstly, to investigate the effect of smoking on complications after orthopaedic surgery. Secondly, to evaluate whether the negative effect of smoking on the complication rate after acute orthopaedic surgery was reversible after smoking cessation therapy and thirdly, to evaluate whether the administered smoking cessation therapy had any long-lasting effect on the smoking abstinence rate.

Study I included 906 patients with surgically treated ankle fractures. Background data were collected from patient charts and the outcome regarding postoperative complications was recorded prospectively in a clinical audit. Studies II and III were based on the same population from a single-blinded, randomized, controlled, clinical, multicenter trial at three hospitals in Stockholm, Sweden. We randomized 105 daily smokers with an acute fracture of a lower or upper extremity requiring acute surgical procedures into an intervention group (smoking cessation therapy) or into a control group. The primary outcome in Study II was any complication occurring, as predefined in the study protocol, within 6–12 weeks. The outcome in Study III was medium- and long-term successful smoking cessation. In Study IV the background data were taken from the SALT cohort in the Swedish Twin Registry. The SALT data were then linked to the Swedish Inpatient Registry, identifying 8773 individuals who had had orthopaedic surgery and who also had had a complication from that surgery.

In Study I it was shown that 30.1% of the smokers had a postoperative complication compared to 20.3% of the non-smokers (OR 1.9, CI: 1.3–2.8, p=0.005). In study II the administered smoking cessation therapy significantly reduced the number of postoperative complications (p=0.048). Study III showed that the administered smoking cessation therapy had a significant effect during the first 6–12 weeks, but not after one year. Study IV demonstrated that smokers had a significantly increased risk of developing complications requiring inpatient care; among the smokers, 14.9%, compared to 11.4% of the non-smokers, had such a complication (HR 1.27, CI: 1.10–1.48, p=0.002).

Smoking is a strong and significant factor associated with development of postoperative complications. Smoking cessation intervention program during the first six weeks after acute fracture surgery decreases the risk of postoperative complications. Smoking patients in need of both acute and elective orthopaedic surgery should be offered an intensive smoking cessation programme.

LIST OF PUBLICATIONS

I. The Impact of Smoking on Complications after Operatively Treated Ankle Fractures – A Follow-up Study of 906 Patients.
Nåsell H, Ottosson C, Törnqvist H, Lindé J, Ponzer S.
Accepted Journal of Orthopaedic Trauma 2011

II. Effect of smoking cessation intervention in acute fracture surgery: A randomised controlled trial.
Nåsell H, Adami J, Samnegård E, Tønnesen H, Ponzer S.
Journal of Bone and Joint Surgery (a) 2010;92:1335-1342.

III. Long-term efficacy of a smoking cessation programme in emergency orthopaedic surgery.
Nåsell H, Ponzer S, Lindström D, Samnegård E, Adami J, Tønnesen H.
Submitted

IV. Smoking and the risk of complications after orthopaedic surgery: a population-based study.
Nåsell H, Ponzer S, Törnqvist H, Benson L, Pedersen N, Eriksson U.
Manuscript

CONTENTS

List of abbreviations

ASA	American society of anesthesiologists physical status score
BMI	Body mass index
CI	Confidence interval
CO	Carbon monoxide
DA	Dopamine
EQ-5D	EQ-5D™ is a trademark of the EuroQol Group.
FEV	Forced expiratory volume
HR	Hazard ratio
ICD	International statistical classification of diseases
IF	Internal fixation
MAO	Monoamine oxidase
nAChRs	Nicotinic cholinergic receptors
NRT	Nicotine replacement therapy
OR	Odds ratio
POMS	Profile of mood states
QUALYs	Quality of life years
RCT	Randomized controlled trial
SF-36	Short Form SF-36

1 INTRODUCTION

WHAT DOES THIS THESIS ADD?

The studies included in this thesis show that smokers have an increased risk of developing postoperative complications after orthopaedic surgery. This risk was increased both in cases of acute and elective surgery. We also found that it is possible to reduce the risk of complications in smokers requiring acute fracture surgery by using smoking cessation therapy. However, the smoking cessation therapy used in our study was effective on smoking cessation rates in a shorter perspective but did not have a lasting effect after one year.

Let the findings inspire patients, health care staff, administrators and politicians to strive towards smoke-free operations!

Personal reflection

"His hair was perhaps whiter than it had been then, and his beard and eyebrows were perhaps longer, and his face more lined with care and wisdom; but his eyes were as bright as ever, and he smoked and blew smoke-rings with the same vigour and delight."

J.R.R. Tolkien, The Lord of the Rings. Page 61.

I was about four years old when it first dawned on me that cigarettes were dangerous. My little brother had found my mother's ashtray and, from what I could understand, the grown-ups were not certain whether he had eaten of the content or not. From my perspective, it was difficult to understand their agony. I had seen my mother and most of her friends use those cigarettes on a daily basis for as long as I could remember, but they still insisted that cigarettes were very poisonous if you ate them. Well, they did smell bad, so why eat them? My brother had to go to the hospital for a gastric lavage.

This episode did not discourage me from joining my classmates' smoking on the sly in the cow pasture out of view of the teacher. He was also a smoker, but we did not discover that until we were 12 years old and went to a school camp. I could not get the smoke to pass my larynx, but the "cool" ones soon became regular smokers and at age 13 were ruling the schoolyard from the assigned smoking area. Doing my military service I once again felt strong enough to explore the effects of nicotine. This time in the form of "snus", Swedish moist snuff. I did not stand it very well and had to spend

the rest of a promising evening in bed pale and nauseated. Relaxed? Well sort of, but certainly not high.

That world is now gone. Among my colleagues and friends, there is only one who still smokes. No names mentioned, because smoking is not considered to be so cool any more. Our hospital is more or less smoke-free and if I go to a restaurant or discothèque (the latter I have not done for some time), it is no longer necessary to take a shower to get rid of the heavy smell of smoke.

What is the thing about nicotine? I have asked a few friends, both users and ex-users, and the most frequent answer is that it tastes good! Or that it is like drinking water when you are really thirsty. Once a male former smoker claimed that he knew from his first cigarette that this was his drug. His mother was a heavy smoker and all his friends were smokers and he immediately had a feeling of alertness and well-being which helped him in his studies. This is in contrast to my mother who had to work hard to learn how to smoke. On the other hand, it did not seem to be so difficult for her to stop smoking. But many ex-users describe (without variance?) that life is greyer and dull compared to the time when they had free access to nicotine.

Without attending med school, would I have known that smoking is a dangerous and addictive habit. Even so, I did not jump with excitement when asked to be part of a group investigating the negative effects of smoking in relation to surgery. I wanted to compare different implants or surgical methods when treating fancy fractures. Meeting Hanne Tönnesen changed that. She convinced me that the possible gains in technology, treating co-morbidities or perioperative care at this stage were, if not minimal, at least not very big. Studying the negative, but reversible effects of smoking, a long ignored lifestyle factor, had far more promising possibilities.

Seeing changes in attitudes and behaviours is always easier in retrospect, but I do hope that the results of our work during the last few years will improve the outcome for smoking patients in need of orthopaedic surgery. It would still be better if this project would change general attitudes a little bit more and thus prevent some of our teenagers from becoming regular smokers.

BACKGROUND

History of tobacco

Christopher Columbus was given a pack of dried leaves as a gift by the “Indians” when he first landed on the new continent in 1492. He did not know that this type of leaf had

been burned and the smoke inhaled for religious, social and psychological effects for at least 2000 years.

Thirty-five years later came the first warning about the addictive effect of smoking, when it became apparent that Spaniards reproached for their bad habit claimed that it was impossible for them to stop smoking. The Indians had used tobacco to induce hallucinations, an effect not seen from today's tobacco products. It is speculated that they might have mixed tobacco with coca leaves or, perhaps more plausible, that they used nicotiana rustica, which has a high content of nicotine and other alkaloids possibly potentiating the effect of nicotine. The smoke was used in religious ceremonies and was also praised for its medical effects, including alleviating hunger and thirst, but not least did it have an important social function.

It did not take more than some hundred years to spread tobacco around world. Initially, tobacco was praised for its medical properties. The use of tobacco was promoted by physicians who claimed that smoking tobacco had several medical effects like curing headache, gastric pain, gout, cancer and also cough and asthma. Interestingly, warmed tobacco leaves were used topically to heal sores and cuts. Today we know that nicotine in low and intermittent doses locally applied promotes wound healing [1]. Within a century the medical reasons were forgotten and tobacco was used for recreation. By the end of the 17th century at least 25% of the adults in England smoked a pipe of tobacco each day. The introduction of tobacco was not unopposed. King James I of England/Scotland wrote, "It is necessary to stigmatize such habits, born in shame and derived from the barbarians" and he tried in vain to introduce a royal ban on tobacco. Later his son, Charles I (also an opponent to smoking) had smoke blown in his face as a final insult when he was led to his execution after losing the last battle against Oliver Cromwell. The Catholic Church forbade smoking under penalty of eternal damnation; only a few years later to promote smoking as a way to dry out the humidity which is the cause of lust among priests and monks. Cigarettes, crushed tobacco wrapped in leaves and later paper, have been documented since the 17th century. The use exploded in the 20th century. One reason was that the tobacco now was flue-cured and produced a smoke that was easier to inhale. The other reasons were the ability to mass produce and, not least, advertising [2, 3].

The tobacco epidemic

Smoking became a mass phenomenon in Europe and America during the early 20th century. The rise in smoking prevalence started with men and was followed by women. In post-World War II times 65% of the men and 40% of the women were regular smokers in Great Britain. Since the 1960s the prevalence of smoking has declined and was first observed among men. Today's smoking prevalence in Western Europe is between 25 and 30%, equally distributed between men and women. Asia has now an

all-time high smoking prevalence among men. In developing countries the smoking epidemic is just in its beginning and in 20–30 years the increase in smoke-related diseases and mortality will probably be seen also in these countries [4].

Reasons to start and continue smoking

Nicotine dependence

Nicotine is the world's most addictive drug with one billion smokers worldwide [5]. Nicotine induces arousal and pleasure and reduces stress and anxiety. It is also believed that nicotine enhances the ability to concentrate, decreases reaction time and diminishes appetite. When dependency is established abstinence will induce the opposite reactions, i.e. irritability, depression, anxiety and increased hunger which may be present for a long time. The smoker gets the positive feedback of stimulation when smoking but also a strong incitement to smoke to avoid the negative effects of abstinence. Smoking a cigarette will allow the nicotine to be absorbed via the 100 square meters of alveolar area and induce a very sharp rise in arterial nicotine concentrations. This is facilitated by the manufacturers' alkalynization of the nicotine to allow it to pass more easily over the mucosa in the lungs. By using the route over the lungs, the liver and the first passage metabolism will be bypassed, which increases the nicotine concentration and allows the nicotine to reach the brain within seconds from the first inhalation. In the brain the nicotine binds to nicotinic cholinergic receptors (nAChRs). These receptors are ligand-gated ion gates that open up to sodium and calcium ions when nicotine binds to the receptor [5, 6].

The classical belief has been that nicotine works by stimulating dopamine release in the midbrain, which is a part of the brain's reward system. A problem with this theory has been to explain the desensitization of the nicotinic cholinergic receptors (nAChRs) and the paradoxical up-regulation of the same receptor. A new model suggests that nicotine inhibits the effect of the nAChRs, which in this model has an inhibitory role in dopamine release. The desensitization is an expected physiological reaction to the effect of nicotine. The up-regulation is then a logical consequence following the need to inhibit the release of dopamine, which is normally done by acetylcholine. The exposure to nicotine will lead to an up-regulated rewarding inhibition system. At this stage a smoker is left with two alternatives, suffer the abstinence symptoms until the nAChRs are down-regulated or consume more nicotine. The positive effect of more nicotine will be rapidly disrupted by new desentization, now followed by a long-standing up-regulation of the reward inhibitory system [7]. This up-regulation is one of the mechanisms believed to explain how the craving for nicotine can last several years after quitting smoking.

Smokers have been shown to have almost complete saturation of their nAChRs throughout the day, a fact that has led to the suspicion that smokers maintain their habit to evade withdrawal and may be rewarded with conditioned reinforcements. That is, smokers get a feeling of positive anticipation in situations linked to intake of nicotine [6]. Even among adolescents with relatively light nicotine dependency, the main reason to continue to smoke seems to be the avoidance of withdrawal symptoms [8].
The short-term effect of withdrawal of tobacco is significant: the distress will be of the same magnitude as seen in a general psychiatric out-patient population. In one study the profile of mood states (POMS) was measured before and after five days of abstinence. The pre-cessation POMS value was 13.6, similar to the adult norm of 17.8. The value during abstinence increased to 27.5, comparable to the value seen among the psychiatric outpatient population of 25.1 [9].

Besides the important dopamine pathway, also inhibition of monoamine oxidase is thought to be important in the development of addiction. Most likely, it is not nicotine itself but some other component in the smoke that inhibits the monoamine oxidase. The inhibitory effect lasts for at least 10 days. The level of inhibition from smoke is within the lower range seen for MAO inhibitors used as antidepressants. One effect of this inhibition is that it is thought to potentiate the dopamine releasing effect of nicotine [10].

Genetics

Fifty per cent of the variability in smoking initiation has been attributed to genetic factors [11]. Nicotine is eliminated via the cytochrome 450 system, and it is theorized that slow elimination might heighten the neurophysiological effect of nicotine and thereby increase the risk of dependence [12]. But there are contradictory findings showing that normal metabolizers are at increased risk to start smoking [13]. What seems to be clear is that those who metabolize nicotine fast need to smoke more to keep their level of nicotine at an appropriate level [14]. Dopamine, and especially the dopamine receptor, is another candidate to explain the initiation of smoking; there is a variant in the gene coding for the receptor that is associated with reduced sensitivity to dopamine and an increased risk for men to become regular smokers [15].

An association between genetic factors and smoking behaviour in adulthood has been demonstrated; slow metabolizers are less likely to smoke and if they do smoke, they smoke fewer cigarettes [14, 16, 17]. However, genes coding for nicotine acetylcholine receptors, dopamine, serotonin pathways, have no convincing relations to smoking behaviour [18]. Genetics might explain to some extent differences in responses to nicotine replacement therapy and to bupropion medication [18]. It is tempting to believe that one could test for a few of these genes and be able to predict the risk of becoming a smoker. In reality, the associations are, so far, weak and a genetic test is marginally better than chance to predict a person's smoking behaviour. In fact, a family

history with information on parents' and relatives' smoking habits will give a better prediction [19].

Social influences on smoking prevalence

Nicotine is very addictive, but people also seem to start smoking because their friends do. At risk to start smoking are individuals with friends who smoke, those who have less good results at school, parents that do not think smoking is bad and those who have easy access to cigarettes. Among the young smoking women in Europe, 62% answered that the reason they started smoking was the influence of friends and 25% reported that smoking made them look cool. Only 8% said they started to smoke because it helped them to manage their stress or depressive feelings [21]. On the other hand, if a smoker quits smoking, the people in their social network will follow. In an American population of 12,000 individuals followed over a 30-year period, it was noted that clusters of smokers simultaneously stopped smoking and that smokers were increasingly marginalized in their social networks [22].

Maternal smoking during pregnancy

There is increasing evidence that smoking during pregnancy is independently associated with an increased risk for the offspring's initiation and onset of regular smoking [23, 24].

Smoking cessation

What do smokers think and do?

Smokers stop smoking. One out of four adults in Canada is a former smoker [25] and 50% of ever-smokers (in the US) will at some point quit smoking for good [26]. The annual successful quit rate is about 1–5%. The absolute majority (85%) will stop smoking without any medication or counseling. Each year at least 4 out of 10 smokers make one serious attempt to stop smoking, but the risk of relapse is high, especially during the first 8 days. The main reason for smokers to stop smoking is health concerns [25, 26]. This is, for example, illustrated by a 6.4% fall in cigarette consumption in 1954 when the first rapport came out describing the causal relationship between smoking and lung cancer [3]. Other reasons to quit smoking are expenses associated with the habit, concern for the effect on others, setting a good example for children, doctor's advice, bad smell, illness of friends and smoking restrictions at work [27]. However, these reasons are only predictive if the smoker has expressed a serious will to quit smoking. The most significant predictor of successful abstinence is the degree of nicotine dependence. A higher number of cigarettes consumed per day and a shorter time to the first cigarette in the morning have been shown to be associated with continuing smoking. Age above 45 years, higher income and less frequent alcohol consumption were associated with higher quit rates [27]. Adolescents seem to be

influenced by the same concerns of future health problems, but also by social influences [28].

Effect of general smoking policy

As mentioned above, neither the English kings' nor the Catholic Church's moral opinions against smoking had any effect on people's smoking habits. At first glance there seems to be no change over the centuries. A Cochrane review from 2002 concludes: "The failure of the largest and best studies to detect any effect (by community interventions) on prevalence of smoking is disappointing. In the best designed trials, light to moderate smokers did slightly better than heavy smokers. A community approach will remain an important part of health promotion activities, but designers of future programs will need take into account these limited effects in determining the scale of projects and the resources devoted to them [29, page 1]." In the same review the authors mentioned two studies that were not included in their analysis. The first study, the "Heart Body and Soul Project", compared a more intensive community intervention with a basic intervention based on minimal self-help intervention with the aid of a pamphlet from the American Lung Association.
The intensive intervention included "sermons" on the negative effects of smoking, individual testimonies on the process of quitting smoking and education in smoking cessation consultation of volunteers who could then go out and assist smokers who wanted to quit. After one year 19.6% in the intensive group were smoke-free compared to 15.1% in the basic group. There was also a control group in which only 2.9% were smoke-free after one year [30]. The second study is "The Four Cities Project" and also compared a more passive intervention with involvement of churches, health educators, site co-coordinators and neighborhood organizations. The difference in the quitting rate between active and passive intervention was significant, 16.7% vs. 11.8% [31]. There is now also some evidence that mass media intervention can be effective in preventing the initiation of smoking in young people [32]. Legislative smoking ban has an impact on exposure to secondhand smoke, and there is increased support for these laws. The impact on smoking prevalence is not clear, but there is a trend towards decreased prevalence of smoking [33].

Effect of smoking cessation therapies

Intensive face-to-face consultations or group sessions combined with medication have been shown to produce the best long-term results regarding quit rates [34]. Medication with nicotine replacement, bupropion or varenicline, is effective but when combined with counseling the effect is further enhanced [35]. Nicotine replacement therapy (NRT) is aimed at reducing the withdrawal symptoms during the acute phase of abstinence. Monotherapy with NRT will add a 70% success rate to the baseline quit rate of 1–5%. [36] Bupropion was initially aimed at treating depression with dopaminegic and adrenergic effects. The exact effect in the treatment of nicotine

addiction is not known. The treatment should start 7–14 days before smoking cessation. The effect size is about the same as for NRT [37]. Varenicline is the newest medicine in the treatment arsenal. It is a partial agonist on the nAChRs and blocks nicotine from binding to the receptor. In monotherapy the success rate is two to threefold compared to no treatment, and there are indications that the effect is better also when compared to NRT and bupropion [38]. The mode of counselling seems to have some importance; motivational interviewing seems to have a better effect than other behavioural therapies. Motivational therapy is about finding the individuals own motives to change behaviour. Traditional methods which rely on advice, information and learning skills are less successful [39] [40]. Group interventions are neither better nor worse than other interventions [41]. Quitting abruptly or cutting down slowly does not seem to affect the final abstinence rate [42]. The absolute effect size of the different treatments varies between 1% and 19%. That is to be compared with no treatment at all: 1–5% will stop smoking and, with treatment, 2–20% will be smoke-free after 6–12 months. The most effective treatment is intensive behavioural support plus medication and the least, but still significantly effective treatment, is a short (< 3 minutes) advice given by a physician [43]. A cost-benefit analysis has shown that the brief intervention is the most cost-effective method, generating both gains in life years saved and in quality of life years (QUALYs). The cost-benefit for intensive intervention is in the same range as breast cancer screening and influenza vaccination for the elderly (1800–4000 Euro per life year gained), which is very favourable compared to other preventive interventions: for example, cholesterol lowering therapy [44].

Effect of smoking cessation interventions in hospitals

Approaching patients who are admitted to inpatient care and discussing behavioural change is a moment of opportunity. The patients will be aware of smoking and its negative effects on their health. Most hospitals have a smoke-free policy, thereby forcing the patients to be abstinent, which provides a possibility to offer professional support to everybody, including those who would not look for such help under other circumstances. Hospitals should offer face-to-face meetings during the admission period and then have supportive contacts for at least four weeks in order to have a significant effect on smoking cessation rates within 6 to 12 months [45, 46]. Patients having surgery are not different from other inpatient groups, insofar as they also require a more intensive programme to remain smoke-free after one year [47].

Alternative treatment methods

Acupuncture, hypnotherapy, anxiolytics (bupropion not included) or exercise has not shown any bias-free evidence of being better than no treatment [37, 48-50]. Vaccination, with the goal of creating antibodies that bind to nicotine and thereby making the molecules too large to cross the blood-brain barrier, still has to prove its

value. The vaccination seems to be well tolerated and there are promising results from phase 2 studies [51].

Doctors' opinions

Doctors are aware of the negative effects of smoking, but beliefs of a significant minority are negative concerning their ability to address the problem. In a review of 19 studies on attitudes among general practitioners, it was found that a large proportion of physicians thought that discussing smoking and smoking cessation was too time-consuming (40%), ineffective (38%), lacked confidence in their ability to help (22%), felt it was unpleasant to discuss (18%) or intruded in the patient's private life (5%) [52]. This seems to be reflected in how doctors act in their meeting with a patient: only 20% of smokers seeing their GP reported that they had been asked whether they smoked or not. Of those that had been asked, only two thirds recalled that they had been given advice to stop smoking [53]. In a more recent survey of attitudes among French cardiologists, it was concluded that they thought smoking cessation had absolute priority for patients with coronary heart disease. Patients were asked about smoking habits and the majority was referred to a smoking cessation centre, but 32% of the doctors never referred their patients to any cessation therapy. The authors concluded that knowledge, involvement and assistance in the management of smokers were poor [54]. Somewhat better results were reached in two other surveys where doctors were asked if they followed the 5 A´s protocol (ask, advice, assess, assist and arrange) when they met a smoker. Adherence to the protocol's first three A's was between 90% and 100%. However, one objection to the results of these studies was that the response rate was low, below 50% [55, 56]. Leaving the objections aside, it does seem that doctors' attitudes are slowly changing. It is important that doctors realize their important function as a role model and also to be aware of the fact that even the briefest advice makes a significant difference [44] . Smoking kills: for example, the longer survival of women is completely cancelled out by smoking [57], but with smoking cessation the increased risk of mortality rapidly diminishes for vascular diseases and for lung disease within 20 years [58]. Furthermore, smoking cessation therapy significantly increases survival after a cardiovascular incident [59]. Therefore, it should be mandatory for all physicians to discuss smoking with their patients.

Smokers' expectations when meeting their doctor

Smokers expect their doctor to ask and advise them about smoking. More than half of the smokers also think that the doctor should assist and follow up their attempts to stop smoking [60]. Not even in stressful situations such as before breast cancer surgery, do the patients mind to discuss and participate in smoking cessation therapy [61].

Orthopaedic surgery and smoking

Smoking and postoperative complications

It is beyond doubt that smoking, through its negative effect on tissue oxygenation [62], has an adverse effect on the outcome after surgical procedures. It has been shown that smokers having a total knee or hip replacement had a postoperative complication rate of 36% compared to 20% in non-smokers. Two thirds of these complications were wound-related [63]. In the treatment of calcaneal fractures smoking is more or less considered to be a contraindication for surgery because of the high infection rates. These results are in line with other studies showing an impaired wound healing capacity among smokers [64-66]. Smokers have an up to 4.5 times higher risk of aseptic loosening of uncemented hip implants. In addition, the same authors concluded that younger age, male gender, and avascular necrosis, previously associated with a worse outcome after a hip replacement, were all also associated with smoking. This finding might indicate that smoking is the true reason for the increased complication rate instead of the other factors [67]. The adverse effects of smoking have also been shown to have a large impact on bone healing with an increased rate of non-unions (i.e. a permanent failure to heal a broken bone) in spinal fusion, in fusion of scaphoid non-unions and in open tibia fractures [68-71]. Furthermore, Turan et al. [72] demonstrated that for smokers undergoing non-cardiac surgery, the odds of having a medical or a wound-related complication were between 1.27 and 1.40.

Are the negative effects of smoking on healing reversible?

Turan et al. estimated by matching 82,304 smokers with the same number of non-smokers that 71% of the increased risk of complications were associated with smoking and the rest with smoke-related chronic diseases [72]. Inhaling smoke from a cigarette decreases the tissue oxygen tension in subcutaneous tissue from 65 to 44 mm Hg within 30 minutes and causes a return to pre-smoking values after some 60 minutes. A typical smoker, consuming 20 cigarettes per day, will have chronic hypoxia in peripheral tissue even if this effect is reversible within one hour [73]. Carbon monoxide (CO) is significantly increased in the blood of smokers. It binds to the haemoglobin molecule and reduces the smoker's ability to transport oxygen to the periphery. The half-life of CO is only 2–6 hours, and after only 6–9 hours of abstinence one can no longer detect increased levels of CO in exhaled air [74]. On the other hand, CO does not only have an acute effect, but there is also a toxic more long-lasting effect on the enzyme cytochrome c oxidase in the mitochondria [75]. Function of the cells in the immune system is negatively affected by smoking; 20 days of abstinence from smoking will normalize the oxidative burst but not restore chemotaxis [76]. Collagen synthesis is markedly decreased in smokers; 20 days of abstinence did not improve its production, but abstinence combined with a nicotine replacement patch did have a significantly positive effect on the synthesis of collagen 1 [77]. Fibroblast proliferation and inflammation in wounds are attenuated in smokers. Abstinence will restore the

inflammatory capacity but not the fibroblast function. Bone healing around titanium implants in rats is seriously affected if the rats are exposed to smoke, but it was normal in the groups where exposure was interrupted 7 days before the implantation [79]. Retrospective cohort studies indicate that those who stop smoking after a spinal fusion will have the same risk of non-union as never-smokers: 17% and 14 %, respectively, compared to 27% for the smokers [80].

Two randomized controlled studies have shown that intensive smoking cessation therapy initiated 4–6 weeks before elective surgery significantly reduces the number of postoperative complications [81, 82]. In a relatively small study including 60 patients, no differences in complication rates could be seen between the groups receiving smoking cessation therapy 2–3 weeks before colorectal surgery and a control group [83]. Nor was any effect on complication rates noted from a brief smoking cessation intervention started a few days before breast cancer surgery [84].

Defining and measuring complications

Definition of complications

The Food and Drug Administration (FDA) has adopted the following definition: "Adverse advents are reportable if they are serious or unexpected. Serious is defined as an event that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or necessitates surgical re-intervention [85, page 3]."

Dekutoski et al. have suggested that there is a difference between an adverse event and a complication, i.e. an adverse event includes any unexpected or undesirable event occurring as a result of surgery. A complication, on the other hand, is a disorder or disease which will negatively affect the outcome for a patient. On exploring definitions and complication rates after spinal surgery, they found that complication rates from different hospital database registries ranged between 3.7% and 19.3%. The re-operation rates ranged between 9% and 19% [85]. Soohoo et al. used California's discharge database to estimate the complication rate in patients who had undergone open reduction and internal fixation of ankle fractures. They found that 3.8% had been re-operated upon, had pulmonary embolism or died within the first three months. An additional 1%t of the patients had had secondary surgery within the first five years postoperatively [86]. These results are in contrast to a study by Bojan et al. who looked at complications among 3006 patients with trochanteric fractures. Almost 11% of these patients suffered from a perioperative or postoperative fracture complication and an additional 4% later had their implant removed for other reasons [87]. Smektala et al. found an overall inpatient complication rate of 25% in 2916 prospectively followed patients with hip fractures. They defined complication as an event requiring any type of

treatment. The mortality rate within a year was 20% in their study [88]. In a review of 112 randomized controlled studies, complications were presented as part of the outcome in only two thirds of them. Only eight of the studies had predefined the anticipated complications. Only 50% of these studies, having complications as part of their outcome, regarded a re-operation of a fracture as a complication. This lack of a general definition of complications may explain the large variation in the reported complication rates [89]. Other obvious reasons for variation are the different surgical procedures chosen [85–91], outcome definitions and differences in follow-up times [92–94], all of which affect the reported occurrence of complications.

Patients and doctors define a complication in almost the same way. However, patients regard certain events to be more serious than judged by their doctors [95]. Bennet-Guerro et al. studied mainly medical complications [92] and did not define wound infections/complications as thoroughly as did Managram et al. [96]. My conclusion is that a broad definition of complications should be used, i.e. an unexpected event in relation to a surgical procedure that requires some kind of intervention. There is a strong need to specify the definition of orthopaedic complications for scientific reasons, but also for clinical use so that the follow-up of patients is done adequately and will contribute to improvement of the outcomes for our patients.

Complications in relation to the final outcome

Having a complication does affect the final outcome for the patient. Patients with superficial wound infections have been found to have a significant decline in their mental health component in SF-12; the decline was of the same magnitude as seen in patients after their first myocardial infarction [97]. On studying both deep and superficial infections after general orthopaedic surgery, the data revealed a clinical and significant reduction in 5 of the SF-36 domains: physical functioning, role-physical, bodily pain, general health and social functioning [98]. In spinal surgery a correlation was seen between the author's definition of a major complication and the decrease of the SF-36 general health score one year postoperatively [99]. Dislocation of a hip arthroplasty had a negative effect on patients' self-perceived health according to the EQ-5D [100].

2 OBJECTIVES

The overall objectives of this thesis were to estimate to what degree smoking is associated with postoperative complications and whether the potential negative effect of smoking in orthopaedic trauma surgery could be reversed with smoking cessation therapy.

STUDY I

The primary objective of this follow-up study on 906 consecutive patients operatively treated for an ankle fracture was to investigate the impact of smoking on postoperative complications, particularly deep wound infections.

STUDY II

The primary objective of this single-blinded, randomized, controlled trial was to evaluate whether a smoking cessation intervention, started during the acute hospitalization period and continuing during the acute postoperative phase of 6 weeks, would reduce the numbers of complications after acute fracture surgery.

STUDY III

The primary objective of this study was to evaluate the efficacy of the smoking cessation intervention programme in terms of post-operative smoking cessation during the first 6–12 weeks and one year after the injury.

STUDY IV

The goal of this study was to describe to what degree smoking contributes to major orthopaedic complications after general orthopaedic surgery. For this purpose, we used two population-based Swedish registers to assess smoking status, type of orthopaedic surgery and all complications severe enough to require hospital re-admission.

3 OVERVIEW OF THE THESIS

ETHICAL CONSIDERATIONS

All studies were conducted according to the Helsinki Declaration and approved by the Regional Ethical Review Board, Stockholm, Sweden.

MATERIAL AND METHODS

Study settings and design

Two study designs were used in this thesis, i.e. retrospective cohort and a prospective randomized controlled trial (RCT). In all, 9784 were patients included in the four included studies (Figure 1).

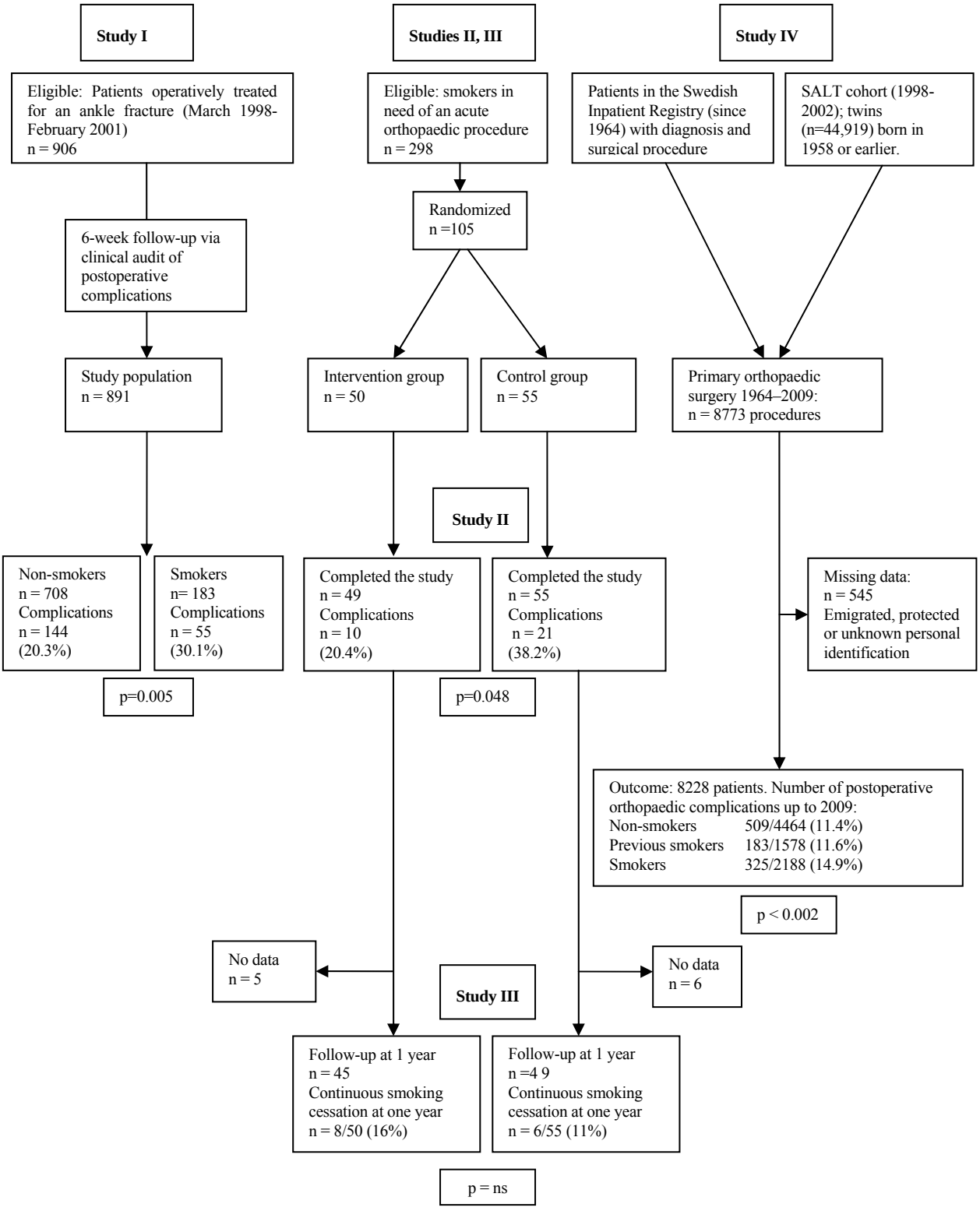
Study I is a retrospective follow-up study, including a consecutive series of 906 patients, aged 15 years or older, operatively treated for an acute ankle fracture during a three-year period (March, 1998–February, 2001) who were identified via the Orthopaedic Department Database at Södersjukhuset.

Studies II and III are based on the same population from a single-blinded, randomized, controlled, clinical, multicenter trial at three hospitals in Stockholm, Sweden. We included 105 daily smokers [101, 102] with an acute fracture of a lower or upper extremity requiring acute surgical procedures and treated for no more than two days prior to inclusion. Inclusion was started in February, 2004, and ended in March, 2006.

Study IV is a cohort study based on the Swedish Twin Registry: 8773 persons from the SALT cohort [103] who had an orthopaedic surgical procedure (index operation) between 1964 and 2009 with primary joint replacement, ligament surgery, arthrodesis, fracture surgery, tendon suturing or discectomy or decompression of the spine were included.

Figure 1

Flowchart of all included patients in Studies I to IV



Assessment of background and outcome data

Background data were assessed in three different ways: compiled from patient charts (Study I), collected prospectively by a study nurse (Studies II and III) and by a computer-assisted telephone interview (Study IV). The outcomes were assessed via data from a clinical routine audit program and medical charts (Study I), collected prospectively by a study nurse (Studies II and III) and from the Swedish Inpatient Register (Study IV)**.**

Study I

Background data

In total, 906 patients were included (Table 1). The patient was regarded as a smoker (n = 185) only if it was stated in the medical chart that the patient was a current smoker; otherwise, the patient was regarded as a non-smoker (n = 721). Background data on all patients, including diabetes mellitus, co-morbidity (e.g. cardiovascular disease) and alcohol/drug misuse, as well as injury and surgical intervention data, were collected from the patients' medical charts from all hospital departments via a computerized patient record system. The accuracy of reduction of the fracture on the postoperative radiographs was assessed from statements in the medical charts. Injury mechanisms were classified as low energy (i.e. simple fall) or high energy (i.e. traffic, sports or fall from a height). It was noted whether the fracture was open or closed.

Outcome data

The outcome data included postoperative complications defined as: superficial wound infections (treated with antibiotics or repeated dressings), deep wound infections (below the deep fascia requiring surgical intervention) [96], deep vein thrombosis (verified by ultrasound or phlebography), pulmonary embolism (CT-verified), urinary tract infection (treated with antibiotics), nerve or vascular injuries including compartment syndrome (clinically verified), plaster-related complications (requiring skin care) and fracture treatment-related complications (inadequately reduced fracture or dislocation of the fracture within 6–8 weeks).

The outcome data were prospectively collected from a clinical audit questionnaire distributed to all patients before discharge from hospital. This audit was part of a routine quality control performed on all operated patients in our department. The patients were asked to fill in the questionnaire and return it 6 weeks after the operation by post. One written reminder was sent to the patient, and if the patient did not respond, a phone contact was established by the study nurse to the patient, the patients' relatives or the staff responsible for the patient. All reported postoperative complications were then confirmed and assessed via medical charts by the orthopaedic surgeon responsible

for the clinical audit. Through these procedures, a 6-week follow-up rate of 98.2% was achieved. An additional review of complications occurring after the first 6 postoperative weeks until June 2002 (i.e. a follow-up period between 1.5 and 3.5 years) was conducted via medical charts. For those patients still under treatment during 2002 due to a deep wound infection related to the fracture treatment, a second review was conducted in 2009, i.e. these patients had a follow-up as long as 11 years.

Table 1

Demographic and injury data for the non-smokers (n=721) and smokers (n=185).

	All patients n = 906		**Non-smokers n = 721**		**Smokers n = 185**		**p-value**
	Mean	SD	Mean	SD	Mean	SD	
Age			50.6	18.4	48.4	13.1	ns
	n	%	n	%	n	%	
Gender (female)	481	53.1	383	53.1	98	53.0	ns
Diabetes mellitus, any kind*	55	6.1	48	6.7	7	3.8	ns
Insulin-dependent diabetes*	27	3.0	24	3.4	3	1.6	ns
Any co-morbidity, except diabetes*	347	38.3	267	37.7	80	43.7	ns
Current alcohol or drug abuse*	67	7.4	24	3.3	43	23.2	0.000
Low-energy trauma	714	78.8	565	78.4	149	80.5	ns
Type of fracture							
Unimalleolar	408	45	323	44.8	85	45.9	ns
Bimalleolar	244	29.6	202	28.0	42	22.4	ns
Trimalleolar	254	28.0	196	27.2	58	31.4	ns
Open fracture	31	3.4	20	2.8	11	5.9	0.042
Surgery within 24 hours	707	78	570	79.1	137	74.1	ns
Method of primary operative fixation							
Plate and screws	642	70.9	519	72.0	123	66.5	ns
Other	264	29.1	202	28.0	62	33.5	ns
Postoperative x-ray Satisfactory*	869	95.9	695	96.4	174	94.1	ns
Secondary surgery due to malreduction	23	2.6	15	2.1	8	4.4	ns

* If stated in the patient's medical records; otherwise, the patient was considered not to have the condition.

Studies II and III

Background data at baseline

Baseline injury and treatment data were collected by a study nurse at inclusion. Data on smoking habits, age, gender, FEV 1.0[104], BMI [105], haemoglobin concentration, social factors, ASA score [106], current illness, fracture location and treatment method were recorded (Table 2).

Outcome data

The *primary outcome* was defined as the number of patients with at least one postoperative complication at 6 to 12 weeks. Postoperative complications were predefined in the study protocol: any unexpected event causing additional medical or surgical treatment, additional investigations (radiography, laboratory tests), a prolonged hospital stay, or unscheduled postoperative check-ups in the outpatient department [92, 96]. All complications were verified via a review of the medical records and case record forms by the orthopaedic surgeons responsible for the study together with an

orthopaedic surgeon not involved in the study. This review was done after the study was finished and before the randomization code was broken.
All patients were followed up at 2–3 weeks (face-to-face), at 4 weeks (telephone interview) and at 6–12 weeks (face-to-face) by the study nurses. The study nurses responsible for recording the complications at each hospital were given the same training in how to define and record possible complications on the case record form. A questionnaire regarding the patients' current smoking status was completed by the patients at the 2–3 and 6–12-week follow-ups. Exhaled carbon monoxide concentrations were measured on the same occasions to verify the smoking status.

The *secondary outcome,* i.e. the outcome in study III, was being continuously smoke-free during the first 6 to 12 weeks and during the first year. The information about the smoking data at one year was collected through questionnaires or by telephone if the questionnaire was not returned. This information was not verified by carbon monoxide measurements.

Table 2

Demographic baseline data and injury and treatment data (Studies II and III).

	Intervention group n = 49		**Control group n = 55***	
	Mean	**SD**	**Mean**	**SD**
Pack years[1]	21.5	11.8	21.5	16.2
Cigarettes per day	12.8	5.7	13.2	6.3
FEV 1.0[2]	2.4	0.9	2.5	0.9
Age (years)	54.7	2.2	51.5	2.0
Body mass index (BMI)	24.3	4.6	25.7	4.1
Haemoglobin (g/L)	136.9	13.9	135.0	11.9
	n	**%**	**n**	**%**
Sex (female)	36	73.5	37	67.3
Living alone	22	44.9	27	49.1
Unemployed	9	18.4	12	21.8
University education	11	22.4	18	32.7
ASA[3]				
1	22	44.9	25	47.2
2	22	44.9	23	43.3
3–4	5	10.2	5	9.4
Current illness				
Heart disease	3	6.1	2	5.8
Lung disease	7	14.3	8	15.4
Diabetes mellitus	3	6.1	2	3.6
Depression	11	22.4	10	19.2
High blood pressure	8	16.3	5	9.1
No other disease	23	49.6	32	61.5
Fracture location				
Ankle	22	44.0	28	53.8
Hip[4]	12	24.0	10	19.2
Tibia/knee	5	10.0	6	11.5
Foot	2	4.0	0	0.0
Upper extremity	9	18.0	8	15.4
Treatment method				
Open reduction/IF[5]	36	73.5	41	78.8
Closed reduction/IF[5]	9	18.4	9	17.3
Closed reduction/ EF[6]	1	2.0	1	3.8
Hip arthroplasty	2	4.0	2	3.8
Shoulder arthroplasty	1	2.0	0	0.0

[1] Pack year = 20 cigarettes/day/year; [2] FEV 1.0 = forced expiratory volume in 1 sec; [3] American Society of Anesthesiologists physical status score; [4] One patient in the control group also had a distal radius fracture; [5] IF = internal fixation; [6] EF = external fixation. * No data on two patients except for age and sex.

Study IV

Background data

Background data were extracted from the SALT Register [103]. Information was available regarding health, social factors and lifestyle, including tobacco use. For the purpose of this study, data were extracted regarding the subjects' smoking status, where they stated whether they were never, former or current smokers. Information about age at onset, total duration and intensity of tobacco use was recorded. We defined those who stated that they had never smoked regularly as non-smokers, those who had stopped smoking the year before their surgery as previous smokers and those who smoked during the year when they had their surgery as smokers.
For the purpose of this study, self-reported information concerning diabetes, self-perceived health, level of education, exercise habits and alcohol consumption were also extracted (Table 3).

Outcome data

Information about complications after orthopaedic surgery was collected via a linkage to the Swedish Inpatient Registry. Predefined ICD diagnosis numbers and surgical procedure numbers were used to identify complications. Patients were followed for complications from the day of the index operation to the first of the following events: date of re-hospitalization with a complication, date of death, date of a second orthopaedic procedure that was not defined as a complication or 31st December 2009. Study participants who emigrated from Sweden after the index operation or had an unknown personal identification number (n = 4) were excluded.

The main outcome was defined as the presence of a complication or not. Complications were defined as being admitted to hospital and diagnosed with a wound infection or wound complication, fracture healing or mechanical complication, secondary joint replacement or reduction of a dislocated prosthesis. Mortality was not included as a complication since the vast majority of the patients had their operation several years prior to when the interview was conducted.

Table 3

Characteristics of the study population in study IV

Background factors	**Never smoked regularly** n = 4462 (54.2%)	**Stopped smoking the year prior to surgery** n = 1578 (19.2%)	**Smoked at the time of surgery** n = 2188 (26.6%)	**p-value***
	Mean (SD)	***Mean (SD)***	***Mean (SD)***	
Age when operated on	61.50 (16.32)	60.44 (13.10)	53.96 (16,53)	< 0.001
	n (%)	***n (%)***	***n (%)***	
Gender				< 0.001
Male	1676 (45.3)	890 (24.2)	1136 (30.6)	
Female	788 (61.6)	680 (15.1)	1061 (23.3)	
Education				0.546
Basic	1857 (55.6)	581 (17.4)	903 (26.9)	
More than basic	2592 (53.2)	996 (20.5)	2190 (26.3)	
Current health				<0.001
Good	3832 (55.2)	1337 (19.3)	1774 (25.5)	
Less good	616 (48.7)	236 (18.8)	413 (32.6)	
Regular physical exercise				<0.001
Yes	2023 (57.4)	713 (20.2)	790 (22.4)	
No	2413 (51.8)	859 (18.4)	1386 (29.8)	
Diabetes				0.443
No	4159 (54.2)	1481 (19.3)	2033 (26.5)	
Yes	302 (54.5)	97 (17.7)	155 (28.5)	
Alcohol dependent (DSM IV)				<0.001
No	4410 (52.2)	1535 (19.2)	2038 (25.5)	
Yes	52 (21.2)	43 (17.6)	150 (61.2)	
Performed surgery				0.000
Soft tissue surgery	741 (47.9)	308 (19.9)	497 (32.1)	
Fracture surgery	1993 (54.4)	635 (17.4)	1028 (28.1)	
Primary joint replacement and arthrodesis	1562 (59.1)	530 (20.0)	551 (20.8)	
Decompression in the spine and fusion	165 (43.2)	105 (27.5)	112 (29.3)	

* Significant difference in age when operated on or in smoking frequency for the varying background factors

Statistical analyses

Study I

Nominal variables were tested with a chi-square test. The results were regarded as significant at $p < 0.05$, two-tailed tests. Student's t-test was used to compare the number of out-patient visits for smokers and non-smokers. Logistic regression modelling was used to study how the participants' background characteristics were associated with any of the measured outcomes. The Hosmer-Lemeshow´s goodness-of-fit test was used to determine if the model adequately fitted the data and a p value of > 0.05 indicated an acceptable fit.

Power analyses: No power analysis was done prior to the data collection. A *post hoc* analysis showed that to detect an absolute difference of 3% (between 4 and 1) in the deep wound infection rate with a power of 80% (B = 0.20) at the significance level of 0.05 alpha would have required 974 patients. To detect a difference between 3% and 1% with the same power would have required 1728 patients.

Study II

Primary analyses were performed according to intention to treat (ITT). We used the chi-squared test to compare the intervention and control groups with regard to the nominal scale and the Mann-Whitney test with regard to ratio and interval scales. The results were regarded as statistically significant if p was less than 0.05 (two-tailed). We also calculated the numbers of patients needed to treat (NNT), i.e. the number of patients that need to be treated for one patient to benefit from the intervention compared with a control. A secondary analysis was performed using an exact binary logistic regression.

Power analyses: We made a conservative estimate for our trial and planned to include 586 patients in total in order to identify a 30% reduction (from 30% to 21%) in the complication rate with a statistical power of 80% ($\beta = 0.20$) at the significance level of 0.05 α. The power calculation was performed with a two-tailed test. However, due to unexpectedly slow inclusion, a *post hoc* power analysis was conducted in December, 2006, and it was concluded that there was a 40% possibility of detecting a 10% absolute difference (30% relative risk reduction) between the groups among the 105 patients included in the study. The study was terminated because it was not likely that it was going to be finalized as planned during a reasonable period of time. No interim analysis was done.

Study III

We used the chi-2 test to compare the intervention and control groups with regard to the frequency of successful smoking cessation. The results were regarded as statistically significant at $p < 0.05$ (two-tailed). Binary logistic regression modelling was used to study how the participants' characteristics could simultaneously affect the likelihood of smoking abstinence. The results were presented as odds ratios (ORs) using the 95% confidence interval (CI). The Hosmer-Lemeshow´s goodness-of-fit test was used to determine if the multivariable model adequately fitted the data and $p > 0.05$ indicated an acceptable fit.

Study IV

Survival was charted by the Kaplan-Meier method and univariable and multivariable Cox proportional hazards regressions, using the Efron method for tie handling, were estimated for the three endpoints using the grouped jack-knife variance estimator in order to take into account the possible correlation between twins. Time at risk of a complication was defined as time from index operation to the first of the following events: date of re-hospitalization with a complication, date of death, date of a second orthopaedic procedure that was not defined as a complication or 31st December 2009. The scaled Schoenfeld residuals from the multivariable models were investigated to assess the proportional hazard assumption; the df betas were inspected to detect outliers, whereas the assumption of linearity for the continuous variable age was

investigated by means of the martingale residuals. No imputation of missing values was done and the level of significance was set to 5%, two-sided.

RESULTS

Study I

Primary outcome

Among the smokers, 30.1% (55/183) had at least one postoperative complication compared to 20.3% (114/708) of the non-smokers ($p = 0.005$). The smokers also had a higher rate of outpatient visits compared to non-smokers (mean: 4.3 and 3.5 visits, respectively, $p = 0.003$) and postoperative antibiotics were prescribed more often for smokers than for non-smokers (21.9% and 11.7%, respectively, $p = 0.003$). The odds ratio (OR) for smokers developing some postoperative complication was 1.9 (CI: 1.3–2.8) (Table 3).

Secondary outcomes

Deep infections were more common in smokers (4.9%) than in non-smokers (0.8%). The multivariable analysis (Table 4) showed that smoking was one of the factors associated with the development of a deep postoperative wound infection; OR 6.1 (CI: 2.1–17.2). Suboptimal operative reduction of the facture, having a trimalleolar fracture or insulin-dependent diabetes were also associated with an increased risk of deep infection with odds of 6.2–8.1 (Table 4).

Superficial wound infections occurred in 10.8% of the study population. All were treated with repeated wound cleansing/dressing changes and 97% were also prescribed antibiotics. These patients had on average of 5.9 outpatient visits compared to 3.1 for patients without superficial wound infections ($p < 0.000$). The multivariable analysis showed that the smokers had an increased risk of developing a superficial wound infection (OR 1.7, CI: 1.01–2.9). The other factors significantly associated with having a superficial wound infection were open fracture, secondary surgery due to initial malreduction of the fracture, age above 60 and an open fracture with odds of 2.8–9.4.

Table 3

Factors associated with risk of having some complication (199/891)

Predictor variable	Level	Crude measures		Univariable		Multivariable	
		n	Any complication %	OR	95% CI	Adjusted for the final model* OR	95% CI
Smoking	Yes	183	30.1	1.6	0.99–2.6	1.9	1.3-2.8
	No	708	20.3	Reference			
Age (years) and diabetes (no/yes)	< 60, no	611	17.7	Reference			
	< 60, yes	22	9.1	0.5	0.1-2.0		
	≥ 60, no	227	32.6	2.3	1.6-3.2	2.2	1.5-3.2
	≥ 60, yes	31	48.4	4.4	2.1-9.1	4.7	2.2-10.0
Trimalleolar fracture	Yes	250	31.2	1.9	1.4-2.7	1.5	1.1-2.2
	No	641	18.9	Reference			
Open fracture	Yes	31	61.3	6.0	2.9-12.6	5.3	2.4-11.8
	No	860	20.9	Reference			

*Associations adjusted for: Smoking, trimalleolar fracture, open fracture, co-morbidity except diabetes, age, diabetes of any kind and gender. Hosmer and Lemeshow: p = 0.878

Table 4

Factors associated with risk of having a deep infection (15/891)

Predictor variable	Level	Crude measures		Univariable		Multivariable	
		n	Deep infection %	OR	95% CI	Adjusted for the final model* OR	95% CI
Smoking	Yes	183	4.9	6.1	2.1-17.2	6.0	2.0-18.7
	No	708	0.8	Reference			
Primary postoperative x-ray unsatisfactory	Yes	37	10.8	9.3	2.8-30.7	8.1	2.2-30.3
	No	854	1.3	Reference			
Trimalleolar fracture	Yes	250	4.4	7.3	2.3-23.2	6.4	1.9-20.8
	No	641	0.6	Reference			
Insulin-dependent diabetes	Yes	27	7.4	5.2	1.1-24.5	6.2	1.1-34.1
	No	864	1.5	Reference			

*Associations adjusted for: Smoking, primary postoperative x-ray unsatisfactory, secondary surgery due to malreduction, trimalleolar fracture, insulin-dependent diabetes, open fracture, diabetes of any type, age, having any co-morbidity except diabetes and gender. Hosmer and Lemeshow: p = 0.450

Study II

Primary outcome according to intention to treat (ITT)

A higher proportion of patients in the control group had a postoperative complication compared to the intervention group (38.2% and 20.4%, respectively, p = 0.048). As shown in table 6. Superficial wound infection was the most frequently recorded complication, followed by complications related to the plaster cast. Both were more common among the controls, but these individual differences were not statistically significant. It was also noted that there were few serious adverse events, i.e. no deep infections occurred, but two patients in the control group developed a deep venous thrombosis and one had a pulmonary embolus. It was also more common among the controls to have more than one postoperative complication (Table 6). The number of patients needed to treat to prevent one patient from having one or more complications was 5.5.

Secondary outcomes and analyses

A secondary analysis showed that the exact odds of having a complication was 2.51 higher in the control group than in the intervention group, but this difference was not statistically significant (CI 0.96–6.9).

Self-reported total smoking abstinence after two weeks amounted to 24 of 48 in the intervention group and 9 of 52 in the control group (p = 0.001). The corresponding numbers at six weeks were 19 of 44 and 10 of 51 (p = 0.013). The *per protocol* analysis did not reveal any significant relationship between the self-reported total smoking abstinence and the complication rate.

Table 6

Frequency of complications in the intervention group (n = 49) and in the control group (n = 55).

	Intervention group n = 49		**Control group n = 55**		p value
	n	**%**	**n**	**%**	
Superficial wound infection (treated with antibiotics or repeated dressings)	4	8.2	11	21.1	ns
Deep wound infection (treated with surgical intervention)	0	0	0	0	ns
Urinary tract infection (treated with antibiotics)	2	4.0	3	5.7	ns
Pneumonia (treated with antibiotics)	1	2.0	1	1.9	ns
Complications related to plaster cast* (skin abrasions and pain, clinical judgment)	1	2.0	6	9.6	ns
Pressure ulcers (pressure ulcers, verified by nurse)	1	2.0	1	1.9	ns
Fracture redislocation (verified by radiographic examination)	1	2.0	1	1.9	ns
Neurological complication (global or focal symptoms emerging after the surgery)	1	2.0	0	0	ns
Deep venous thrombosis (verified by ultrasound)	0	0	2	3.6	ns
Pulmonary emboli	0	0	1	1.8	ns
Patients with at least one complication	10	20.4	21	38.2	0.048

* Requiring a total of 15 additional outpatient visits. Three patients developed a pressure ulcer during the follow-up period.

Study III

Primary outcome

Uninterrupted smoking cessation at 2-3 weeks and at 6–12 weeks was significantly more common among the patients in the intervention group compared with the patients in the control group (30% vs. 13%, p = 0.03), but no significant difference between the groups could be detected at 12-month follow-up (16.0% vs. 10.9%, p = 0.44) as shown in Tables 7 and 8.

After 6–12 weeks the only baseline characteristic associated with continuous cessation was a BMI over 25 (Table 7). No baseline characteristics were associated with continuous cessation at one year.

Table 7

Factors associated with continuous smoking cessation at 2 and 6 weeks

Predictor variable	Level	Crude measures		Univariable		Multivariable	
			Smoke-free			Adjusted for the final model*	
		n	%	OR	95% CI	OR	95% CI
Smoking cessation therapy	Yes	50	30	Reference			
	No	55	12.7	0.3	0.1–0.9	0.3	0.09–0.9
BMI ≤ 25		48	14.6	Reference			
BMI > 25		43	27.9	2.2	0.8–6.4	3.1	1.003–9.3

*Hosmer and Lemeshow: p = 0.278

Table 8

Factors associated with self-reported continuous smoking cessation at one year

Factor	Level	Crude measures		Univariable		Multivariable*	
			Smoke-free			Adjusted for the final model*	
		n	%	OR	95% CI	OR	95% CI
Smoking cessation therapy	Yes	50	16.0	Reference			
	No	55	10.9	0.6	0.2–2.0		

No factors included in the multivariable analyses as none of the factors in the univariable analyses had a p value < 0.150

Study IV

Descriptive data

The median follow-up period from the date of the index operation until the first complication or censoring occurred was 5.0 years. The median time until a complication occurred was 8.5 months (25 percentile 1.8 months and 75 percentile 24.0 months). Two thousand one hundred eighty-eight patients were current smokers at the time of surgery, and 30 of them had ceased smoking before they had their complication. For these 30 patients, the median period of smoking abstinence before the occurrence of a complication was 4 years.

Smokers at the time of surgery were, on the average, 6 years younger than those who had never smoked or had ceased smoking prior to surgery. The results also showed that smoking was more common among men than among women. Those with good health, who exercised more or had a joint replacement, smoked less than their counterparts.

Outcome data

The overall complication rate was 12.6% (n = 1103). Fracture-related or mechanical complications were most common and occurred in 8.8% of the patients (n =725); 8.3% of the non-smokers, 8.7% of the ex-smokers and 10.0% of the smokers. Postoperative wound infection and other wound-related complications were the second most common type of complication with 1.8% (n = 146), followed by secondary joint replacement, 0.7% (n = 54), non-union, 0.5% (n = 44) and dislocation of a joint prosthesis, 0.5% (n = 44).

Smoking and the risk of complications

Having any complication was significantly associated with smoking at the time of surgery; HR 1.27 (CI 1.10–1.48, p = 0.002) (Table 9). Having a wound infection or other wound-related complication was also significantly associated with smoking at the time of surgery; HR 1.71 (CI 1.16–2.51, p = 0.007) (Table 10). An analysis of the subgroup of patients who had had fracture surgery showed a significant association between smoking at the time of surgery and the development of a non-union; HR 3.68 (CI 1.87–7.23, p < .001) (Table 11). All variables included in the multivariable models were tested for interactions with smoking. For the endpoints "any/some complication" and non-union, smoking did not have any interactions with p value < 0.1, but for the secondary endpoint wound infection/complication, gender (p=0.015) interacted with smoking with an increased risk for smoking women.

The corresponding HR for current smokers to have a complication occurring within a year are: any complication, HR 1.43 (CI 1.17–1.73, p < 0.001), wound infection/complication, HR 1.77 (CI 1.09–2.88, p = 0.02) and non-union, 3.87 (CI 1.78–8.42, p = 0.001)

Table 9
Hazard ratio for major complications after orthopaedic surgery.

	Patients n = 8228	**Any complication n = 1017**		**Univariable**		**Multivariable***	
	n	**n**	**%**	**Hazard ratio**	**95% Confidence interval**	**Hazard ratio**	**95% Confidence interval**
Never smoked	4462	509	11.4	ref			
Stopped smoking	1578	183	11.6	1.07	0.9-1.27	1.17	0.98-1.38
Smoked	2188	325	14.9	1.26	1.10-1.45	1.27	1.10-1.48

*Adjusted for all background variables

Table 10
Hazard ratios for wound infection/complications after orthopaedic surgery.

	Patients n = 8228	**Wound infection/ complication n = 146**		**Univariable**		**Multivariable***	
	n	**n**	**%**	**Hazard ratio**	**95% Confidence interval**	**Hazard ratio**	**95% Confidence interval**
Never smoked	4462	63	1.4	ref			
Stopped smoking	1578	26	1.6	1.23	0.78–1.94	1.16	0.72–1.87
Smoked	2188	57	2.6	1.76	1.23–2.52	1.71	1.16–2.51

*Adjusted for all background variables

Table 11
Hazard ratios for non-union after orthopaedic surgery.

	Patients surgically treaded for a fracture n = 3656	**Non-union n = 44**		**Univariable**		**Multivariable****	
	n	**n**	**%**	**Hazard ratio**	**95% Confidence interval**	**Hazard ratio**	**95% Confidence interval**
Never smoked	1993	15	0.8	ref			
Stopped smoking	635	6	0.9	1.32	0.51-3.41	1.44	0.55-3.74
Smoked	1028	23	2.2	3.01	1.57-5.76	3.68	1.87-7.23

**All background factors included, except the four types of surgery

GENERAL DISCUSSION

Our results show that smoking affects the outcome after orthopaedic surgery by increasing the risk of short and long-term postoperative complications (Studies I and IV). The main and novel finding in Study II was that a six-week smoking cessation programme, started at the time of emergency fracture surgery, significantly reduces the postoperative complication rate. In Study III it was concluded that it is possible to help orthopaedic trauma patients to achieve short-term smoking cessation, but the chosen smoking cessation intervention had no effect on smoking rates at one year in this patient group.

Increased risk of complications for smokers

Studies I and IV are consistent with previous findings in the literature showing the negative impact of smoking on postoperative complications both in acute and elective orthopaedic surgery [63, 107] [64-66, 68-72]. With these two studies we have been able to estimate the degree the risk of complications among smokers as compared to non-smokers. After general orthopaedic surgery, 14.9% of the smokers had a complication requiring inpatient care, compared to 11.4% of the never smokers and 11.6% of the former smokers (HR 1.27). After ankle fracture surgery, 30.1% of the smokers had a complication within the first six postoperative weeks, compared to 20.3% of the non-smokers (OR 1.9). Smokers had an even higher risk of deep wound infections in Studies I and IV: 2.6% and 4.8% of the smokers in Study I and IV, respectively, compared to 0.8 and 1.4% for non-smokers (OR of 6.0 in Study 1 and with a HR of 1.71 in Study IV).

The outcomes in Studies I and IV were measured in two different ways. In Study I the patients were followed up prospectively for six weeks as part of a routine clinical audit. Those who did not return their questionnaires were contacted by telephone which resulted in the very high follow-up rate of 98%. This method, which allows recording of even minor adverse events renders higher complication rates than seen in studies using only inpatient register data.[93] However, the accuracy of the complication rate depends also on the chosen diagnostic criteria [92, 96]. In study IV we only included patients with complications that had required hospital care, but, on the other hand, a register follow-up of this type allows a much longer follow-up time compared to clinical studies. The weakness of using registers is the uncertainty of the accuracy of the complications registered at discharge. However, validation studies of the Swedish Inpatient Registry have found the data to be trustworthy [108, 109]. The overall complication rate within 6 weeks was 22% in Study I and 12% in Study IV. This difference in complications rates most likely reflects the different ways of follow-up and the definition of a complication in each of the studies. In addition, the overall complication rate in Study II was even somewhat higher (29%). The patients

in Study II were followed up over the same time period as those in Study I, but each patient had a face-to face meeting and also underwent a physical examination by a doctor and by a study nurse, which probably increased the probability of having a complication recorded.

It should be noted that in Study I we also identified other known risk factors for developing postoperative complications: elderly patients, especially those with diabetes mellitus, those with an open or more severe fracture, secondary surgery as well as cases where the fracture reduction was suboptimal were at high risk of developing a postoperative complication [86, 110–112]. These findings, confirming previously reported findings by others, strengthen the reliability of our data. Furthermore, the consistent finding of increased complication risks among smokers in Studies I and IV, together with previous findings [62, 72, 73, 76–82], strongly supports our conclusion that smoking is not only associated with, but also the direct cause of, the increased complication rate.

Fewer complications with smoking cessation therapy in orthopaedic trauma surgery

The main and novel finding of Study II is that a six-week smoking cessation programme, started at the time of emergency fracture surgery, significantly reduces the postoperative complication rate. Others have shown that intensive smoking cessation therapy started 4–6 weeks before elective surgery diminishes the complication rate [81, 82]. Smoking cessation therapy initiated less than four weeks preoperatively has not been shown previously to have any effect on complication rates. A brief smoking cessation intervention a few days before breast cancer surgery was found to have no effect on postoperative complications [84]. Nor was any effect seen from a programme started 2–3 weeks before colon cancer surgery [83].

In Study II we found that a significantly higher proportion of patients in the control group had a postoperative complication compared to the intervention group. It was also more common among the controls to have more than one complication. However, our secondary regression analysis could not confirm a statistically significant difference between the groups even though the exact odds of having a complication were 2.51 in favour of the intervention group. The low number needed to treat (5.5 patients) also indicates a strong effect of the treatment.

RCTs in acute patient populations are not easy to perform due to several factors such as the narrow time window for inclusion. This was also the case in Study II; during the study period it became clear that we would not be able to include the expected 586 patients (according to the original power calculation) within a reasonable time frame. In

spite of our efforts, we succeeded in including only 18% of all smokers. Therefore, we chose to terminate the study. However, even though we only succeeded in including one fifth of the initially planned number of patients, significant differences between the randomized groups could be detected. Our interpretation is that primary and secondary outcomes added together constitute an indication that there was a significant and clinically important difference in the complication rates between the intervention and control groups.

We chose to include patients with all types of extremity fractures requiring surgery, which might be questioned since fracture treatment methods and healing vary depending on the fracture. However, this choice can be justified since the focus of our study was short-term complications, and the main problems were assumed to be related to wound healing as shown previously with regard to elective patients [63, 82]. Furthermore, we also hoped that it would be possible to generalize our results for a heterogeneous fracture patient population.

The patients who declined to participate (n = 193) must be considered when interpreting our results. They might have continued to smoke or they could have quit smoking without help. They were older, they had a hip fracture more often than the rest of the cohort, and their complication rate was high. Even though the decliners' older age could have affected the complication rate, the patients in the control group had approximately the same number of complications as the decliners. These equivalent levels of complications strengthen our conclusion that our assessment of complications among patients participating in the study is valid.

Our primary end-point was defined as the total number of patients with at least one complication, a method used previously by others [81, 82]. Most of the established postoperative complications were minor, even though they were in accord with definitions (and frequencies) in previous studies [81, 82, 92, 96, 113]. However, one may question whether some of the complications are of clinical significance**.** Superficial wound infections, the most common complication noted, must be considered to be of clinical importance. Although minor superficial infections are usually easy to treat and exert a minor impact on the final medical outcome, they are more costly than expected and have a negative impact on the patient's health and well-being [97]. Skin abrasions and pain caused by the plaster cast were the second most common complication and also appeared more often in the control group. These problems required one or more extra outpatient visits, which was also the definition for a complication to be recorded as such. The clinical significance can be debated, but considering that the seven patients with plaster cast-related problems required a total of 15 outpatient visits resulting in unnecessary health care costs and suffering for the patients, we believe this type of complication should not be neglected.

In Study IV it was noted that those who were former smokers had about the same hazard ratio for having a complication as never-smokers. From this data we could not draw any conclusions about the necessary abstinence period before surgery but could conclude that abstinence from smoking somewhere between 1 and 731 days will help in reducing the risk of having a complication.

We conclude that our results in Study II indicate that this type of smoking cessation programme, requiring a total of two to three hours of support from a nurse with adequate training, decreases the risk of early postoperative complications.

Smoking cessation in an orthopaedic trauma population

Study III shows that smoking cessation therapy makes it possible to stop smoking for the first weeks after orthopaedic trauma surgery. However, in the long term, the smoking cessation intervention used in this study was not successful.

Almost one in three patients in the intervention group were continuously smoke-free for up to 12 weeks after injury compared to about one in seven patients in the control group. These results are comparable to or worse than the results from other intensive preoperative smoking cessation interventions [114-116]. However, there are some studies which indicate that trauma populations in general might have more difficulties in stopping smoking compared to the general population. Injuries are generally more common in patients with lower educational and economic levels [117-119], which in turn seems to be associated with less good results in quitting smoking [120-122]. On the other hand, patients with a lower socioeconomic status are less likely to have been offered evidence-based methods to achieve smoking cessation [123]. Introducing smoking cessation therapy to all trauma patients would at least equalize this last difference.

At one-year follow-up we could not find any difference in smoking cessation between our intervention and control groups. This is in contrast to the long-term results from other preoperative intensive smoking cessation interventions [115, 116, 124]. The discrepancy in results could be explained by fewer face-to-face appointments in our programme, most of which was administered as telephone contacts. Also the patients in the preoperative programmes had other personal contacts with staff more often due to the elective surgical pathway itself in comparison with our emergency pathway. Our intervention with one or two face-to-face interventions followed by weekly telephone contacts is somewhere between the intensity of the intervention given in Azodi and Möller's protocols and those described as brief interventions (the latter of which had no effect on the cessation rate at one year) [84, 125]. Most other similar studies have had fewer patients who declined to participate and therefore our study population might run

the risk of selection bias. Participation was voluntary and patients in both the intervention and control groups might have been more motivated to stop smoking than an average smoking trauma population. In a previously published paper a subgroup of our study population stated that their reason for participating in the study was that they wanted to receive smoking cessation therapy [126]. One interpretation of the fact that no long-term effects could be detected is that since it was not possible to have the randomization blinded to the participants, those allocated to the control group may have been keen to quit smoking [26]. It should also be noted that four of the patients in the control group and one in the intervention group who did smoke the first six weeks, developed a complication and were then smoke-free at the one-year follow-up. The complications may have worked as a motivating factor in stopping smoking. One of the most common motivations cited for wanting to quit smoking is health-related problems [27] with awareness of the medical problems [127]. Briefer interventions seem to be effective in the short perspective of a few weeks, but not in the longer run [47].

Motivating patients to participate in smoking cessation therapy

Almost two thirds of the eligible patients declined to participate and half of them gave as a reason that they simply did not want to participate in a study. One in four did not want to quit smoking at all.

It should be remembered that an accidental injury followed by hospital admission and surgery presumably raises an individual's stress level and might affect the wish to quit smoking due to the fact that nicotine is known to reduce feelings of anxiety [128] and also has a minor analgesic effect [129]. In patients scheduled for elective surgery, nicotine replacement therapy does seem to positively affect postoperative smoking behaviour, but not anxiety levels [130].

Furthermore, 35–100% of people trying to give up smoking report that they relapsed while experiencing some sort of stress [131, 132]. This fact seemed to be important to our non-participants; however, only 12% of them reported that they were unable to quit smoking because there were "too many things happening at this moment." Disease and surgery, are, on the one hand, a stress factor but, on the other hand, a motivating factor that increases the chances of achieving smoking cessation [133]. Based on the fact that almost half of our non-participants did not seem to mind the ideas of the intervention but the trial itself, we believe that a higher percentage of smokers would participate in a smoking cessation programme if it was part of routine hospital care.

Strengths and limitations of this thesis

The major strengths of this thesis are that our findings were confirmed via three different study designs. There is a consistent strong association between smoking and postoperative complications, as demonstrated in two studies based on different study populations. Due to the register data design used in Study IV, it was not possible to estimate how long before surgery it would be necessary to quit smoking in order to decrease the risk of complications. However, former smokers did not have an increased risk of complications compared to never smokers, thus underlining the fact that it is always worthwhile to stop smoking. Furthermore, our results in Study II showing that an acute six-week smoking cessation programme significantly reduces the postoperative complication rate strengthen this conclusion. The strength of Study II is that it is a randomized controlled trial in a multicentre setting and that the intervention and the follow-up were standardized and conducted by well-trained staff, as well as that the outcome assessment was conducted single-blinded by study nurses and regular staff were not aware of the randomization groups.

The major limitation in Studies II and III is the low numbers of participants. Study II was designed according to intention-to-treat principles and the aim was to find out whether smoking cessation therapy initiated at the time of acute fracture treatment could reduce the number of complications. According to the intention-to-treat analyses, there was a significant effect of the therapy, but the *per protocol* analysis did not show any significant association between those who reported to be smoke-free and the number of complications. Study III looked at secondary outcomes of successful smoking cessation during the first 6–12 weeks and during the first year. It was noted that that the therapy given was effective within the first follow-up period, but there was no difference between the groups at one year.

Since we wanted to explain the effect seen in Study II with successful abstinence from smoking, is it troublesome that the *per protocol* analysis was negative. There are several possible explanations. In our view, the most plausible one is that the number of patients included was too low, i.e. the study was underpowered. In Studies II and III we had no absolute knowledge concerning the treatment allocation. The primary outcome in Study II was well defined in our study protocol, thereby minimizing the risk of bias and random mistakes. The outcome in Study III was, both because it was a secondary outcome and because abstinence from smoking is not that easy to verify [134–136], somewhat more uncertain. The patients in the treatment arm had regular weekly contacts with the nurse responsible for the smoking cessation treatment and in these contacts discussions about smoking and relapse were included. This might have made the patients in the treatment arm more prone to report that they had not been smoke-free at the follow-ups, compared to those in the control group who only met the nurse responsible for the outcome measures on two occasions.

The hypothetical effect of the smoking cessation is partly supported in our data. If, in the analysis of complications, we selectively sort out those that occurred during the in-patient treatment, when all patients were by necessity more or less smoke-free, there will be a fairly decent absolute, but not significant, difference in the *per protocol* analysis. Seventeen per cent of those who were smoke-free at two weeks had a complication, compared to 27% among the smokers.

General health aspects

Always worthwhile to stop smoking

The studies included in this thesis, as well other previously published papers, demonstrate the importance of stop smoking and related factors: Former smokers have the same complication risk after orthopaedic surgery as never- smokers (Study IV). Smoking cessation therapy initiated at the time of fracture surgery yields a significant reduction of the number of complications (Study II). Successful smoking cessation gives a very quick decrease in the excess risk of vascular disease and, within 20 years, the risk of lung diseases are the same as for never-smokers [58]. Smoking cessation therapy in high-risk smokers reduces cardiovascular mortality [59] and an aggressive tobacco control programme seems to reduce the number of deaths from heart diseases [137]. The majority of smokers want to quit smoking and up to 40% of them do try to quit every year. Only 20–30% of the quitters search for help and find an effective treatment [123]. Professional support is less frequently utilized among the less strong socioeconomic groups with the highest smoking rates [123].

Five to ten per cent [47] of the population will undergo some kind of surgical procedure annually, and this is a window of opportunity to offer evidence-based help to stop smoking to a large part of the population, including those that seldom ask for or get the most qualified help.

Doctors play an important role in motivating and helping patients to quit smoking [44, 60]. Our results, together with previously published data, should motivate orthopaedic surgeons to discuss smoking with their patients. And, finally, one patient succeeding in being smoke-free might also inspire others in his or her immediate social network to stop smoking [22].

The future

Future research

We have shown that smoking cessation therapy results in a significant reduction of postoperative complications. It would also be beneficial to confirm that smoking cessation per se reduces the number of complications in a trauma population. This would require both a larger population than we had in our randomized study and a more thorough follow-up of the smoking status of all participants. Smoking status could be evaluated with measurements of cotinine and self-reported tobacco use. The advantage with cotinine is that it gives a picture of smoking habits during the last week [74].

Nicotine in low doses applied locally and perhaps systemically seems to stimulate angiogenesis and soft tissue healing [1, 77, 138]. The principles of healing are the same in skin and bone, and in some laboratory studies nicotine in low doses has been shown to stimulate bone healing [139, 140]. It would therefore be interesting to investigate whether nicotine has any clinical effect on bone healing. On comparing healing time after open gap osteotomy in proximal tibias, it was found that moist snuff users healed as fast as non-smokers and that smokers had significantly longer healing times [141]. The main problem with clinical evaluation of bone healing is how to define a healed fracture. To my knowledge, there is no generally accepted definition of how to decide if a fracture is healed or not. The next problem is that different fractures have such great variance in healing time, depending both on location and whether they are high or low-energy fractures. A first step could be a case control study with, for example, non-united humeral fractures and moist snuff as the factor of interest.

According to some papers, Swedish snus, a moist oral tobacco, increases the risk of cardiovascular mortality [145, 146] and pancreatic cancer [147]. But the results are uncertain and in one review, the author came to the conclusion that there are no certain negative health effects from snus [148]. We would like to know if snus users have any increased or decreased risk of complications after general orthopaedic surgery. A suitable design to test this would be as in our Study IV.

Smoking cessation units

The future is already here in the form of smoking cessation units starting at an increasing number of surgical departments in Sweden. Smoking patients who are undergoing elective surgery will benefit from this new policy [81, 82] and, according to our data, so will also those requiring acute orthopaedic surgery. Patients will have a better outcome of their surgery, but there will also be general health benefits. The intervention should be based on some type of behavioural counselling and preferably in

personal meetings. It should also be continued for at least one month after discharge from hospital to achieve smoking cessation for longer than a year [45]. Thereby, the short-term risk of complications and the long-term risk of general smoke-related disease will be reduced. By accomplishing short and long-term smoking cessation, these new smoking cessation units will most probably be very cost effective [44].

4 CONCLUSIONS

Smoking is an independent and significant risk factor associated with the development of complications after orthopaedic surgery.

Smoking cessation therapy significantly decreases the number of complications in a smoking orthopaedic trauma population requiring acute surgery.

It is possible to achieve short-term smoking cessation in an acute orthopaedic trauma population with a smoking cessation programme started at the time of admission.

Smoking patients in need of orthopaedic surgery should be offered an intensive smoking cessation programme.

5 SAMMANFATTNING PÅ SVENSKA

Rökning har förödande generella hälsoeffekter och påtaglig negativ inverkan på resultaten av kirurgiska ingrepp. Denna avhandling hade tre huvudmålsättningar. Första målet var att undersöka hur stor är riskökningen för rökare att drabbas av postoperativa komplikationer. Det andra målet var att undersöka om rökavvänjning kan minska antalet postoperativa komplikationer i samband akut frakturkirurgi. Det tredje målet var att följa upp om ett rökavvänjningsprogram leder till rökfrihet på längre sikt.

I studie I inkluderades 906 patienter opererade för fotledsfraktur. Bakgrundsdata inklusive uppgifter om rökning samlades in från befintliga journaler. Uppgifter om komplikationer (primärt utfall) inhämtade från ett prospektivt insamlat lokalt kvalitetsregister. Studie II och III baserades på samma studiepopulation, nämligen, på 105 frakturpatienter i behov av akut ortopedisk kirurgi, och som inkluderades i en randomiserad kontrollerad multicenter studie. Det primära utfallet i studie II var att undersöka om det förelåg någon skillnad avseende förekomsten av postoperativa komplikationer mellan de som randomiserats till att delta i ett rökavvänjningsprogram eller ej (kontrollgrupp). Utfallet i studie III var om den insatta rökavvänjningen gav ett rökstopp eller ej inom 6-12 veckor och om rökfriheten kvarstod efter ett år. Studie IV baserades på bakgrundsdata från Svenska Tvillingregistrets SALT-cohort. Dessa data samkördes med Slutenvårdsregistret för att identifiera de individer som hade genomgått minst en ortopedisk operation (n=8773) och också för att identifiera vilka av dessa hade drabbats av någon postoperativ komplikation.

Resultaten av studie I visade att 30.1% av rökarna hade minst en postoperativ komplikation jämfört med 20.3% av icke-rökarna (OR 1.9; CI 1.3–2.8, p = 0.005). I studie II hade patienter som randomiserats till rökavvänjning ett signifikant lägre antal komplikationer jämför med kontrollgruppen (p = 0.048). Studie III visade att rökavvänjningen hjälpte patienterna att vara rökfria under de första sex till tolv veckorna men effekten kvarstod inte efter ett år. Studie IV konkluderade att rökare hade en signifikant ökad risk (14.9 %) jämfört icke-rökarna (11.4 %) att drabbas av inläggningskrävande komplikation (HR 1.27, CI 1.10–1.48, p = 0.002).

Rökning är en starkt och statistiskt signifikant faktor för uppkomst av postoperativa komplikationer. Rökavvänjning som påbörjas i samband med akuta ortopediska ingrepp minskar antalet postoperativa komplikationer. Rökare i behov av akuta eller planerade ortopediska ingrepp ska erbjudas att delta i ett rökavvänjningsprogram.

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