

# Smoking cessation before coronary artery bypass grafting improves operative outcomes

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**Background:** The detrimental effect of active smoking on operative outcome after coronary artery bypass grafting (CABG) is still debated and smoking cessation programs are usually deferred until after surgery. The potential benefit from smoking cessation on postoperative outcomes is investigated in this study.

**Methods:** A retrospective analysis on a large cohort of patients who underwent CABG at a single institution was performed. Generalized boosted regression modeling was used to estimate the multinomial propensity scores for smoking status categories and the average treatment effect on the treated was calculated for all outcomes of interest.

**Results:** A total of 6113 patients who underwent isolated CABG for the first time were included. At baseline, there were 640 (10.4%) current smokers, 3309 (54.1%) ex-smokers, and 2164 (35.3%) nonsmokers. Multilevel propensity score weighted analysis showed a beneficial effect of smoking cessation compared with current smoking, which increased the risk for all major pulmonary complications (odds ratio [OR], 1.54; 95% confidence interval [CI], 1.13-2.10;  $P = .006$ ), including reintubation (OR, 1.95; 95% CI, 1.17-3.25;  $P = .01$ ), full tracheostomy (OR, 3.04; 95% CI, 1.49-6.18;  $P = .002$ ), lung infection/consolidation (OR, 1.44; 95% CI, 1.02-2.02;  $P = .03$ ). Although smoking cessation did not significantly improve other outcomes, it was associated with a nonsignificant trend toward a decreased risk for in-hospital mortality (OR, 1.83; 95% CI, 0.85-3.91;  $P = .1$ ).

**Conclusions:** This study showed that smoking cessation before CABG reduced the risk of serious pulmonary complications. The present findings indicate that embarking on a smoking cessation program should not be deferred until after surgery. (*J Thorac Cardiovasc Surg* 2014;148:468-74)

Tobacco smoking remains the leading cause of preventable morbidity and mortality in the world<sup>1</sup> and smoking cessation is associated with important benefits.<sup>2</sup> In addition to the general health risks associated with smoking, it has been shown that smokers are more likely to have postoperative complications including delayed wound healing, pulmonary complications, and mortality.<sup>3</sup>

Smoking cessation has been consistently shown to offer important benefits in reducing complications in patients undergoing noncardiac surgery.<sup>3</sup>

Cigarette smoking is a major contributor to the risk of coronary heart disease<sup>4</sup> and a large number of active smokers are referred for coronary artery bypass grafting

(CABG) worldwide. Although smoking cessation after CABG has been found to improve late outcomes,<sup>5,6</sup> cardiac surgeons continue to debate whether patients who have stopped smoking should wait for a definite period of time before undergoing surgery.<sup>7</sup> Few limited studies have investigated the effect of active smoking on CABG operative outcomes and discordant results have been reported.<sup>8-12</sup>

The main risk scoring systems in cardiac surgery such as EuroSCORE and STS score failed to investigate the effect of active smoking on operative mortality.<sup>13</sup> As a consequence, active smoking at the time of surgery is not commonly perceived as a main risk factor for operative morbidity and mortality, and smoking cessation programs are usually deferred until after surgery.

Therefore, we investigated the potential benefit of smoking cessation on operative outcomes after CABG by conducting a detailed analysis on a large cohort of patients from a single institution.

## PATIENTS AND METHODS

### Study Population

The study was conducted in accordance with the principles of the Declaration of Helsinki.

Prospectively collected data from the institutional surgical database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) were analyzed

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### Abbreviations and Acronyms

ATT	= average treatment effect on the treated
CABG	= coronary artery bypass grafting
CI	= confidence interval
GBM	= generalized boosted regression modeling
IR	= incomplete revascularization
NYHA	= New York Heart Association
POAF	= postoperative atrial fibrillation
SWI	= sternal wound infection

retrospectively. The PATS database captures detailed information on a wide range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients undergoing cardiac surgery in our institution. The data are collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain & Ireland database criteria. The database is maintained by a team of full-time clinical information analysts, who are responsible for continuous prospective data collection as part of a continuous audit process. Data collection is validated regularly. Patients undergoing isolated first-time CABG from April 2001 to May 2013 were included in the present analysis.

Patients were scheduled for surgery according to internal guidelines for the scheduling of patients on the waiting list: emergency (within 24 hours), very urgent (0-4 weeks), urgent (4-8 weeks), soon (8-12 weeks), and routine (18 weeks from referral to surgery). Patients on the waiting list complaining of worsening of symptoms were reviewed in the clinic by the allocated consultant or given a theatre slot with the first available consultant as appropriate.

Patients were queried about their smoking habits at index admission. The study population was divided into 3 groups based on smoking habits: (1) never smoked, defined as patients who had never smoked cigarettes regularly; (2) ex-smokers, defined as those who had quit smoking at least 4 weeks before the index procedure; and (3) current smokers, defined as those who smoked within 4 weeks before the index procedure. Four weeks was chosen as the smoking cessation cut-off according to a previous meta-analysis of randomized controlled trials enrolling patients undergoing noncardiac surgery demonstrating that trials of at least 4 weeks' smoking cessation had significantly larger treatment effects on postoperative complications than shorter trials.<sup>3</sup>

Smoking cessation services were provided for all prospective surgical candidates and brief intervention counseling was offered during surgical preadmission checks. All smokers and ex-smokers (within 5 years) had preoperative pulmonary function testing. When an airflow obstruction (defined as an FEV<sub>1</sub>/FVC ratio <0.7, where FEV<sub>1</sub> is forced expiratory volume in the first second of expiration and FVC is forced vital capacity, and a predicted FEV<sub>1</sub> <80%) was demonstrated, bronchodilators were started before surgery. During the study period, no case was delayed to achieve a period of smoking cessation.

### Outcomes

The following postoperative complications were investigated: major lung complications including full tracheostomy, reintubation, lung infection/consolidation; low cardiac output syndrome defined as the need for inotropes and/or an intra-aortic balloon pump after surgery, need for renal replacement therapy, a postoperative cerebrovascular accident, both transient or permanent, reexploration for bleeding, sternal rewiring for instability, sternal wound infection (SWI) either superficial or deep, postoperative atrial fibrillation (POAF), pleural effusion requiring drainage, prolonged postoperative hospital stay (defined as length of stay ≥75th percentile of postoperative stay length distribution), and in-hospital mortality.

### Statistical Analysis

For baseline characteristics, variables were summarized as the mean ± standard deviation for continuous variables and number and percentage for categorical variables. The standardized mean difference was used to quantify differences in means or prevalence among groups using ex-smokers as reference; a value >0.10 represented meaningful imbalance in a given covariate.<sup>14</sup>

The following risk factors were investigated: age, gender, diabetes mellitus, body mass index (BMI) ≥30 kg/m<sup>2</sup>, renal impairment defined as a baseline serum creatinine level ≥200 mmol/L, previous myocardial infarction, history of congestive heart failure, chronic obstructive pulmonary disease (defined as long-term use of bronchodilators or steroids for lung disease or evidence of airflow obstruction on preoperative pulmonary function testing), history of cerebrovascular accident, functional New York Heart Association (NYHA) class III or IV, reduced left ventricular ejection fraction (<50%), peripheral vascular disease, nonelective surgery, use of cardiopulmonary bypass, number of grafts, and incomplete revascularization.

The incidence of postoperative complications was compared among groups by means of the  $\chi^2$  test or analysis of variance for continuous variables. To separate the effect of smoking cessation on outcomes from observed confounding factors that influenced smoking status at the time of surgery, nonparsimonious, generalized boosted regression modeling (GBM) was implemented to estimate the multinomial propensity scores (number of interactions = 3000) for smoking status categories including all preoperative risk factors. This method relies on tree-based regression models that are built in an iterative fashion. As the iterations or number of regression trees added to the model increases, the model becomes more complex. However, at some point, more complex models typically result in worse balance and therefore are less useful in a propensity score weighting context. The key assumption that each unit had a nonzero probability of belonging to each group was assessed by the overlap of the empirical propensity score distributions. Balance among smoking status groups was assessed by means of comparisons of effect size standardized as the mean difference of the effect size before and after weighting.

The propensity score weights were used as case weights in a generalized linear logistic model to estimate the average treatment effect on the treated (ATT) for all outcomes of interest.<sup>13</sup> In brief, the ATT answers the question of how the average outcome would change if everyone who received surgery without smoking cessation had instead received surgery after a smoking cessation period. These models estimated the odds ratio (OR) and 95% confidence interval (CI) for each smoking status category using ex-smokers as the treatment group.

The following programs were used for the statistical analysis: R version 2.15.2 (R Foundation for Statistical Computing, Vienna, Austria; <http://www.R-project.org/>), twang (Toolkit for weighting and analysis of nonequivalent groups, R package version 1.3-18; <http://CRAN.R-project.org/package=twang>), and survey packages (Survey: analysis of complex survey samples, R package version 3.28-2; <http://cran.r-project.org>).

## RESULTS

### Baseline Characteristics

A total of 6113 patients who underwent isolated first-time CABG were included. At baseline, there were 640 (10.4%) current smokers, 3309 (54.1%) ex-smokers, and 2164 (35.3%) nonsmokers. Baseline characteristics stratified by smoking status are shown in Table 1. Eight of 16 variables were different among smoking status groups (standardized mean difference >0.1) including age, female gender, previous myocardial infarction, chronic obstructive pulmonary disease, reduced left ventricular ejection fraction, peripheral vascular disease, nonelective indication, and the use of cardiopulmonary bypass.

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