Smoking is a risk factor of organ/space surgical site infection in orthopaedic surgery with implant materials

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Abstract

Purpose In recent guidelines, smoking is reported as a factor increasing the risk of surgical site infection (SSI). The accurate analysis of the literature shows that this recommendation relies on low level of evidence in orthopaedic surgery with material implantation (arthroplasty components or implants for internal fixation). This study aimed to assess the attributable risk of smoking on organ/space SSI in orthopaedic surgery with implants.

Methods Risk factors of organ/space SSI were studied in a prospective cohort including 3,908 patients from June 2003 to December 2006.

Results Smoking was found as a significant risk factor for organ/space SSI. We also observed a significant difference between smokers and non-smokers for surgical wound complications (hematoma, discharge or wound dehiscence) during the period between surgical procedure and discharge from hospital.

Conclusion This is the first large prospective report of a significant association between smoking and organ/space SSI in orthopaedic surgery with implants.

Introduction

The risk of surgical site infection (SSI) is estimated at 1 % to 5 % and the attributable cost is from \$3,000 to \$29,000 per patient, depending on the type of surgery [1]. Some of patient-related risk factors are modifiable, such as glucose control, obesity, immunosuppressive treatment, and smoking [1]. Indeed, after guidelines for prevention of SSI were released in 1999 by Mangram et al., cigarette smoking has been considered as an independent risk factor for SSI, probably by delaying primary wound healing [2]. The limitation of these guidelines, however, is that terms like *current cigarette smoking*, *prior smokers* and *non-smokers* were not always defined, the distinction between incisional superficial, incisional deep and organ/space-SSI was not specified, and studies were made in cardiothoracic surgery [2, 3]. To appropriately determine the contribution of tobacco use to SSI risk, standardized definitions of smoking history must be adopted and used in studies designed to control for confounding variables. Some publications support this evidence, but only in retrospective studies in orthopaedic surgery and with controversial results [4–6]. A prospective study including 108 patients attending orthopaedic surgery showed that smoking was a risk factor only for superficial incisional SSI [7]. In a recent systematic review and meta-analysis, SSI was assessed in 51 studies, including 408,428 smokers and non-smokers [8]. The study disclosed significantly more SSI in smokers, but there were only three orthopaedic studies, showing more deep SSI in smokers, but not space/organ SSI, two in spine surgery [9, 10], and one in limb-threatening open tibia fractures [11]; none addressing prospectively the specific problem of material-related infections, especially prosthesis. In the largest retrospective cohort study evaluating the attributable risk of current smoking on postoperative complications for all surgical specialties, current smokers have increased rates of major respiratory complications and SSI, included in the adjusted analysis

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made for orthopaedic surgery, but without distinction between the different types of SSI [12]. In a previous study, we analysed *Staphylococcus aureus* nasal carriage as a risk factor for SSI in orthopaedic surgery with implant materials [13]. An ancillary objective of our study was to investigate the association between smoking and the risk of SSI. This is a prospective report of a large multicentre cohort of patients focused on orthopaedic procedures with implantation of arthroplasty or internal fixation devices.

Patients and methods

Study sample

Seventeen centres enrolled consecutive patients with orthopaedic indications for implantation arthroplasty or internal fracture-fixation devices, from June 2003 to December 2006. All patients provided written consent for their participation in the study, according to the Regional Ethical Research Committee. Patient identities remained confidential and data was managed by the co-ordinating study center.

Study variables

Beside detailed patient characteristics (age, sex, body mass index), underlying medical conditions were recorded, including diabetes mellitus, cancer, malnutrition, immunodeficiency, renal deficiency, rheumatoid arthritis, medication (particularly antibiotics one month before surgery and immunosuppressive drugs such as corticosteroids), and tobacco use. Data concerning surgery was collected, such as the kind of procedure performed and the type of arthroplasty, cement use, antimicrobial prophylaxis, date of hospital admission, date of surgery, date of discharge, follow-up schedule, class of wound contamination, American Society of Anesthesiologist (ASA) score, duration of surgery, arthroplasty first implantation or revision, blood transfusion, hematological diseases, and significant blood collection after surgery. Patients were followed up at hospital discharge (period 1), a month later (period 2) and one year after surgery (period 3). If a SSI was suspected, numerous bacteriological samples were obtained peri-operatively or by aseptic aspiration using ultrasound guidance. The primary outcome was surgical site infection at any time during the follow-up period. The secondary outcome was surgical wound complications, phlebitis and other infections at any time during the follow-up period.

For the purposes of this study, each patient was classified into current smoker (patient has smoked cigarettes in the year before admission for surgery), and non-smokers.

Definitions for SSI (superficial incisional SSI, deep incisional SSI, organ/space SSI) were those edited by the Centers

for Disease Control (CDC) [14]. The diagnosis was made by a surgeon or an attending physician. Briefly, a superficial incisional SSI involves only skin and subcutaneous tissue of the incision. A deep incisional infection involves deep soft tissues of the incision (e.g., fascial and muscle layers). An organ/space SSI involves bone or joint, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure. Delay between operation and occurrence of infection, purulent drainage, histopathologic examination, imaging test, bacteriologic cultures are precisely described in the National Institute for Health and Clinical Excellence (NICE) clinical guidelines for prevention and treatment of SSI [14].

Statistics

Categorical variables were compared with Fischer's exact test. The Wilcoxon non-parametric test was used for mean comparison. Multivariate analyses were carried out to evaluate risk factors for SSI. To adjust for confounding factors, the tobacco use variable was entered in a multiple logistic regression model. The software used to collect the recorded data was Epi-info, version 6.04d Fr (CDC-WHO). The SPSS software, version 16.0 (Chicago, Illinois, USA) was used for the statistical analysis.

Results

As of December 2006, a total of 4,046 patients were enrolled in seventeen French centres; 3,908 (96.6 %) were evaluated, 642 of whom (16.4 %) were current smokers and 3,266 (83.6 %) non-smokers. One hundred and thirty eight patients were excluded for the following reasons: 120 mainly because no nasal sampling was performed, and 18 patients were secondarily excluded because of lack of clinical data.

Concerning the type of surgery, 2,321 (59.4 %) underwent total hip arthroplasty, 1,162 (29.7 %) total knee arthroplasty, 292 (7.5 %) uni-compartmental knee arthroplasty, and 133 (3.4 %) others orthopaedic types of surgery with implantation of internal fixation devices.

Smokers were younger, more often male patients, and presented with arterial disease more frequently, with a higher American Society of Anesthesiologist (ASA) score (Table 1). During surgical intervention, non-smokers had a significantly increased incidence of blood transfusion compared to smokers. The initial indication for scheduled orthopaedic surgery significantly varied between smokers and non-smokers. Smokers presented more often with osteonecrosis (9.2 % vs. 2.8 %, OR, 3.5; 95 % CI [2.5–4.9], $p < 0.001$), but less often with osteoarthritis (84.9 % vs. 89 %, OR, 0.7; 95 % CI [0.5–0.9], $p < 0.001$).

Table 1 Main clinical and surgical data of patients included in the study

Characteristics	Non-smokers n (%)	Smokers n (%)	p value Smokers vs. Non-smokers
Patients, <i>n</i>	3,266	642	
Male (%)	1,216 (37.2)	462 (72.0)	$p<0.001$
Mean age (y, $\pm$ SD)	71($\pm$ 18.0)	65 ($\pm$ 11.0)	$p<0.001$
BMI ($\pm$ SD)	27.5 ($\pm$ 4.5)	28 ($\pm$ 4.4)	NS
Comorbidities :			
Diabetes mellitus	338 (10.4)	82 (12.8)	NS
Immunocompromised patients	8 (0.3)	3 (0.5)	NS
Arterial disease	116 (3.6)	38 (5.9)	$p<0.001$
Neuropathy	47 (1.4)	10 (1.6)	NS
Cancer	340 (10.4)	70 (10.9)	NS
Malignant blood disease	13 (0.4)	1 (0.2)	NS
Psychiatric history	363 (11.1)	63 (9.8)	NS
Rheumatoid arthritis	77 (2.4)	13 (2.0)	NS
Renal insufficiency	10 (0.3)	2 (0.3)	NS
Medication :			
Immunosuppressive drugs	98 (3.0)	24 (3.7)	NS
Antibiotics (less than 1 month before)	142 (4.4)	22 (3.5)	NS
Indication :			$p<0.001$
- Osteoarthritis	2,906 (89.0)	545 (84.9)	
- Revision THR	167 (5.1)	25 (3.9)	
- Osteonecrosis	92 (2.8)	59 (9.2)	
- Inflammatory arthritis	32 (1.0)	4 (0.6)	
- Fracture	13 (0.4)	1 (0.2)	
- Other	49 (1.5)	8 (1.2)	
Blood transfusion	325 (9.9)	38 (5.9)	$p<0.001$
Surgical significant hematoma	43 (1.3)	5 (0.8)	NS
ASA score:			$p<0.001$
- 1	651 (19.9)	146 (22.7)	
- 2	2,278 (69.7)	398 (62.0)	
- 3	337 (10.3)	97 (15.1)	
- 4	0	1 (0.2)	

BMI Body mass index, calculated as weight in kilograms divided by height in meters squared; SD Standard deviation; ASA American Society of Anesthesiologist; THR Total hip replacement NS nonsignificant *p* value

After 12 months, a total of 77 organ/space SSIs were diagnosed. No superficial nor deep incisional SSI was observed. Smokers had an increased incidence of SSI compared to non-smokers (OR, 2.2; 95 % CI [1.3–2.6], $p=0.003$) (Table 2). In univariate analysis, the association between smoking and surgical site infection occurs only during period 1 (at hospital discharge), but not one month or one year later. In multivariate analysis, smoking was an independent variable associated to an increased risk for SSI

in the first period. The adjusted relative risk for smokers was 2.2 (95 % CI, 1.4–3.7)⁷. Concerning other events, in the early postoperative period (surgery to hospital discharge, mean: nine days), surgical wound complications (hematoma, discharge, or wound dehiscence) were significantly increased in smokers, but phlebitis and other infections (mostly urinary infection) were less common in smokers ($p=0.002$ and $p=0.001$ respectively). In periods 2 (hospital discharge to one postoperative month follow-up consultation), and 3 (one postoperative month follow-up to one postoperative year consultation), only phlebitis was still significantly much more frequent in non-smokers compared to smokers. The rate of *Staphylococcus aureus* nasal carriage was not statistically different between smokers and non-smokers [120/642 (18.7 %) vs. 670/3266 (20.5 %), $P=0.3$].

Discussion

In a large prospective study of 3,908 patients undergoing scheduled orthopaedic surgery with implanted devices (arthroplasty components or implants for internal fixation), our study showed that smoking is an independent risk factor for organ/space SSI, during the one-year follow-up. This risk difference between smokers and non-smokers is mainly observed during the period between surgical procedure and discharge from hospital. In recent guidelines, smoking is reported as a factor increasing the risk of SSI [14]. However, the accurate analysis of the literature shows that this recommendation relies on low level of evidence in orthopaedic surgery with material implantation. A prospective observational study reported a higher risk of wound-related complications in smokers vs. non-smokers undergoing hip and knee replacement (31 % vs. 5 %, $p=0.001$), but not of prosthesis infections [7]. Two studies in orthopaedic surgery reported that smoking was an independent risk factor for SSI, but they are retrospective observational studies with few patients, 69 and 50 respectively [4, 5]. In retrospective studies, using multivariate logistic regression analysis, smoking history was not recovered as a risk factor for SSI in 223 patients underlying spine surgery [6], nor as a risk factor for aseptic loosening around total hip arthroplasty [15]. In a retrospective study including 34 patients with 37 operations, smoking was significantly associated with failure of operative treatment of established non-union of the scaphoid bone [16].

In a retrospective cohort study of 3,309 patients undergoing primary total hip replacement to examine the impact of tobacco use and body mass index on the length of stay in hospital and the risk of short-term postoperative complications, heavy tobacco use was associated with an increased risk of systemic postoperative complications, but there was no significant association between smoking status and the

Table 2 Univariate analyses of the association of smoking and clinical outcomes at hospital discharge, one month after surgery, and one year after surgery

	Non-smokers <i>n</i> =3,267 (%)	Smokers <i>n</i> =642 (%)	<i>p</i> value	OR (95 % CI)
Surgical site infection overall	1.7	3.7	<i>p</i> =0.003	2.21 [1.34–3.62]
Surgical wound complications:				
- diagnosed in period 1	30.1	35.4	<i>p</i> =0.009	1.27 [1.06–1.52]
- diagnosed in period 2	22.1	21.2	<i>p</i> =NS	0.95 [0.77–1.17]
- diagnosed in period 3	11.3	13.4	<i>p</i> =NS	1.21 [0.94–1.56]
Phlebitis:				
- diagnosed in period 1	3.1	1.1	<i>p</i> =0.002	0.34 [0.16–0.73]
- diagnosed in period 2	2	0.6	<i>p</i> =0.01	0.31 [0.11–0.85]
- diagnosed in period 3	0.3	0.3	<i>p</i> =NS	0.93 [0.19–4.23]

SSI Surgical site infection; period 1: hospital discharge; period 2: between hospital discharge and 1 month follow-up consultation; period 3: between 1 month follow-up consultation and 1 year follow-up consultation;

BMI Body mass index, calculated as weight in kilograms divided by height in meters squared; SD Standard deviation; ASA American Society of Anesthesiologist; THR Total hip replacement; NS nonsignificant *p* value

incidence of local complications [17]. Detection of factors affecting the survival of the prosthesis need long follow-up periods, and their analysis of tobacco status on local complications may lack the statistical power to detect a significant difference in rates of complication between the different groups.

As discussed in NICE clinical guidelines, factors that are significant for one type of surgery may not be applicable to other surgical procedures [18]. For instance, in a very large prospective study (16,000 patients, 9,398 smokers), in cardiovascular surgery, smoking was not a risk factor for SSI (OR, 0.9; 95 % CI [0.7–1.2]) [3].

The association between smoking and SSI in the immediate postoperative period but not at one month or one year suggests that the mechanism for early vs. later infections may differ. Indeed, we also observed that smoking significantly increased the proportion of complications such as wound hematoma, discharge, or dehiscence in the immediate postoperative period. This may support the fact that smoking affects the normal wound healing process and may induce more infectious complications.

Among smokers, numerous factors are responsible for the increased risk of postoperative complications. Nicotine, nitric oxide, and carbon monoxide directly alter the wound healing process [19, 20]. Smoking causes endothelial dysfunction, inflammation, and progression of atherothrombotic disease. Moreover, smokers have evidence of an impaired systemic immune response with suppressed immunoglobulin levels, an altered CD4 to CD8 cell ratio, and reduced phagocyte activity. These factors may explain the relationship between smoking and community-acquired pneumonia, postoperative pneumonia, wound infection and invasive pneumococcal disease, and the increased fatality of bacteraemia in smokers [21].

Given that the prevalence of *S. aureus* nasal carriage is not statistically different (*P*=0.3) in smokers and in non-smokers in our study, we think that the nasal colonisation rate does not explain the difference in the occurrence of organ/space SSI between smokers and non-smokers. Today and to our knowledge, nasal screening of *S. aureus* carriage remains a matter of debate.

In our study, the main criticism is that the exposure variable (smoking) was not quantified, and we took into account only current smokers at the time of implant assessment. So, among non-smokers, the time between smoking ceased and the inclusion is unknown. The prevalence of active smoking was 16 % in our study, which is less than the French national average of 22 % for women and 35 % for men [22]. We have no epidemiological data in the French population of the same range of age.

Our large prospective study of patients undergoing orthopaedic surgery with implant materials confirmed that smoking is as an independent risk factor for organ/space SSI, and suggested, as other studies have, that smoking cessation should be encouraged in the pre-operative period. Perioperative smoking cessation seems to be an effective measure to reduce postoperative complications even if it is introduced as late as four weeks before surgery, except for wound infections in one prospective randomized study [23], or only on superficial SSI in the other [7]. How long it is necessary to stop smoking to get the same risk of deep SSI in smokers as in non-smokers needs further research.

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