

Preoperative cigarette smoking and short-term morbidity and mortality after cardiac surgery: a meta-analysis

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/heartasia-2018-011069>).

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Received 15 May 2018

Revised 7 September 2018

Accepted 2 October 2018

ABSTRACT

Currently, the choice of whether or not to electively operate on current smokers is varied among cardiothoracic surgeons. This meta-analysis aims to determine whether preoperative current versus ex-smoking status is related to short-term postoperative morbidity and mortality in cardiac surgical patients. Systematic literature searches of the PubMed, MEDLINE and Cochrane databases were carried out to identify all studies in cardiac surgery that investigated the relationship between smoking status and postoperative outcomes. Extracted data were analysed by random effects models. Primary outcomes included 30-day or in-hospital all-cause mortality and pulmonary morbidity. Overall, 13 relevant studies were identified, with 34 230 patients in current or ex-smoking subgroups. There was no difference in mortality ($p=0.93$). Current smokers had significantly higher risk of overall pulmonary complications (OR 1.44; 95% CI 1.27 to 1.64; $p<0.001$) and postoperative pneumonia (OR 1.62; 95% CI 1.27 to 2.06; $p<0.001$) as well as lower risk of postoperative renal complications (OR 0.82; 95% CI 0.70 to 0.96; $p=0.01$) compared with ex-smokers. There was a trend towards an increased risk of postoperative MI (OR 1.29; 95% CI 0.95 to 1.75; $p=0.10$). No difference in postoperative neurological complications ($p=0.15$), postoperative sternal surgical site infections ($p=0.20$) or postoperative length of intensive care unit stay ($p=0.86$) was seen. Cardiac surgical patients who are current smokers at the time of operation do not have an increased 30-day mortality risk compared with ex-smokers, although they are at significantly increased risk of postoperative pulmonary complications.

INTRODUCTION

Variations exist between cardiothoracic surgeons as to willingness to electively operate on existing smokers. Current cigarette smoking status is thought to be related to perioperative morbidity in a number of surgical fields, most particularly in cardiac surgery. While past retrospective cohort studies in cardiac surgical patients have explored the relationship between current smoking status and perioperative morbidity and mortality,^{1–5} there is conflicting evidence regarding a number of perioperative complications such as postoperative myocardial infarction (MI),^{1–6} surgical site infections (SSI)^{7–8} and prolonged postoperative intensive care unit (ICU) stay,^{1–4–9–11} with no comprehensive systematic reviews or meta-analysis on the subject available. Furthermore, there is a lack of evidence directly comparing current smokers with ex-smokers, and fewer still that compare current

smokers with recent (within 12 months of operation) ex-smokers.

Recent evidence suggests that perioperative smoking cessation is often successful,¹² and thus surgical teams should have a firm understanding of the benefits of preoperative smoking cessation to improve outcomes. The present meta-analysis evaluates whether preoperative smoking status (current vs ex-smokers) influences short-term postoperative morbidity and mortality outcomes in adult cardiac surgery.

METHODS

Literature search strategy

Electronic searches were performed on PubMed, MEDLINE and the Cochrane Library (Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials) from inception through August 2017 for relevant studies. A broad search strategy was developed after reviewing similar searches in related literature. To maximise the initial scope of the search, ‘smoking AND ((thoracic surgery) OR (thoracic AND surgery) OR (cardiac surgery) OR (cardiac AND surgery) OR (coronary artery bypass))’ was used as the search strategy. All records were systematically assessed using established inclusion and exclusion criteria. References of included studies were manually assessed for possible inclusion in the present review. Two researchers independently conducted an initial search, and any discrepancies in inclusions were resolved by discussion and mutual agreement.

A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the literature search strategy of studies investigating the impact of smoking status at the time of cardiac surgery is presented in the online supplementary file 1.

Selection criteria

Primary inclusion criteria were any observational or interventional study of adult cardiac surgery patients that presented short-term postoperative mortality or complication data and presented sub-group analysis of outcomes for ex-smokers and current smokers. Current smoking was defined as smoking at least one cigarette per day within 1 week of the date of operation, and ex-smokers were defined as patients who had ceased smoking over 1 week prior to the date of operation. The primary outcomes were defined as 30-day or in-hospital all-cause mortality and overall postoperative pulmonary complications (including pneumonia,



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To cite: Bayfield NGR, Pannekoek A, Tian DH. *Heart Asia* 2018;**10**:e011069. doi:10.1136/heartasia-2018-011069

clinically significant atelectasis, prolonged mechanical ventilation, ARDS, pneumothorax and pleural effusion requiring drainage). Secondary outcomes were defined as postoperative pneumonia (in isolation), postoperative myocardial infarction, postoperative neurological event (stroke or TIA), new postoperative renal failure or dialysis requirement, sternal wound infection (superficial or deep) and length of postoperative ICU stay. The definition of ex-smoking status for each source study was recorded.

Quality assessment

Included studies were screened for quality with a Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.¹³ A numerical checklist of criteria was used to assist with judgement of study quality. Each study was scored from 1 to 14 based on the criteria, and the numerical scores were assessed for outliers. Studies were rated 'good' (10–14 points), 'fair' (7–9) or 'poor' (<7). Quality assessment was performed independently by two reviewers.

Statistical analysis

Patient demographic data for ex-smokers and current smoker groups were extracted from each study, as well as postoperative outcomes. Baseline demographics were pooled as meta-analysis of proportions or means as appropriate. For each dichotomous postoperative complication, a random effect model was used to generate a Mantel-Haenszel OR, as a high chance of statistical heterogeneity was assumed. For the analysis of the continuous data of length of intensive care stay, a random effect model was used to generate a mean difference (in hours) with the inverse variance statistical method. Statistical heterogeneity was assessed using the I^2 statistic. Publication bias was tested for in both primary outcomes using funnel plots and Egger's linear regression method. Subgroup analysis was performed on studies which defined current smoking as any smoking within 4 weeks of operation and coronary artery bypass grafting-only studies. Further subgroup analysis was performed on the primary endpoints in studies rated 'good' as a sensitivity analysis. The median year of patient recruitment was assessed in meta-regression to determine

temporal influences on the heterogeneity on overall pulmonary complications. Data were analysed with Review Manager (V.5.3, Cochrane Collaboration, Software Update, Oxford, UK) and Comprehensive Meta-Analysis Software (V.3, Biostat, Englewood, USA).

RESULTS

Literature search

Overall, 5805 records were identified in the literature search. Following application of the inclusion and exclusion criteria, 17 studies were deemed suitable for inclusion in the systematic review, of which 13 were quantitatively analysed.^{1–6 14–20} Four studies were analysed qualitatively due to incompatible data presentation or data presentation that was not able to be reconciled into statistical analysis; results from all of these studies were in concordance with our meta-analytical findings.^{21–24} The characteristics of the included studies are summarised in table 1.

Thirteen studies were eligible for inclusion in the statistical meta-analysis. Of these, eight investigated mortality.^{1–6 15 19} Ten investigated overall pulmonary complications,^{1–4 6 14 15 18 19} and six specifically investigated pneumonia.^{1–3 5 18 19} Five studies investigated postop MI.^{1–3 6 19} Seven studies investigated renal complications.^{1–6 15} Eight studies investigated neurological complications.^{1–6 15 19} Eight studies investigated a variety of sternal wound complications.^{1–3 5 6 16 18–20} Seven studies reported mean length of ICU stay with CIs.^{1–4 6 15 17}

Seven studies defined current smokers as smoking within 4 weeks of operation. Four studies did not define the time period of smoking cessation prior to operative date that they used to classify ex-smokers.^{14 16 19 20} Guan *et al*¹⁷ included a robust stratification of patients into sustained quitters (quit 1 month—1 year preop), recent quitters (quit 1 month—1 week preop) and current smokers.

Quality assessment

Quantitatively, studies ranged from 8 to 11 points out of the possible maximum 14 points. There were no significant outliers. Significant variations existed as to the sample sizes and the

Table 1 Study characteristics

| Lead author | Year | Type of study | Included surgeries | Location | Current smoking status definition | Quality score and rating (if in meta-analysis) |
|---------------------------------------|------|----------------------------|--------------------------------|-------------------------|---------------------------------------|--|
| Ngaage <i>et al</i> ¹⁸ | 2002 | Retrospective cohort study | All elective cardiac surgeries | UK, single centre | <3 month preop smoking | 11, Good |
| Saxena <i>et al</i> ¹ | 2013 | Retrospective cohort study | CABG | Australia, multi-centre | <1 month preop smoking | 11, Good |
| Saxena <i>et al</i> ² | 2013 | Retrospective cohort study | AVR | Australia, multi-centre | <1 month preop smoking | 11, Good |
| Saxena <i>et al</i> ³ | 2014 | Retrospective cohort study | AVR+CABG, concomitant | Australia, multi-centre | <1 month preop smoking | 11, Good |
| Ji <i>et al</i> ⁶ | 2015 | Retrospective cohort study | CABG | China, single centre | <1 month preop smoking | 10, Good |
| Benedetto <i>et al</i> ⁵ | 2014 | Retrospective cohort study | CABG | UK, single centre | <4 weeks preop smoking | 11, Good |
| Al-Sarraf <i>et al</i> ⁴ | 2008 | Retrospective cohort study | CABG | Kuwait, single centre | <4 weeks preop smoking | 11, Good |
| Al-Sarraf <i>et al</i> ¹⁵ | 2007 | Retrospective cohort study | All valvular surgeries | Kuwait, single centre | <4 weeks preop smoking | 11, Good |
| Shih <i>et al</i> ²¹ | 2014 | Retrospective cohort study | All cardiac surgeries | USA, multi-centre | <2 weeks preop smoking | – |
| Guan <i>et al</i> ¹⁷ | 2016 | Prospective cohort study | On-pump CABG | China, single centre | <1 week preop smoking | 9, Fair |
| Warner <i>et al</i> ²³ | 1984 | Retrospective cohort study | CABG | USA, single centre | Smoking up to date of operation | – |
| Mortasawi <i>et al</i> ¹⁹ | 2004 | Retrospective cohort study | CABG | UK, single centre | Current versus ex (no time specified) | 10, Good |
| Olsen <i>et al</i> ¹⁶ | 2002 | Retrospective cohort study | CABG | USA, single centre | Current versus ex (no time specified) | 9, Fair |
| Nagachinta <i>et al</i> ²⁰ | 1984 | Prospective cohort study | All elective cardiac surgeries | USA, single centre | Current versus ex (no time specified) | 11, Good |
| Siddiqui ¹⁴ | 2012 | Retrospective cohort study | All cardiac surgeries | Pakistan, single centre | Current versus ex (no time specified) | 8, Fair |
| Harrington <i>et al</i> ²² | 2004 | Prospective cohort study | CABG | Australia, multicentre | Current versus ex (no time specified) | – |
| Warner <i>et al</i> ²⁴ | 1989 | Prospective cohort study | CABG | USA, single centre | Urinary cotinine <0.5 ug/mL | – |

AVR, aortic valve replacement; CABG, coronary artery bypass grafting.

Table 2 Baseline characteristics

| | Current smokers | Ex-smokers | Number of patients (studies) for which data were retrievable |
|---|---------------------|---------------------|--|
| Total | 8402 | 25 828 | 34 230 (13) |
| Age (mean±SD, years) | 65.5±1.6 | 60.9±1.5 | 22 079 (7) |
| Female (%) (95% CI) | 11.8 (5.3 to 24.4) | 11.4 (6.4 to 19.6) | 14 397 (6) |
| Preoperative hypertension (%) (95% CI) | 60.0 (49.1 to 70.0) | 63.3 (52.9 to 72.6) | 22 079 (7) |
| Preoperative hypercholesterolaemia (%) (95% CI) | 50.1 (22.9 to 77.3) | 57.5 (36.3 to 76.2) | 19 940 (5) |
| Preoperative left main disease (%) (95% CI) | 23.5 (20.8 to 26.3) | 21.6 (17.8 to 26.0) | 26 918 (5) |
| Preoperative congestive heart failure (%) (95% CI) | 23.3 (12.6 to 38.9) | 24.0 (13.3 to 39.4) | 21 703 (5) |
| Preoperative PHx of MI or recent MI (%) (95% CI) | 28.5 (18.4 to 41.2) | 18.6 (10.7 to 30.3) | 23 889 (6) |
| Preoperative diabetes mellitus (%) (95% CI) | 20.6 (15.8 to 26.5) | 23.8 (18.9 to 29.5) | 28 993 (8) |
| Preoperative peripheral vascular disease (%) (95% CI) | 13.4 (10.7 to 16.8) | 12.0 (9.7 to 14.7) | 26 507 (6) |
| Preoperative PHx of CVA/CVD (%) (95% CI) | 9.9 (7.0 to 13.9) | 12.8 (9.2 to 17.5) | 23 552 (5) |
| Preoperative COPD (%) (95% CI) | 17.6 (11.6 to 25.9) | 14.6 (9.7 to 21.3) | 30 532 (8) |
| Preoperative renal failure (%) (95% CI) | 2.6 (2.0 to 3.4) | 3.3 (2.7 to 4.0) | 26 170 (5) |
| Cardiopulmonary bypass time (mean±SD, min) | 102.5±5.2 | 97.0±8.9 | 20 240 (6) |
| Cross clamp time (mean±SD, min) | 81.0±5.2 | 78.6±8.5 | 19 940 (5) |

COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; CVD, cardiovascular disease; MI, myocardial infarction; Phx, past history.

classification of ex-smokers according to the period of smoking cessation. Studies with higher scores had a larger group of subjects and a more robust stratification of smoking status. There were overall low rates of incomplete data impacting on inclusion rate of patients. There was no clear reason that would bias the researchers in one way or another. Classifications of postoperative complications were well-defined across studies. All studies were rated either 'good' or 'fair' and thus judged suitable for inclusion in the meta-analysis. There were no disagreements in classification of 'good/fair' between the two researchers. Quantitative scores and good/fair ratings are presented in [table 1](#).

Clinical outcomes

Overall, 34 230 patients were included in the statistical meta-analysis. There was no overlap between studies. Baseline data are presented in [table 2](#).

Current smokers were shown to have a significantly increased risk in postoperative overall pulmonary complications (OR 1.44; 95% CI 1.27 to 1.64; $p<0.001$, $I^2=45\%$) and in postoperative pneumonia (OR 1.62; 95% CI 1.27 to 2.06; $p<0.001$, $I^2=67\%$) compared with ex-smokers. There was a trend towards an increased risk in postoperative MI (OR 1.29; 95% CI 0.95 to 1.75; $p=0.10$, $I^2=18\%$) for current smokers. There was no difference in mortality ($p=0.93$), postoperative neurological complications ($p=0.15$) or postoperative sternal surgical site infections ($p=0.20$). Current smokers were shown to have a statistically significant decrease in risk of postoperative renal complications (OR 0.82; 95% CI 0.70 to 0.96; $p=0.01$, $I^2=0\%$). There was no difference in postoperative length of ICU stay ($p=0.86$). Statistical outcomes are presented in [table 3](#). Forest plots of primary and secondary outcomes presented in the online supplementary files 2-9.

Subgroup analysis did not change the significance or effect of any results. Meta-regression identified the median year of patient recruitment as a significant influence on the heterogeneity of the results for postoperative pulmonary complications ($\beta=-0.05$, $p<0.001$, $R^2=1.0$), suggesting that increased risk for current smokers has reduced in recent years. Egger's linear regression test did not identify any publication bias on assessment of both primary outcomes (two-tailed $p=0.20$ and $p=0.52$, respectively), although the small amount of studies may limit the sensitivity of the test. Forest plots of subgroup analysis

are presented in the online supplementary files 10-12. Funnel plots are presented in the online supplementary files 13; 14.

DISCUSSION

The present meta-analysis found that there is no tangible relationship between current smoking status and short-term mortality after cardiac surgery, as consistent with data from other surgical specialties.⁹ However, other studies have shown that continued smoking results in increased mortality from 1 year postoperatively through to long-term outcomes²⁵⁻²⁸ and that postoperative smoking cessation improves life expectancy.²⁹ Thus, while there is no clear evidence of mortality benefit in the perioperative period, smoking cessation is certainly a desirable long-term goal. A preoperative approach to initiating smoking cessation should be considered, as recent evidence suggests that preoperative smoking cessation is often successful and may have an improved success rate with interventions.¹² The period prior to cardiac surgery is a time that lends itself towards educating patients on the harms of smoking, especially as the relationship between smoking and cardiovascular disease is not apparent to many patients.³⁰

The pathophysiology of smoking and its effect on the lungs is well known. Cigarette smoking accelerates lung function decline over time,³¹ and inflammatory effects on the small

Table 3 Clinical outcomes for current smokers and ex-smokers undergoing cardiac surgery

| | OR (95% CI) | I^2 | P values |
|------------------------------------|-----------------------|-------|----------|
| Mortality | 0.99 (0.78 to 1.25) | 18% | 0.93 |
| Pulmonary complications | 1.44 (1.27 to 1.64) | 45% | <0.00001 |
| Pneumonia | 1.62 (1.27 to 2.06) | 67% | <0.0001 |
| Renal complications | 0.82 (0.70 to 0.96) | 0% | 0.01 |
| Myocardial infarction | 1.29 (0.95 to 1.75) | 18% | 0.1 |
| Neurological complications | 1.19 (0.94 to 1.52) | 15% | 0.15 |
| Surgical site infections | 1.14 (0.94 to 1.38) | 0% | 0.2 |
| Intensive care unit length of stay | 0.19* (-2.01 to 2.40) | 63% | 0.86 |

*Mean difference.

airways increase the susceptibility of the lungs to respiratory complications such as infection and atelectasis.¹⁸ Postoperative pulmonary complications thus are an unsurprising outcome postcardiac surgery, and the present review subsequently shows that the odds of developing such complications in current smokers was increased by 44%. Postoperative pneumonia is the most common infection following open-heart surgery and is a major cause of perioperative morbidity and mortality.³² Taking reasonable measures to reduce the risk of postoperative pneumonia is a desirable perioperative goal, and advocating preoperative smoking cessation seems justifiable to reduce the risk of these complications.

There is conjecture over where smoking cessation within 6–8 weeks of surgery may increase risk of pulmonary complications in the perioperative period¹⁰ and calls for further research in this area.⁹ This conjecture is related to a known transient increase in sputum production within the first 6–8 weeks of smoking cessation.³³ The stratification of smokers in the studies contributing to this meta-analysis was inadequate to investigate the possibility of this effect. In future studies, more robust stratification of smokers should be considered. Furthermore, there is a paucity of evidence exploring the effects of smoking cessation 0–4 weeks preoperatively. The results of this meta-analysis are most valid when applied to patients who ceased smoking <1 month preoperatively, as these patients constitute the vast majority of the sample size.

Smoking is also a known significant contributor to cardiovascular disease, with long-term effects of atherosclerosis,³⁴ hypertension³⁵ and direct myocardial remodelling.³⁶ It has unfavourable effects directly on the coronary endothelium, causing coronary arterial vasoconstriction and increased myocardial oxygen demand.³⁷ However, the included studies herein have invariably failed to find a significant rate of postoperative MI in current smokers. The results of this meta-analysis show a non-significant trend towards an increased risk of postop MI in current smokers; however, only five studies presented postoperative MI data. Further studies may be beneficial in exploration of this result.

An unexpected result of this meta-analysis was the association between preoperative smoking cessation and an increased risk of renal complications postoperatively. This is a counter-intuitive result, as smoking overall is a known risk factor for both chronic kidney disease³⁸ and postoperative acute kidney injury,^{39 40} although these studies did compare non-smokers to current smokers. This result may be due to some confounding variable that was unable to be controlled for herein, or there may be some true underlying effect. Further research should be directed at exploring this result.

There are several limitations to the present study that must be considered when interpreting the findings. First, there were no stratifications in the data set to account for pack-year history in either ex-smokers or current smokers. Smoking status was assessed primarily by history and confirmation of ex-smoking status in particular is difficult. In all but one study, the ex-smoking groups were not differentiated by the duration prior to surgery when the patients quit. In future studies, more robust analysis incorporating the time frames of smoking cessation will allow for closer analysis of the effects of smoking cessation prior to surgery.

The results of this meta-analysis are clinically significant in reinforcing the significant pulmonary morbidity associated with current cigarette smoking at the time of cardiac surgery. Clinical urgency of need for elective open-heart surgery should be counterbalanced against the pulmonary morbidity

associated with operating on current smokers and consideration given to aiming for a significant preoperative period of smoking abstinence.

In conclusion, cardiac surgical patients who are current smokers at the time of operation do not have an increased mortality risk compared with ex-smokers, although they are at significantly increased risk of postoperative pulmonary complications including pneumonia. There is no difference in postoperative ICU admission length between current and ex-smokers. With known impact on long-term mortality, smoking cessation should continue to be encouraged at all points. Pulmonary morbidity outcomes justify a decision to be cautious of electively operating on current smokers.

Contributors NGRB and DHT contributed to the conception or design of the work. All authors contributed to the data collection, data analysis and interpretation, drafting the article, critical revision of the article and final approval of the version to be published.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Raw data used to perform statistical analysis will be available by directly contacting the corresponding author and requesting it. However, as this data is synthesised from a series of studies included in the meta-analysis, all of this data is already available online in the text of each respective article.

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