Effect of Smoking Cessation Intervention on Results of Acute Fracture Surgery

A Randomized Controlled Trial

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Background: Tobacco smoking is a major health and economic concern and is also known to have a significant negative effect on surgical outcomes. The benefits of a smoking cessation intervention prior to elective orthopaedic surgery have been evaluated previously. Our aim was to assess whether a smoking cessation program, initiated during the acute hospitalization period and carried out for six weeks, could reduce the number of complications following emergency surgical treatment of fractures.

Methods: In a multicenter, single-blinded, randomized, controlled clinical trial, 105 smokers with a fracture of the lower or upper extremity that needed acute surgical treatment were randomized to an intervention group (n = 50) or a control group (n = 55). The intervention group was offered a standardized smoking cessation program for six weeks, and all patients were followed at two to three weeks, four weeks, and six to twelve weeks.

Results: The proportion of patients with at least one postoperative complication was significantly larger in the control group than it was in the intervention group (38% and 20%, respectively; p = 0.048). The development of two or more postoperative complications was also more common among the controls (p = 0.039). The rates of superficial wound infection, the most frequently recorded complication in both groups, were 20% and 8%, but this difference was not significant. A secondary analysis showed that the odds of having a complication were 2.51 times (95% confidence interval, 0.96 to 6.9 times) higher in the control group than in the intervention group, but this difference was not significant.

Conclusions: Our results indicate that a smoking cessation intervention program during the first six weeks after acute fracture surgery decreases the risk of postoperative complications.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.

Smoking tobacco is a major health and economic problem, and it is also known to have a negative effect on surgical outcomes. To our knowledge, the first study to show an association between smoking and increased postoperative complications was published in 1944[1]. Since then, more than 300 papers have confirmed this association. It has been shown that smoking impairs healing of skin, bone, and soft tissues, thus resulting in flap necrosis[2-4], nonunions, delayed unions, failure of wound-healing, and infections[5-8] as well as anastomotic leakage[9]. The LEAP (Lower Extremity Assessment Project) Study Group[10] showed that current smokers were more than twice as likely to develop an infection and 3.7 times as likely to develop osteomyelitis at the site of a limb-threatening open tibial fracture. The effect of a smoking cessation intervention prior to elective orthopaedic surgery has been evaluated previously[11]. In one study of 120 patients, a smoking cessation intervention initiated six weeks prior to elective hip or knee replacement reduced the postoperative complication rate from 52% to 18%[12]. Another study[13], of patients undergoing general surgery, confirmed that a smoking cessation intervention for as short as three to four weeks preoperatively could reduce the complication rate from 41% to 21%. However, in a smaller

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study, of sixty patients, a smoking cessation intervention starting one to three weeks before colorectal surgery did not influence the complication rate[14].

We are not aware of any prospective, randomized, controlled studies of the effect of a smoking cessation program on the complication rate following emergency surgical treatment of a fracture in patients who smoke. Furthermore, the effect of such an intervention initiated and carried out during the acute postoperative phase has not been reported, to our knowledge.

We hypothesized that a smoking cessation intervention instituted during the immediate postoperative period after acute fracture surgery would reduce the prevalence of postoperative complications. The primary objective of this single-blinded, randomized, controlled trial was to determine whether a smoking cessation intervention, started during the acute hospitalization period and continuing during the acute postoperative phase of six weeks, would reduce the numbers of patients with complications following surgical treatment of an acute fracture.

Materials and Methods

We conducted a multicenter, single-blinded, randomized, controlled, clinical trial at three hospitals in Stockholm, Sweden. The study was planned according to the International Conference on Harmonization guidelines for good clinical practice and was approved by the Ethics Committee of the Karolinska Institute (reference number, 03-215), Stockholm, and registered at ClinicalTrials.gov (NCT00533000).

Participants

Potentially eligible patients were daily smokers[15,16] (more than two cigarettes per day for at least one year prior to inclusion) with an acute fracture of the lower or upper extremity that required an acute surgical procedure and was treated no more than two days prior to inclusion. Patients with a history of alcohol or drug abuse; those who were pregnant or had a severe mental illness, including dementia; and those who were unable to read and understand Swedish were excluded. The flowchart for patient inclusion is shown in Figure 1, and the baseline

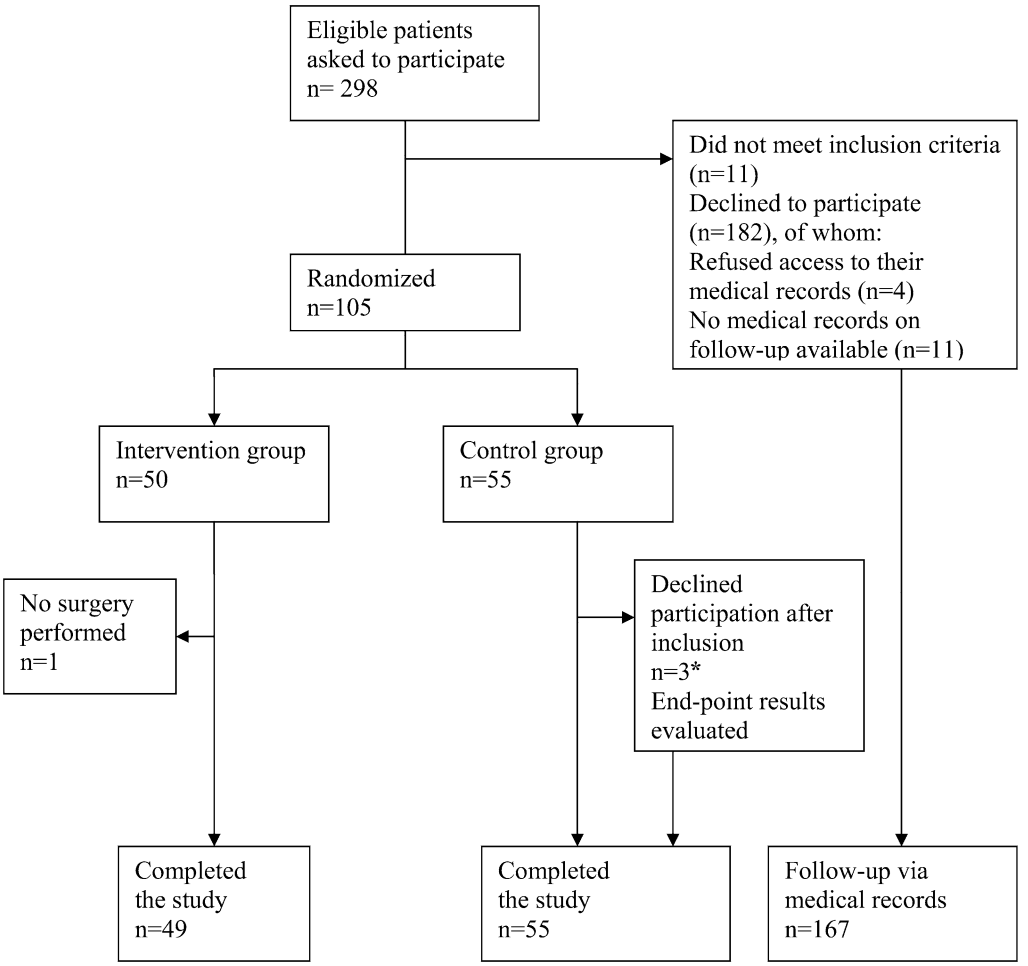

Fig. 1

Flowchart pertaining to the patient recruitment, inclusion, randomization, and follow-up. *The study was planned according to the intention-to-treat principle; we therefore included the three patients who declined to participate in our final analyses.

data for all patients are presented in Table I. The study took place between February 2004 and December 2006. The patients were followed for between six and twelve weeks after surgery.

Randomization

The patients were included after confirmation of the inclusion and exclusion criteria by one of the orthopaedic surgeons responsible for the study (H.N., E.S., or S.P.). All patients gave informed oral and written consent before inclusion. The patients were randomized in a 1:1 ratio to the control group or to the intervention group with use of opaque, sealed envelopes in blocks of ten, stratified for each hospital. The envelopes were then mixed, consecutively numbered, and put in a box. The treating orthopaedic surgeon, other medical staff, and the study team (except for the nurse responsible for conducting the smoking cessation program) were blinded to the allocation. Two study nurses were involved at each hospital: one was responsible for inclusion of the patients and for evaluation of the outcomes and was blinded to the randomization, and the other was responsible for randomization and the smoking cessation intervention. All nurses had had a long experience with randomized clinical trials and were highly aware of the importance of blinding. To further ensure blinding, all patients were asked not to reveal their randomization group, or to discuss it, with the nurse responsible for the outcome assessment or with the staff responsible for the fracture treatment. Both groups received medical and surgical treatment according to the routines in the hospital departments.

Intervention

Nurses specifically trained to carry out the chosen smoking cessation program[17] contacted the included patients on the orthopaedic wards and performed the randomization. The program, initiated within two days during the initial hospitalization period, included one or two personal meetings and weekly telephone contacts for six weeks with the nurse. At the first meeting, the Fagerström score[18] was assessed in order to estimate the degree of nicotine dependence and to help plan the smoking cessation program. The patients were continuously encouraged not to smoke, and free nicotine substitution was offered to those who needed it. No other drug therapy was used. The intervention was aimed primarily at keeping the patients from smoking for the first six postoperative weeks. The control group received general advice to stop smoking, but no additional support was offered.

Follow-up Data

All patients were followed by the study nurses at two to three weeks with a face-to-face meeting, at four weeks with a telephone interview, and at six to twelve weeks with a face-to-face meeting. The time range of six to twelve weeks for the final follow-up visit was chosen for the practical reason that it could be conducted simultaneously with the follow-up evaluation of fracture-healing. The study nurses responsible for recording the complications at each hospital received the same training

TABLE I Demographic Baseline Data and Injury and Treatment Data

	Intervention Group (N = 49)	Control Group (N = 53*)
Pack-years†‡	21.5 ± 11.8	21.5 ± 16.2
Cigarettes per day†	12.8 ± 5.7	13.2 ± 6.3
Forced expiratory volume in 1 sec† *(L)*	2.4 ± 0.9	2.5 ± 0.9
Age† *(yr)*	54.7 ± 2.2	51.5 ± 2.0
Body mass index† *(kg/m²)*	24.3 ± 4.6	25.7 ± 4.1
Hemoglobin level† *(g/L)*	136.9 ± 13.9	135.0 ± 11.9
Female sex§	36 (74)	37 (70)
Living alone§	22 (45)	27 (51)
Unemployed§	9 (18)	12 (23)
University education§	11 (22)	18 (34)
American Society of Anesthesiologists physical status score§		
1	22 (45)	25 (47)
2	22 (45)	23 (43)
3-4	5 (10)	5 (9)
Current illness§		
Heart disease	3 (6)	2 (4)
Lung disease	7 (14)	8 (15)
Diabetes mellitus	3 (6)	2 (4)
Depression	11 (22)	10 (19)
High blood pressure	8 (16)	5 (9)
No other disease	23 (50)	32 (60)
Fracture location§		
Ankle	23 (47)	31 (56)
Hip#	11 (22)	11 (20)
Tibia/knee	4 (8)	5 (9)
Foot	2 (4)	0 (0)
Upper extremity	9 (18)	9 (16)
Treatment method§		
Open reduction + internal fixation	36 (74)	43 (78)
Closed reduction + internal fixation	9 (18)	10 (18)
Closed reduction + external fixation	1 (2)	0 (0)
Hip arthroplasty	2 (4)	2 (4)
Shoulder arthroplasty	1 (2)	0 (0)

*No data, except for age, sex, fracture type, and treatment method, were available for two patients. †The values are given as the mean and standard deviation. ‡A pack-year equals twenty cigarettes per day per year. §The values are given as the number of patients with the percentage in parentheses. #One patient in the control group also had a distal radial fracture.

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 two to three-week and six to twelve-week follow-up visits.

Outcome Measures

The primary outcome was defined as the number of patients with at least one postoperative complication at six to twelve weeks. Postoperative complications, which were predefined in the study protocol, consisted of any unexpected event causing additional medical or surgical treatment, additional investigations (radiography or laboratory tests), a prolonged hospital stay, or unscheduled postoperative check-ups in the outpatient department[19,20]. The complications recorded for our patients are listed and defined in Table II.

All complications were verified with a review of the medical records and case record forms by two of the orthopaedic surgeons responsible for the study (H.N. and S.P.) together with an orthopaedic surgeon who was not involved in the study. This review was done after the study was finished and before the randomization code was broken.

Sample Size

Our initial power calculation was based on the results of a previously published randomized clinical trial on a smoking cessation intervention for patients undergoing elective hip and knee surgery[12]. That study showed a 65% relative risk reduction in postoperative complications, which were assessed until the patient was discharged from the hospital (assessment only until discharge most likely resulted in a complication rate that was lower than it would have been had it been recorded for a longer period[21]). Making a conservative estimate for our trial, we planned to include 586 patients in total in order to identify a 30% reduction in the complication rate (from 30% to 21%) with a statistical power of 80% ($\beta = 0.20$) at the significance level (α) of 0.05. The power calculation was performed with a two-tailed test.

During the study period, it became clear that enrolling patients was more difficult than had been expected. Only about 12% of our patient population smoked, and many were not willing to quit at the time of an acute injury. A major reason for the enrollment slowing down was the introduction of a non-smoking policy at the participating hospitals, which probably, as a result of an increased awareness of the negative effects of smoking, negatively affected the patients' interest in participating in a study. As a result of the 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 9% absolute difference (a 30% relative risk reduction) between the groups among the 105 patients already in the study. Furthermore, the analysis showed that the power would remain low until about 500 patients had been included. In spite of the low power, the study enrollment was terminated since it was not likely that it was going to be finalized as planned during a reasonable period of time. No interim analysis was done.

Statistical Methods

Primary analyses were performed according to the intention-to-treat principle—i.e., the patients included in the study were analyzed according to their original allocation (to the intervention or control group) regardless of whether or not they reported total smoking abstinence during the treatment period. We used the chi-square test to compare the intervention and control groups with regard to nominal values, and we used the Mann-Whitney U test to compare them with regard to

TABLE II Frequency of Complications in the Intervention and Control Groups

	Intervention Group* (N = 49)	Control Group* (N = 55)	P Value†
Superficial wound infection (treated with antibiotics or repeated dressings)	4 (8)	11 (20)	NS
Deep wound infection (treated with surgical intervention)	0 (0)	0 (0)	NS
Urinary tract infection (treated with antibiotics)	2 (4)	3 (5)	NS
Pneumonia (treated with antibiotics)	1 (2)	1 (2)	NS
Complications related to plaster cast‡ (skin abrasions and pain, verified by clinical judgment)	1 (2)	6 (11)	NS
Pressure ulcers (verified by nurse)	1 (2)	1 (2)	NS
Fracture redislocation (verified by radiographic examination)	1 (2)	1 (2)	NS
Neurological complication (global or focal symptoms emerging after surgery)	1 (2)	0 (0)	NS
Deep venous thrombosis (verified by ultrasound)	0 (0)	2 (4)	NS
Pulmonary embolus	0 (0)	1 (2)	NS
Patients with at least one complication	10 (20)	21 (38)	0.048

*The values are given as the number of patients with the percentage in parentheses. †NS = not significant. ‡Requiring a total of fifteen additional outpatient visits. Two patients developed a pressure ulcer in the gluteal region during the follow-up period.

ratios and interval values. The results were regarded as significant if p was <0.05 (two-tailed). We also calculated the number of patients who needed to be treated for one patient to benefit from the intervention compared with a control.

A secondary analysis was performed with use of an exact binary logistic regression, which is a viable alternative to the asymptotic logistic regression for analyzing small data sets or when the number of positive or negative events is low[22]. The probability of a complication occurring was the dependent variable. Predictor variables for the analysis were age, sex, socioeconomic status, American Society of Anesthesiologists score[23], number of pack-years (a pack-year is defined as twenty cigarettes per day per year), current diseases, and the randomization group. Due to the large number of variables, the small number of cases, and the lack of prior knowledge of the degree of association between baseline factors and the primary outcome, forward selection was used to decide on a model. Age was regarded as a clinically relevant prognostic factor; hence, it was included in the first step of the selection process, as was the randomization group. A p value of <0.05 was used as an inclusion criterion.

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Results

Study Population

A total of 298 eligible patients were asked to participate in the study (Fig. 1); 105 patients (35%) were enrolled and also randomized, eleven (4%) did not meet the inclusion criteria at the final assessment (e.g., the surgery had been canceled or delayed), and 182 (61%) declined to participate. All randomized patients were followed according to the study protocol, and all but four of the 182 who had declined to otherwise participate agreed to a follow-up by a review of their medical records.

The 298 patients belonged to the total population of about 4800 patients who had fracture surgery performed at the participating departments during the study period and of whom 12% were smokers (according to the hospital databases). The expected prevalence of smokers in Sweden is 14%[24,25] and, if adjusted[26] for age, the expected prevalence of smokers in our population would be 11%, indicating that our register data are fairly valid. On the basis of these data, we estimated that 18% of all smokers were included, 32% declined to participate, and 50% did not meet the inclusion criteria.

Primary Outcome According to Intention-to-Treat Analysis

As shown in Table II, the proportion of patients who had a postoperative complication was significantly higher in the control group than it was in the intervention group (38% and 20%, respectively; p = 0.048). 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 significant. There were few serious adverse events—i.e., no deep infections occurred—but a deep venous thrombosis developed in two patients in the control group and a pulmonary embolus developed in one patient in that group. The development of more than one postoperative complication was also more common among the controls (Table III).

The number of patients needed to treat to prevent one patient from having one or more complications was 5.5.

Secondary Outcomes and Analyses

The secondary analysis showed that the exact odds of having a complication were 2.51 times (95% confidence interval, 0.96 to 6.9 times) higher in the control group than in the intervention group, but this difference was not significant.

Twenty-four of forty-eight patients in the intervention group and nine of fifty-two in the control group reported total abstinence from smoking at two weeks (p = 0.001). The corresponding numbers at six weeks were nineteen of forty-four and ten of fifty-one (p = 0.013). The per-protocol analysis did not reveal any significant relationship between the self-reported total abstinence from smoking and the complication rate.

Analysis of the Outcomes for the Nonparticipants

We were able to use medical records to follow 167 of the 182 patients who declined to otherwise participate in the study. Seventy (42%) of these 167 nonparticipants had had at least one complication, and seven of them had had a deep wound infection. There were no significant differences between the

TABLE III Number of Patients with Two, One, or No Postoperative Complications in the Intervention and Control Groups*

	Intervention Group† (N = 49)	Control Group† (N = 55)
Two complications	1‡ (2)	5§ (9)
One complication	9 (18)	16 (29)
No complications	39 (80)	34 (62)

*Eleven complications occurred in ten patients in the intervention group and twenty-six complications occurred in twenty-one patients in the control group (p = 0.039; Mann-Whitney U test). †The values are given as the number of patients with the percentage in parentheses. ‡One patient experienced confusion and a urinary tract infection. §One patient had a superficial wound infection and a deep venous thrombosis, one had a deep venous thrombosis and a pulmonary embolus, one had a superficial wound infection and a urinary tract infection, one had pneumonia and a urinary tract infection, and one had a plaster-cast-related complication and a fracture redislocation.

nonparticipants and the controls regarding the frequency of postoperative complications. We had no information regarding whether the nonparticipants continued to smoke during the study period.

Discussion

The main and novel finding of our study is that a six-week smoking cessation program started immediately after emergency fracture surgery significantly reduced the postoperative complication rate. There is convincing evidence that smokers have a generally increased risk of postoperative complications. Randomized studies have shown that a smoking cessation intervention introduced prior to elective surgery significantly reduces the rate of postoperative complications[12,13]. However, to the best of our knowledge, this is the first randomized controlled trial showing that smoking cessation intervention starting in the acute hospitalization period after an acute injury and continued for a short period of six weeks is sufficient to decrease the number of postoperative complications. The proportion of patients who experienced a postoperative complication was significantly higher in the control group than it was in the intervention group. The development of more than one complication was also more common among the controls. However, our secondary regression analysis could not confirm a significant difference between the groups, although the exact odds of having a complication were 2.51 times lower in the intervention group. The low number of patients that needed to be treated (5.5) to prevent one patient from having one or more complications also indicates a strong effect of the treatment.

We were not able to confirm whether a patient had quit smoking completely, smoked less, or continued smoking as before, which is a difficulty also noted previously by others[27,28]. However, according to self-reports, a significantly larger number of the patients in the intervention group did quit smoking totally during the study period. It is not unlikely that patients in the control group also smoked less, which could explain the discrepancy between the results of the intention-to-treat analysis and those of the per-protocol analysis. It should also be noted that the intention of our trial was not to evaluate the ability of the intervention to induce patients to quit or decrease smoking but to assess whether the smoking intervention reduced the number of postoperative complications. Compliance with an intervention is probably higher in a trial than it is in clinical practice, but we noticed that some of the patients in the control group also ceased smoking, which suggests that the difference in smoking abstinence between the groups could also be expected in routine health care. The total staff time used for the intervention was less than three hours per patient, indicating that the cost of this well-validated and frequently used intervention[17,29] is modest.

In spite of our efforts, we succeeded in including only 18% of all smokers who had fracture surgery performed at the participating departments, which probably reflects a "real life" situation of patients in need of acute fracture surgery. It was more difficult to enroll patients than expected. First, only about 12% of our study population were smokers. Second, as expected, many smokers were not willing to quit at a time when they were going to undergo acute fracture surgery. Third, the inclusion rate in our study was rather low, and it declined during the second year. One explanation is that the prevalence of smoking in Sweden decreased from 24% in the 1990s to 14% in 2006[24,25], and another is that during the study period the participating hospitals introduced a nonsmoking policy, which decreased the patients' interest in participating in such a study and the chance of being included in the control group. The eleven eligible patients not meeting the inclusion criteria were mostly non-Swedish-speaking persons or patients who were not operated on at all. Patients with a history of alcohol dependency were excluded because they were not considered to be amenable to follow-up within a study. However, it has been shown by others[30] that patients with alcohol dependence are interested in stopping smoking and are able to abstain from smoking if offered adequate support.

We chose to include patients with all types of extremity fractures requiring surgery, which might be questioned since fracture treatment and healing vary. However, this choice can be justified since the focus of our study was on the short-term complications and the main problems were assumed to be related to wound-healing, as has been shown with regard to patients treated with elective surgery[8,12]. Furthermore, we also hoped that it would be possible to generalize our results to a heterogeneous fracture patient population.

The patients who declined to participate must also 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 higher rate of hip fractures than the rest of the cohort, and their complication rate was high. Even though the older age of those who declined to participate could have affected the complication rate, the patients in the control group had approximately the same number of complications as those who declined to participate. 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 the total number of patients with at least one complication, a method used previously by others[12,13], and our analysis showed a significant difference between the groups. Most of the established postoperative complications were minor, although they were in accordance with definitions (and frequencies) in previous studies[12,13,19-21].

One may question whether some of the complications are clinically relevant. However, 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, these infections are more costly than expected and have a negative impact on the patient's health and well-being[31]. Skin abrasions and pain caused by the plaster cast were the second most common complication, and they also were more common in the control group. These problems required one or more additional outpatient visits, which was one of the definitions of a complication. The clinical relevance

can be debated, but the seven patients with plaster-cast-related problems required a total of fifteen outpatient visits, resulting in unnecessary health-care costs and suffering for the patients. We believe that the relevance of this type of complication should not be discounted.

The strengths of this study are that it was a randomized controlled trial in a multicenter setting and that the intervention and the follow-up were standardized and conducted by well-trained staff. Another strength is that the outcome assessment was conducted in a single-blinded manner by study nurses and regular staff not aware of the randomization groups. The major limitation of the study is the relatively small number of patients. During the study period, it became clear that we were not going to be able to include the 586 patients required according to the original power calculation within a reasonable time frame. Therefore, we chose to terminate the study enrollment. However, although we succeeded in including less than one-fifth of the initially planned number of patients, significant differences between the groups could be detected. The fact that the differences in absolute numbers were substantial—for example, regarding superficial wound infection rates (20% compared with 8%)—is also worth noting. In spite of this study being a randomized trial, we chose to further explore the results by using an exact binary logistic regression analysis, a method specifically developed for small data sets and small numbers of events. Even though the exact odds of having a postoperative complication were 2.51 times higher in the control group, this finding was not significant. Despite this, our interpretation is that the primary and secondary outcomes added together indicate that there was a difference in the complication frequency between the groups.

The large number of patients who declined to participate in our study is also a weakness and could indicate that a large proportion of smokers may not be reachable for any kind of smoking intervention. On the other hand, 60% to 80% of all smokers are known to want to quit smoking and have made one or more attempts[24,32]. It is possible that the randomized controlled study setting made the patients hesitate to participate. Therefore, it is likely that a higher percentage of smokers with acute injuries could be reachable if the smoking cessation program were to be offered as part of a clinical routine.

We concluded that our results indicate that this type of smoking cessation program, requiring a total of two to three hours of support from a nurse with adequate training, decreases the risk of early postoperative complications. Therefore, we believe that smokers with an acute fracture requiring emergency surgery should be offered a smoking cessation intervention during the hospitalization period after the injury. ■

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References

1. Morton HJV. Tobacco smoking and pulmonary complications after operation. Lancet. 1944;243:368-70.

2. Kroll SS. Necrosis of abdominoplasty and other secondary flaps after TRAM flap breast reconstruction. Plast Reconstr Surg. 1994;94:637-43.

3. Padubidri AN, Yetman R, Browne E, Lucas A, Papay F, Larive B, Zins J. Complications of postmastectomy breast reconstructions in smokers, ex-smokers, and nonsmokers. Plast Reconstr Surg. 2001;107:342-51.

4. Kuri M, Nakagawa M, Tanaka H, Hasuo S, Kishi Y. Determination of the duration of preoperative smoking cessation to improve wound healing after head and neck surgery. Anesthesiology. 2005;102:892-6.

5. Little CP, Burston BJ, Hopkinson-Woolley J, Burge P. Failure of surgery for scaphoid non-union is associated with smoking. J Hand Surg Br. 2006;31:252-5.

6. Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. Ann Surg. 2003;238:1-5.

7. Schmitz MA, Finnegan M, Natarajan R, Champine J. Effect of smoking on tibial shaft fracture healing. Clin Orthop Relat Res. 1999;365:184-200.

8. Moller AM, Pedersen T, Villebro N, Munksgaard A. Effect of smoking on early complications after elective orthopaedic surgery. J Bone Joint Surg Br. 2003;85:178-81.

9. Sørensen LT, Jørgensen T, Kirkeby LT, Skovdal J, Vennits B, Wille-Jørgensen P. Smoking and alcohol abuse are major risk factors for anastomotic leakage in colorectal surgery. Br J Surg. 1999;86:927-31.

10. Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM; LEAP Study Group. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. J Orthop Trauma. 2005;19:151-7.

11. Tønnesen H, Nielsen PR, Lauritzen JB, Møller AM. Smoking and alcohol intervention before surgery: evidence for best practice. Br J Anaesth. 2009;102:297-306.

12. Møller AM, Villebro N, Pedersen T, Tønnesen H. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. Lancet. 2002;359:114-7.

13. Lindström D, Sadr Azodi O, Wladis A, Tønnesen H, Linder S, Nåsell H, Ponzer S, Adami J. Effects of a perioperative smoking cessation intervention on postoperative complications: a randomized trial. Ann Surg. 2008;248:739-45.

14. Sørensen LT, Jørgensen T. Short-term pre-operative smoking cessation intervention does not affect postoperative complications in colorectal surgery: a randomized clinical trial. Colorectal Dis. 2003;5:347-52.

15. Korhonen T, Broms U, Levälahti E, Koskenvuo M, Kaprio J. Characteristics and health consequences of intermittent smoking: long-term follow-up among Finnish adult twins. Nicotine Tob Res. 2009;11:148-55.

16. Luoto R, Uutela A, Puska P. Occasional smoking increases total and cardiovascular mortality among men. Nicotine Tob Res. 2000;2:133-9.

17. Rigotti NA, Munafo MR, Stead LF. Smoking cessation interventions for hospitalized smokers: a systematic review. Arch Intern Med. 2008;168:1950-60.

18. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict. 1991;86:1119-27.

19. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol. 1999;20:250-78.

20. Bennett-Guerrero E, Welsby I, Dunn TJ, Young LR, Wahl TA, Diers TL, Phillips-Bute BG, Newman MF, Mythen MG. The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery. Anesth Analg. 1999;89:514-9.

21. Byrne DJ, Lynch W, Napier A, Davey P, Malek M, Cuschieri A. Wound infection rates: the importance of definition and post-discharge wound surveillance. J Hosp Infect. 1994;26:37-43.

22. King E, Ryan T. A preliminary investigation of maximum likelihood logistic regression versus exact logistic regression. Am Stat. 2002;56:163-70.

23. Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: a study of consistency of ratings. Anesthesiology. 1978;49:239-43.

24. Thyrian JR, Panagiotakos DB, Polychronopoulos E, West R, Zatonski W, John U. The relationship between smokers' motivation to quit and intensity of tobacco control at the population level: a comparison of five European countries. BMC Public Health. 2008;8:2.

25. Idris BI, Giskes K, Borrell C, Benach J, Costa G, Federico B, Helakorpi S, Helmert U, Lahelma E, Moussa KM, Ostergren PO, Prättälä R, Rasmussen NK, Mackenbach JP, Kunst AE. Higher smoking prevalence in urban compared to non-urban areas: time trends in six European countries. Health Place. 2007;13:702-12.

26. Hellqvist L, Rolandsson M, Birkhed D, Hugoson A. Tobacco use in relation to socioeconomic factors and dental care habits among Swedish individuals 15-70 years of age, 1983-2003. Int J Dent Hyg. 2009;7:62-70.

27. Britton GR, Brinthaupt J, Stehle JM, James GD. Comparison of self-reported smoking and urinary cotinine levels in a rural pregnant population. J Obstet Gynecol Neonatal Nurs. 2004;33:306-11.

28. Vartiainen E, Seppälä T, Lillsunde P, Puska P. Validation of self reported smoking by serum cotinine measurement in a community-based study. J Epidemiol Community Health. 2002;56:167-70.

29. Feenstra TL, Hamberg-van Reenen HH, Hoogenveen RT, Rutten-van Mölken MP. Cost-effectiveness of face-to-face smoking cessation interventions: a dynamic modeling study. Value Health. 2005;8:178-90.

30. Zullino D, Besson J, Schnyder C. Stage of change of cigarette smoking in alcohol dependent patients. Eur Addict Res. 2000;6:84-90.

31. Perencevich EN, Sand KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis. 2003;9:196-203.

32. Marbella AM, Layde PM, Remington P. Desire and efforts to quit smoking among cigarette smokers in Wisconsin. Wis Med J. 1995;94:617-20.