Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial

Ann M Møller, Nete Villebro, Tom Pedersen, Hanne Tønnesen

Summary

Background Smokers are at higher risk of cardiopulmonary and wound-related postoperative complications than non-smokers. Our aim was to investigate the effect of preoperative smoking intervention on the frequency of postoperative complications in patients undergoing hip and knee replacement.

Methods We did a randomised trial in three hospitals in Denmark. 120 patients were randomly assigned 6–8 weeks before scheduled surgery to either the control (n=60) or smoking intervention (60) group. Smoking intervention was counselling and nicotine replacement therapy, and either smoking cessation or at least 50% smoking reduction. An assessor, who was masked to the intervention, registered the occurrence of cardiopulmonary, renal, neurological, or surgical complications and duration of hospital admittance. The main analysis was by intention to treat.

Findings Eight controls and four patients from the intervention group were excluded from the final analysis because their operations were either postponed or cancelled. Thus, 52 and 56 patients, respectively, were analysed for outcome. The overall complication rate was 18% in the smoking intervention group and 52% in controls (p=0·0003). The most significant effects of intervention were seen for wound-related complications (5% vs 31%, p=0·001), cardiovascular complications (0% vs 10%, p=0·08), and secondary surgery (4% vs 15%, p=0·07). The median length of stay was 11 days (range 7–55) in the intervention group and 13 days (8–65) in the control group.

Interpretation An effective smoking intervention programme 6–8 weeks before surgery reduces postoperative morbidity, and we recommend, on the basis of our results, this programme be adopted.

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Department of Anaesthesiology, Bispebjerg University Hospital, Copenhagen 2400 NV, Denmark (A M Møller MD, N Villebro RN, T Pedersen MD); **and Clinical Unit of Preventive Medicine and Health Promotion, Bispebjerg University Hospital, Copenhagen** (H Tønnesen MD)

Correspondence to: Dr A M Møller
(e-mail: docamm@yahoo.com)

Introduction

About a third of all patients who undergo surgery are smokers. Smoking has repeatedly proved an important risk factor for intraoperative and postoperative complications.[1–4] Smokers have an increased frequency of pulmonary, circulatory, and infectious complications, impaired wound healing,[5,6] and postoperative admittance to the intensive-care unit.[7]

The mechanism leading to this increased risk could include smoking-induced chronic pulmonary changes—such as increased closing capacity, reduced clearance of pulmonary secretions, and chronic obstructive lung disease[8]—and impaired cardiovascular function,[9] immune function,[10,11] and collagen production.[6] Findings of physiological studies have shown that most of the smoking-induced changes are reversible to some degree, and that the period needed for a substantial improvement is about 6–8 weeks.[12–15] Warner and colleagues[16,17] showed that patients who stopped smoking 8 weeks before cardiac surgery had fewer pulmonary complications than smokers. The effect of preoperative smoking intervention on the postoperative complication rate, however, needs to be established. We postulated that smoking intervention from 6–8 weeks before surgery could reduce the frequency of postoperative complications after elective surgery. Our objective was to investigate postoperative morbidity and mortality in patients undergoing elective knee and hip replacement.

Patients and methods

Patients

Patients scheduled for primary elective hip or knee alloplasty at three university-affiliated hospitals in Copenhagen were invited to enter the study. All daily smokers were eligible for the study. Exclusion criteria included patients with a weekly alcohol intake greater than 35 units.[18] The ethics committee for all hospitals in Copenhagen and Frederiksberg approved the study and patients gave oral and written informed consent. The intervention period was 6–8 weeks before and 10 days after operation.

Procedures

Patients were randomly assigned—by block randomisation—to either the control (standard care) or smoking intervention group by opaque sealed envelopes containing treatment allocation. Equal distribution of patients between the three hospitals and hip and knee surgery was assured by stratification (table 1). A project nurse, trained in smoking cessation techniques, was attached to the study. All patients who agreed to enter the study had an introductory meeting with the project nurse, at which the study was explained in detail. At the meeting, the patient's height, weight, and forced expiratory volume in 1 s were recorded. The controls received standard care, which meant little or no information about the risk of tobacco smoking or smoking cessation counselling.

The patients in the intervention group were offered a meeting every week with the project nurse. At the first meeting a Fagerstöm test[19] was done, to estimate the magnitude and profile of nicotine dependence. A

	Intervention group (n=56)	Control group (n=52)	p
Preoperative factors			
Age (years)	66 (41–83)	64 (30–85)	0·37
Women	32 (57%)	30 (58%)	0·85
Body-mass index (kg/m²)	27 (15–43)	26 (17−44)	0·64
ASA class			
I	23 (41%)	16 (31%)	0·86
II	31 (56%)	33 (63%)	
III	2 (3%)	3 (6%)	
History of disease			
Chronic heart disease	7 (12%)	8 (15%)	0·33
Chronic obstructive lung disease	7 (13%)	5 (10%)	0·52
Diabetes mellitus	1 (2%)	3 (5%)	0·41
Preoperative laboratory tests			
Haemoglobin (g/L)	139 (118–174)	135 (96–155)	0·22
Creatinine (μmol/L)	84 (61–121)	81 (57–170)	0·38
FEV₁ (L/s)	2·2 (0·8–4·5)	2·3 (1·2–4·6)	0·63
Smoking habits			
Cigarettes per day	15 (5–30)	15 (3–30)	0·71
Pack years*	35 (11–65)	37 (1–102)	0·61
Intraoperative factors			
General anaesthesia	28 (50%)	33 (63%)	0·22
Knee replacement	16 (29%)	17 (33%)	0·68
Hip replacement	40 (71%)	35 (67%)	0·68
Duration of surgery (min)	90 (35–160)	90 (45–190)	0·92

Data are median (range) or number (%). ASA=American Society of Anesthesiology Physical Status Score; FEV₁=forced expiratory volume in 1 s. *Smoking years×daily consumption=20.

Table 1: **Patients' baseline characteristics**

personalised nicotine substitution schedule was devised in accordance with the test results and patient's preference. Patients were strongly encouraged to stop smoking completely, but they also had the option to reduce their tobacco consumption by at least 50%. Smoking status was monitored by carbon monoxide in expired air. Nicotine substitution products were given to the patients without charge. At all subsequent meetings, tobacco consumption was recorded. Patients were given advice about smoking cessation or reduction; benefits and side-effects, how to manage immediate withdrawal symptoms, and how to keep weight gain to a minimum. Patients could also discuss other general issues related to smoking intervention or hospitalisation.

Anaesthesia was done in accordance with the general practice of the hospital—either general anaesthesia of sevoflurane, fentanyl, propofol, and rocuronium in appropriate doses or regional anaesthesia with bupivacaine. Surgical procedures were done in accordance with hospital routine, including prophylaxis with antibiotics and for venous thromboembolism.

An assessor masked to the intervention recorded all intraoperative or postoperative complications from the onset of surgery to discharge from hospital. Patients were observed from the day of surgery until either discharge from or death in hospital. Postoperative complications were the primary outcome of this study, and were defined as either death or postoperative morbidity requiring treatment within 4 weeks after surgery. Additionally, we recorded duration of hospital stay, defined as number of days from day of operation until discharge from or death in hospital.

Statistics
A sample size of 120 patients was chosen to allow for safety assessment and to determine the effect of smoking intervention on postoperative events. Power calculations suggested that this number of patients should be recruited to identify a 50% reduction in events with a power of 80% at the 5% significance level. Statistical analysis was by

Formulas used in statistical analysis

$$RRR = \frac{CER - EER}{CER}$$

$$ARR = CER - EER$$

$$NNT = \frac{1}{ARR}$$

CER=control event rate; EER=experimental event rate; RRR=relative-risk reduction; NNT=number of patients needed to treat; ARR=absolute-risk reduction.

Mann-Whitney U and Fisher's exact tests, and $p < 0.05$ was judged significant. The main analysis was by intention to treat, with data for patients who discontinued intervention included up to the time of withdrawal. We also analysed data per protocol—ie, we compared patients in accordance with their actual behaviour, irrespective of which group they were randomised to. We calculated the relative risk for an event, the relative risk reduction, and number of patients needed to treat (panel).

Role of the funding source
The study sponsors had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
166 patients were eligible for the study, but 46 refused to participate. Thus, 120 were randomly assigned to intervention or control groups (figure 1). Table 1 shows patient's baseline characteristics. 12 patients dropped out of the study because their operation was cancelled or postponed. More than twice as many patients randomised to the intervention group chose to stop smoking than chose to reduce their tobacco consumption (figure 1).

The overall postoperative complication rate was significantly reduced in the intervention group compared with the controls (table 2). The largest effect of intervention was seen for wound-related complications. A non-significant effect was also seen for cardiovascular complications and second surgery complications. The relative-risk reduction for wound complications was 83% and the number needed to treat was four (95% CI 2–8). For cardiovascular insufficiency, the respective values were
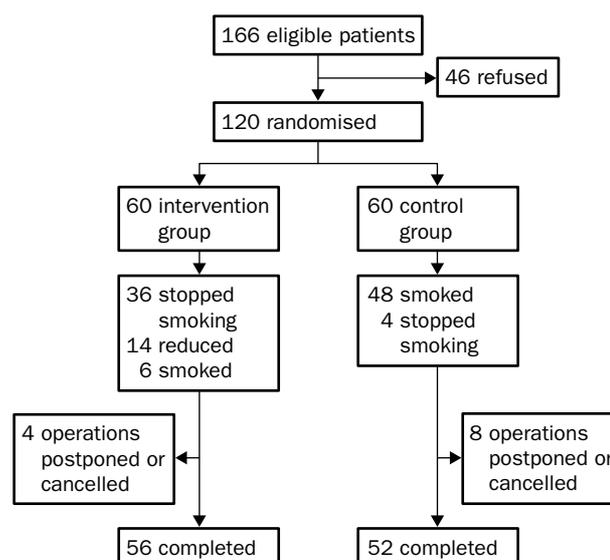

Figure 1: **Trial profile**

	Intervention group (n=56)	Control group (n=52)	p
Complications*			
Respiratory insufficiency†	1 (2%)	1 (2%)	0·97
Cardiovascular insufficiency‡	0	5 (10%)	0·08
Renal insufficiency§	0	1 (2%)	0·98
Delirium or confusion¶	1 (2%)	4 (8%)	0·15
Gastrointestinal bleeding¶	0	1 (2%)	0·98
Wound-related	3 (5%)	16 (31%)	0·001
Haematoma	1 (2%)	4 (8%)	
Infection (positive culture)	2 (4%)	12 (23%)	
Subfascial involvement	1 (2%)	4 (8%)	
Urinary tract infection‖	5 (9%)	6 (12%)	0·66
Any	10 (18%)	27 (52%)	0·0003
Death	0	0	··
Secondary surgery	2 (4%)	8 (15%)	0·07
Replacement	0	0	
Reposition	1 (2%)	0	
Wound-related	1 (2%)	7 (13%)	
Vascular	1 (2%)	1 (2%)	
Hospital stay			
Orthopaedic department (days, median [range])	11 (7–55)	13 (8–65)	0·41
Total days in orthopaedic department	750	767	
Total days in non-orthopaedic department	2	49	
In medical or surgical departments	0	17	
In intensive-care unit	2	32	

Data are number of patients (%) unless otherwise indicated. *Patients might have more than one complication; †requiring ventilatory support in intensive-care unit; ‡myocardial infarction or congestive heart failure; §creatinine >300 μmol/L or dialysis; ¶requiring treatment; ‖positive culture treated with antibiotics.

Table 2: **Outcomes in the two study groups**

100% and ten (6–52), and for secondary surgery, 77% and nine (4–111). Overall relative risk reduction was 65% and the number needed to treat to gain an extra patient free of complications was three (2–6). Figure 2 shows the relative risks.

Length of stay in the orthopaedic department did not differ between the groups (table 2). One patient in the intervention group and six controls were admitted to other departments. The proportion of days spent in non-orthopaedic departments was 6·0% (49/816) in the control group and 0·3% (2/752) in the intervention group (p=0·0001).

In the per protocol analysis, we recorded a significant difference in complication rate between patients who stopped smoking and those who did not, whereas those who reduced their cigarette use did not differ from the smokers (table 3).

Discussion

The results of our trial show that postoperative complications can be substantially reduced by smoking intervention 6–8 weeks before hip or knee replacement. The reduction in postoperative complications was most evident for wound-related complications, and, to a lesser extent, cardiovascular complications. The pathophysiological background for these findings could be the reversibility of the effect of tobacco smoking on the vascular system and delayed wound healing.[20–22]

Cessation of smoking for 3 weeks was shown to improve wound healing in an experimental study.[6] The mechanism probably involves recovery of the amount or structure of collagen and of the immune capacity, reduced oxygenation of peripheral tissues, and vasoconstriction induced by nicotine.[5] In our study, we recorded a very low frequency of postoperative pulmonary complications (2%) in both groups. Joint replacement surgery is generally associated with a low risk of pulmonary complications, probably because of the distance of the operation site from the diaphragm and early mobilisation.[23] In abdominal and gynaecological surgery, smokers have been shown almost consistently to have an increased risk of pulmonary complications, and the possible effect on these patients should be assessed.[3,4,24] When analysed per protocol, we reported an even greater difference between patients who stopped smoking and those who were smokers than when the data were analysed by intention-to-treat, and we saw no beneficial effect of smoking reduction. These data must be interpreted very carefully, since this analysis is based on non-randomised material, and these patients probably have very different baseline risk—motivation for smoking cessation is determined by many factors that act as confounders in this analysis, such as health status, social life, and age.

Length of hospital stay is, first of all, dependent on hospital practice, and might not suggest a difference in minor complication rate or mobilisation. We did show that the controls stayed on average 2 extra days in the orthopaedic department; furthermore, they spent many more days in other departments than did the intervention group. More than two-thirds of these days were spent in the intensive-care unit. This longer time means increased costs, if we extrapolate the data to the entire population of smoking patients presenting for joint replacement surgery. The data for intensive care admittance should be
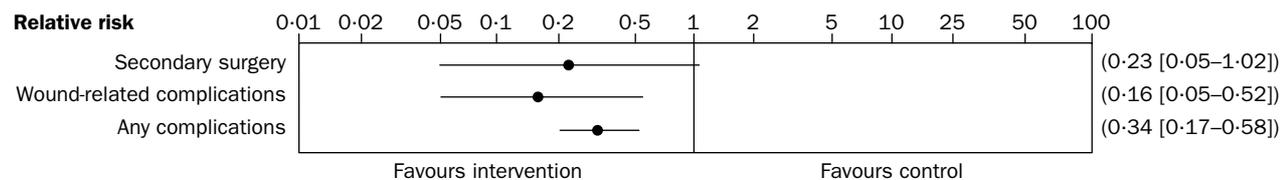

Relative risk	0·01 0·02 0·05 0·1 0·2 0·5 1 2 5 10 25 50 100	
Secondary surgery		(0·23 [0·05–1·02])
Wound-related complications		(0·16 [0·05–0·52])
Any complications		(0·34 [0·17–0·58])
	Favours intervention Favours control	

Figure 2: **Relative risk of postoperative events**
Bars=95% CI.

	Smokers	Reduced cigarette use	p*	Stopped smoking	p†
Complications					
Wound	12 (26%)	7 (27%)	0·98	0	0·0004
Any	20 (44%)	12 (46%)	0·89	4 (10%)	0·001

*Difference between smokers and those who reduced their cigarette use.
†Difference between smokers and those who stopped smoking.

Table 3: **Per protocol analysis**

interpreted with caution because of the low numbers. Nevertheless, the data point to potentially great savings in patient morbidity and costs, since postoperative complications are expensive to treat.[25] Lengthy hospital stay because of infection is well documented.[26,27]

The reduction in complication rate is a result of the smoking intervention programme. All parts of the intervention (smoking cessation and smoking reduction, use of nicotine replacement, increased information, and personal relation to the project nurse) could have contributed to the positive effects. A successful smoking intervention could also change other lifestyle factors, such as exercise, eating, or drinking habits, which are all factors that might contribute to the results.

46 (28%) of the 166 eligible patients refused to participate in the study, for various reasons. We do not know whether these patients had a different baseline risk to the included patients, or in what way they would have changed the study findings if they had been included. The results might have been changed in either direction, dependent on an increased benefit from, or a reduced compliance to, smoking intervention.

Smoking is a risk factor for wound infection and cardiopulmonary complications in almost any type of surgery; smokers make up a considerable proportion of the total number of postoperative complications. If preoperative smoking intervention can reduce these complications, the savings in personal suffering and financial expense should be substantial. The results of our study should be consolidated by a health technology assessment, to test applicability and cost benefit when the intervention is implemented in general practice.

An effective smoking intervention programme applied 6–8 weeks before surgery more than halved the frequency of postoperative complications, with the greatest effect on wound-related and cardiovascular complications. Although the exact duration of smoking abstinence necessary cannot be concluded from these data, we recommend cessation of smoking for at least 6 weeks on the basis of our results.

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