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Association of Smoking with Early Postoperative Outcomes in Patients

Who Underwent Isolated Heart Valve Surgery

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ABSTRACT

Background: There is limited published evidence on the association of smoking with early postoperative outcomes in patients who underwent isolated heart valve surgery.

Methods: Data prospectively collected from 1,024 patients with surgical aortic valve replacement (SAVR) or mitral valve replacement/repair (SMVR) between January 2002 and September 2017 at Emory University hospitals (Atlanta, Georgia, US) and entered into the Society of Thoracic Surgeons (STS) national database were retrospectively analyzed. Descriptive summary statistics were provided for demographic characteristics, risk factors, preoperative cardiac status and operative factors, stratified by smoking status. Linear regression was used to assess the association between smoking and continuous outcomes, namely: postoperative stay days in hospital and total ICU hours, which were both log-transformed. Logistic regression was used to evaluate the association between smoking and dichotomous outcomes, namely: postoperative in-hospital events, 30-day mortality, and 30-day re-admission. Finally, age, race, gender, family history of premature CAD, hypertension, obesity, dyslipidemia, prior MI, surgeon's experience in heart valve surgery, diseased vessels, emergent/urgent status, procedure type, and cardioplegia use were added to the regression models to estimate adjusted measures of effect.

Results: Among 1,024 patients with SAVR or SMVR included in the study, 120 (11.7%) were current smokers, 288 (28.1%) were former smokers and 616 (60.2%) were never smokers. While there were no significant differences in postoperative stay days, total ICU hours, postoperative in-hospital events or 30-day re-admission between former and current smokers and never smokers, current smokers had significantly higher overall postoperative 30-day mortality (OR = 3.22, 95% CI (1.26, 8.28)) compared to never smokers. Moreover, higher postoperative 30-day mortality occurred in both former and current smokers aged $\geq$ 70 years (former: OR = 3.36, 95% CI (1.33, 8.51); current: OR = 8.76, 95% CI (2.01, 38.1)), who were white (former: OR = 2.41, 95% CI (1.13, 5.12); current: OR = 4.04, 95% CI (1.42, 11.5)) or who were male (former: OR = 3.15, 95% CI (1.13, 8.78); current: OR = 4.85, 95% CI (1.41, 16.7)).

Conclusion: Smoking is significantly associated with higher postoperative 30-day mortality among patients who underwent isolated heart valve surgery, particularly among those aged $\geq$ 70 years, who were white or who were male.

KEYWORDS

Isolated heart valve surgery, Smoking, Early postoperative outcomes, 30-day mortality.

INTRODUCTION

Valvular heart disease (VHD) is a common cardiovascular disease characterized by damage or defect in heart valves (1). Five million Americans are diagnosed with VHD every year (2, 3). Heart valve surgery is performed to repair or replace affected valves, and accounts for 10% to 20% of all heart surgeries in the United States. Most heart valve surgeries involve mitral and aortic valves (4, 5).

It is well-documented that smoking is a significant risk factor for developing cardiovascular diseases, including VHD (6). To date, however, there are only two published studies to specifically document the association of smoking with early postoperative outcomes in patients undergoing heart valve surgery (7, 8). In one study, data obtained prospectively between June 2001 and December 2009 by the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (SCTS) Cardiac Surgery Database Program were analyzed retrospectively (8). Isolated aortic valve (AV) replacement surgery was performed in 2,790 patients and smoking status was recorded in 2,784 cases. The impact of smoking on 14 short-term complications and long-term mortality was determined by using binary logistic and Cox regression, respectively. The authors concluded that smoking does not necessarily portend a poorer perioperative outcome in patients undergoing isolated aortic valve replacement surgery (8). The other study consisted of 590 patients who underwent isolated AV and/or mitral valve (MV) surgery (replacement and/or repair) in Dendrite Clinical in UK from February 2000 to July 2007 (7). The authors found no significant impact of smoking on early postoperative outcomes, including in-hospital mortality, length of both hospital and intensive care unit stays, and postoperative complications in patients undergoing isolated heart valve surgery (7). Apparently, the specific evidence is very limited for the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery.

In this study, to provide more evidence about the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery, we analyzed data from 1,024 patients who underwent SAVR or SMVR from January 2002 to September 2017 at Emory University hospitals (Atlanta, Georgia, US).

METHODS

This study was approved by the Emory University Institutional Review Board (IRB) in compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations. The individual patient consent was waived by the IRB because this study was a secondary data analysis. Patients included in this study underwent SAVR or SMVR from January 2002 to September 2017 at Emory University hospitals (Atlanta, Georgia, US). Surgical data for these patients are stored in the Society of Thoracic Surgeons (STS) national database. Patients with missing smoking status, transcatheter aortic valve replacement (TAVR), other concomitant cardiac surgery or who were not white or black were excluded from the study (see Figure 1).

In this study, current or former smokers were compared to never smokers in five early postoperative outcomes. Current smokers were defined as patients who had smoked at least five packs of cigarettes during his/her lifetime and still regularly smoked every day or periodically, yet consistently within 30 days prior to admission (9). Former smokers were patients who had smoked at least five packs of cigarettes during his/her lifetime but did not currently smoke prior to admission, and never smokers were patients who had not smoked five or more packs of cigarettes during his/her lifetime (9). Five early postoperative outcomes included postoperative stay days in hospital, total ICU hours, postoperative in-hospital events, 30-day mortality, and 30-day re-admission. In hospital postoperative events indicated whether a postoperative event occurred during the entire postoperative period up to discharge, even if over 30 days. They included but not limited to sepsis, stroke, transient ischemic attack, pneumonia, superficial wound infection, deep wound infection, wound interventions, venous thromboembolism, mediastinal bleeding, valve dysfunction, sternotomy, sterile dehiscence of the sternal edges requiring surgical intervention, new requirement for dialysis and new dysrhythmia requiring insertion of a permanent device. The postoperative 30-day mortality indicated whether the patient was alive or dead at 30 days post-surgery (whether in hospital or not).

Three demographic characteristics of age, race and gender as female and 24 risk factors, preoperative cardiac status and operative factors were compared between current smokers or former smokers and never smokers during the analysis. The 24 risk factors are family history of premature coronary artery disease (CAD), diabetes, hypertension, obesity, cerebrovascular diseases, chronic lung diseases, peripheral arterial disease, renal fail dialysis, last creatinine level, dyslipidemia, endocarditis, immunosuppressive therapy, preoperative hemoglobin, preoperative hematocrit, previous cardiac intervention, prior myocardial infarction (MI), angina, heart failure within 2 weeks, surgeon's experience in heart valve surgery, cardiac arrhythmia, diseased vessels, emergent/urgent status, procedure type, and cardioplegia use (see Table 1).

Categorical variables were summarized as counts and percentages. Quantitative variables were summarized as mean ± standard deviation [or median (interquartile range)]. The association between smoking and ordinal variables (e.g., age category, obesity and surgeon's experience in heart valve surgery), nominal variables (e.g., race and procedure type) or dichotomous (e.g., sex, immunosuppressive therapy) was assessed by using the either univariable or multivariable logistic regression. Moreover, Firth penalized likelihood was used to address the issue of small number of events (10, 11). The association between smoking and continuous variables with normal distributions (e.g., last creatinine level, preoperative hemoglobin and preoperative hematocrit) was assessed using analysis of variance. The Tukey method was used to adjust for multiple comparison. Continuous variables that did not appear to have a normal distribution were first log-transformed prior to incorporating them in the regression model. In the regression analysis, smoking was treated as a nominal categorical variable, with never smokers as the reference group. The impact of smoking on early postoperative outcomes was first analyzed independently, and then adjusted by covariates which were significantly different between former and current smokers and never smokers. These covariates included age, race, gender, family history of premature CAD, hypertension, obesity, dyslipidemia, prior MI, surgeon's experience in heart valve surgery, diseased vessels, emergent/urgent status, procedure type, and cardioplegia use. Chronic lung disease status was not included in the multivariable model because it is a well-established mediator between smoking and cardiovascular diseases (12-17). In all outcomes, the association of smoking with early postoperative outcomes was further stratified by age, race and gender. Age had three levels (namely, < 55 years, 55-69 years and ≥ 70 years). Race had two levels: white and black. Gender also had two levels: male and female. All statistical analyses were performed by using SAS Version 9.4. All *p* values were twosided and the type I error rate was set at 0.05. Confidence intervals were constructed using a 95% level of confidence.

RESULTS

A total of 1,024 patients who underwent SAVR or SMVR were included in the study, of whom, 120 (11.7%) were current smokers, 288 (28.1%) were former smokers and 616 (60.2%) were never smokers. Their demographic characteristics and 24 risk factors, preoperative cardiac status and operative factors were stratified by smoking status and summarized in Table 1. The percentage of female patients as current or former smokers was significantly lower than as never smokers ($p < 0.001$, see Table 1). There were significant differences in age, race, surgeon's experience in heart valve surgery, and procedure type between current or former and never smokers ($p < 0.001$, $p = 0.002$, $p = 0.09$, and $p = 0.01$, respectively. see Table 1). Former and/or current smokers had a significantly higher percentage of family history of premature CAD ($p < 0.001$), hypertension ($p = 0.006$), obesity ($p = 0.017$), chronic lung diseases ($p < 0.001$), dyslipidemia ($p = 0.009$), prior MI ($p = 0.001$), and diseased vessels ($p = 0.006$), but a significantly lower percentage or level of emergent/urgent surgical status ($p < 0.001$), and cardioplegia use ($p = 0.03$) (see Table 1).

Estimated differences in postoperative in-hospital stay days, total ICU hours, postoperative in-hospital events or postoperative 30-day re-admission in all levels of age, race and gender were significant between current and former and never smokers in both unadjusted and adjusted analyses (see Table 2 and 3).

The overall incidence of 30-day mortality was 2.6% (16 out of 616) in never smokers, 5.2% (15 out of 288) in former smokers, and 5.0% (6 out of 120) in current smokers. When not adjusted for covariates, former smokers had significantly higher overall postoperative 30-day mortality (OR = 2.06, 95% CI (1.01, 4.23)), but this significant finding was not observed among current smokers. It is interesting that after adjusting for covariates, current smokers had significantly higher overall postoperative 30-day mortality (OR = 3.22, 95% CI (1.26, 8.28), see Figure 2), but former smokers did not (see Table 3). The incidence of 30-day mortality among patients aged ≥ 70 years was 3.0% (7 out of 234) in never smokers, 9.1% (11 out of 121) in former smokers, and 21.4% (3 out of 14) in current smokers. In the unadjusted analysis, both former and current smokers aged ≥ 70 years had significantly higher postoperative 30-day mortality (OR = 2.49, 95% CI (1.03, 6.01) and OR = 6.68, 95% CI (1.74, 25.7), respectively. see Table 3). After adjusting for covariates, the association of postoperative 30-day mortality with former and current smokers became significant (OR = 3.36, 95% CI (1.33, 8.51) and OR = 8.76, 95% CI (2.01, 38.1), respectively. see Table 3 and Figure 2). The incidence of 30-day mortality among whites was 2.5% (12 out of 486) in never smokers, 5.7% (14 out of 248) in former smokers, and 5.8% (5 out of 86) in current smokers. Without adjustment for covariates, among patients who were white, only former smokers had significantly higher postoperative 30-day mortality (OR = 2.35, 95% CI (1.08, 5.09)), but current smokers did not. After adjustment, however, both former and current smokers who were white had significantly higher postoperative 30-day mortality (OR = 2.41, 95% CI (1.13, 5.12) and OR = 4.04, 95% CI (1.42, 11.5), respectively. see Table 3 and Figure 2). The incidence of

30-day mortality among male patients was 1.6% (5 out of 320) in never smokers, 5.1% (9 out of 175) in former smokers, and 4.9% (4 out of 81) in current smokers. In the crude analysis, only former male smokers had significantly higher postoperative 30-day mortality (OR = 3.27, 95% CI (1.12, 9.53)), but current male smokers did not. After adjustment by covariates, however, both former and current male smokers had significantly higher postoperative 30-day mortality (OR = 3.15, 95% CI (1.13, 8.78) and OR = 4.85, 95% CI (1.41, 16.7), respectively. see Table 3 and Figure 2).

DISCUSSION

Smoking is a significant risk factor for a number of cardiovascular diseases (6). To date, there are two studies that investigated the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery, both of which failed to observe a significant association (7, 8). In addition to the limitations acknowledged by the researchers in both studies, we found that neither studies clarified the impact of TAVR on the analysis. Many patients have been treated with TAVR worldwide since 2002 when Dr. Alain Cribier performed the first-in-man TAVR (18). TAVR may be associated with higher rates of mortality than SAVR in patients with severe aortic valve stenosis at intermediate surgical risk (19). Despite having a higher cardiovascular disease burden, smokers were reported to have better outcomes compared to non-smokers among patients with TAVR (20). The smoker's paradox appears to be applicable to patients with TAVR (20-22). Therefore, inclusion of patients with TAVR had a potential to conceal the authentic association of smoking with early postoperative outcomes in isolated heart valve surgery. Considering the limitations in both studies (7, 8), the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery is not entirely clear. Given the great number of isolated heart valve surgery and smoking people in the US and the known risk of smoking in cardiovascular diseases (2, 5, 23), it is necessary to further examine the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery.

In this study, we retrospectively analyzed data prospectively collected from 1,024 patients with SAVR or SMVR between January 2002 and September 2017 at Emory University hospitals (Atlanta, Georgia, US) and entered in the STS national database. Among demographic characteristics, risk factors, preoperative cardiac status and operative factors, we found there were significant differences in age, gender, hypertension, chronic lung diseases, surgical emergent/urgent status, and obesity between former and current smokers and never smokers, consistent with previous studies (7, 8). We also found there were significant differences in race, family history of premature CAD, dyslipidemia, surgeon's experience level, diseased vessels and procedure type, but no difference in preoperative endocarditis, not consistent with or not reported by previous studies (7, 8). For early postoperative outcomes, our results confirmed that there were no significant differences in postoperative stay days, total ICU hours, in-hospital events or 30-day re-admission between current and former smokers and never smokers in both univariate and multivariate analysis (7, 8).

Different from previous studies (7, 8), our results revealed that current smokers had significantly higher postoperative 30-day mortality compared to never smokers in the adjusted analysis (OR = 3.22, 95% CI (1.26, 8.28)), although there was no significant difference when not adjusted by covariates. The difference in postoperative 30-day mortality between current and former smokers and never smokers was further analyzed across age, race and gender. Both before and after adjustment by covariates, the significantly higher postoperative 30-day mortality was found in former smokers aged ≥ 70 years (Before: OR = 2.49, 95% CI (1.03, 6.01); After: OR = 3.36, 95% CI (1.33, 8.51)), who were white (Before: OR = 2.35, 95% CI (1.08, 5.09); After: OR = 2.41, 95% CI (1.13, 5.12)), or who were male (Before: OR = 3.27, 95% CI (1.12, 9.53); After: OR = 3.15, 95% CI (1.13, 8.78)). Although only current smokers aged ≥ 70 years had significantly higher postoperative 30-day mortality before adjusted by covariates (OR = 6.68, 95% CI (1.74, 25.7), the significantly higher postoperative 30-day mortality was found in current smokers aged ≥ 70 years (OR = 8.76, 95% CI (2.01, 38.1)), who were white (OR = 4.04, 95% CI (1.42, 11.5)), or who were male (OR = 4.85, 95% CI (1.41, 16.7)) in the adjusted analysis.

We concluded that smoking is significantly associated with higher postoperative 30-day mortality among patients who underwent isolated heart valve surgery, particularly among those aged ≥ 70 years, who were white or who were male (see Figure 2). Besides the different conclusion, our study is different from previous studies in at least four aspects (7, 8). First, our study only included patients with SAVR or SMVR and patients with TAVR were excluded from our analysis. Second, there were no patients with combined AV and MV surgery in our study cohort. Third, patients in our study were Americans who lived in the US, including 820 (80.1%) whites and 204 (19.9%) blacks. While race information was not provided, data collected from Australians, New Zealanders and Irish were used in previous studies (7, 8). Fourth, data in our study were assessed across age, race and gender, but previous studies did not (7, 8). These differences may explain why conclusions in this study are different from those previously reported (7, 8).

In the present study, while both former and current smokers aged ≥ 70 years, who were white or who were male had significantly higher postoperative 30-day mortality, only current smokers had significantly higher overall postoperative 30-day mortality (see Table 3 and Figure 2). At the same time, we noticed that the association of smoking with postoperative 30-day mortality was stronger in current smokers than in former smokers not only in the overall level but also across age, race and gender (see Table 3). Our results revealed the adverse health effects of smoking in both former and current smokers undergoing isolated heart valve surgery.

Our study is subject to at least three limitations. First, our study was limited to patients with SAVR or SMVR at Emory University hospitals (Atlanta, Georgia, US). These patients might not be representatives of all patients with isolated heart valve surgery in the US. Second, our data did not include variables about cigarette packs smoked per year in former and current smokers, cross-clamp time, and NYHA classification or ejection fraction due to incomplete data. These variables might be different between former and current smokers and never smokers, and the difference may influence the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery. Third, the smoking status of never, former and current smokers in our study was determined by patient self-report, which can introduce patients' bias.

Despite these limitations, our study supports what many people hold to be true: history of smoking or current smoking is associated with worse postoperative outcomes. Our study provides additional evidence on the association of smoking with early postoperative outcomes in patients undergoing isolated heart valve surgery. More studies should be conducted to further validate these findings.

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Figure 1: Flow Diagram of Study Participants

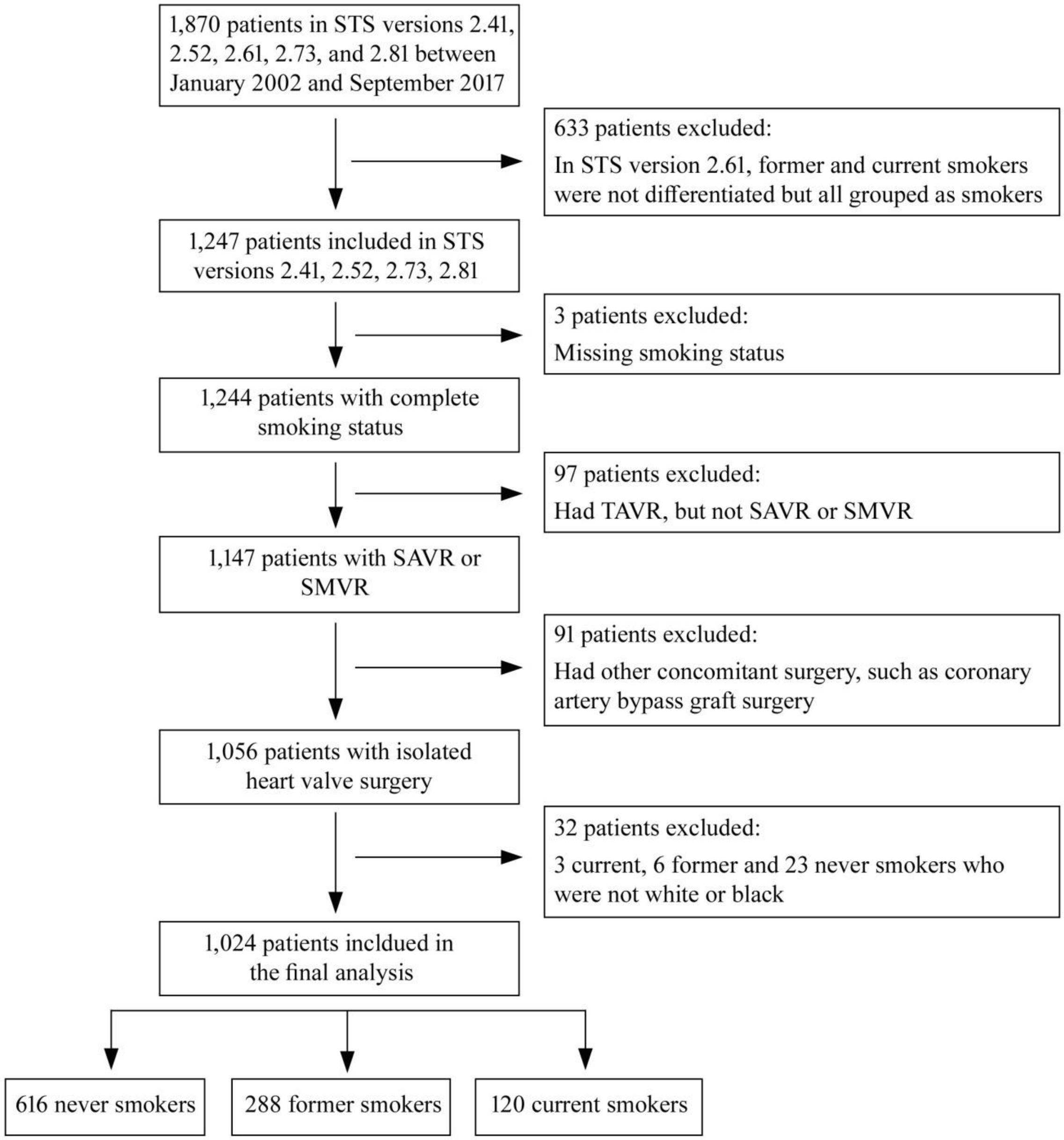

Figure 2: Odds ratio (OR) and 95% confidence interval (CI) for postoperative 30-day mortality. ORs and 95% CIs in the overall level and across age, race and gender were displayed as solid cycles and horizontal lines, respectively. ORs were considered statistically significant if their 95% CIs did not contain the null value of 1.

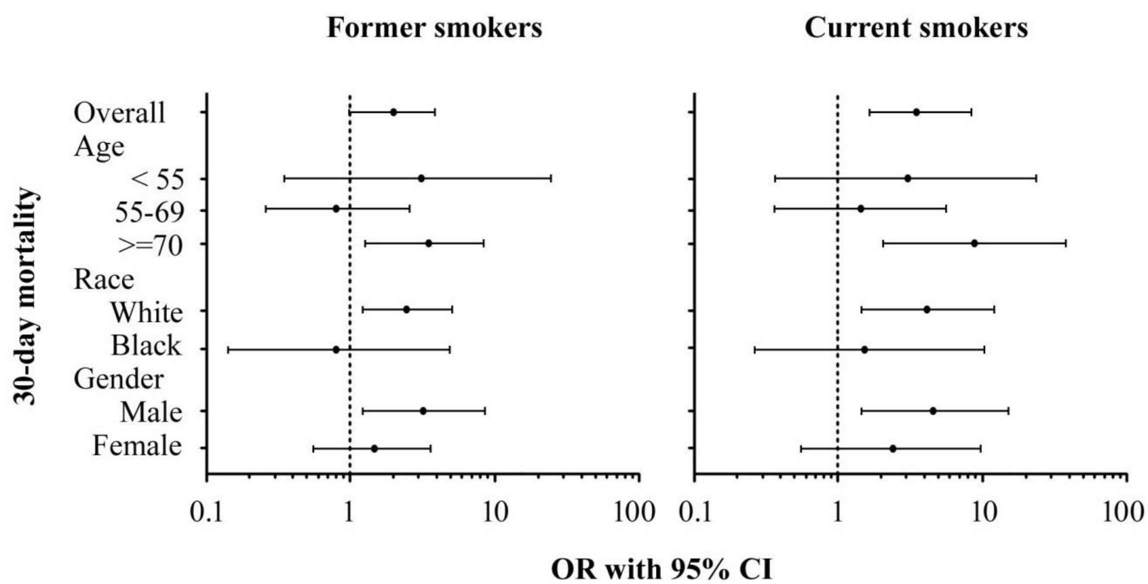

Table 1. Demographics, risk factors, preoperative cardiac status, and operative factors stratified by smoking status.

Variables *	Never smoker (n = 616)	Former smoker (n = 288)	Current smoker (n = 120)	*p*
Age (%)				**<0.001**
< 55 years	178(28.9)	51(17.7)	61(50.8)	-
55 – 69 years	204(33.1)	116(40.3)	45(37.5)	-
≥ 70 years	234(38.0)	121(41.0)	14(11.7)	-
Race (%)				**0.002**
White	486(78.9)	248(86.1)	86(71.7)	-
Black	130(21.1)	40(13.9)	34(28.3)	-
Female	296(48.1)	113(39.2)	39(32.5)	**0.001**
Family history of premature CAD (%)	58(9.4)	52(18.1)	18(15.0)	**<0.001**
Diabetes (%)	144(23.4)	84(29.2)	30(25.0)	0.174
Hypertension (%)	441(71.6)	234(81.3)	86(71.7)	**0.006**
Obesity (BMI) (%)				**0.017**
Normal weight	217(35.2)	81(28.1)	49(40.8)	-
Overweight	211(34.3)	106(36.8)	47(39.2)	-
Obesity	188(30.5)	101(35.1)	24(20.0)	-
Cerebrovascular diseases (%)	100(16.2)	59(20.5)	27(22.5)	0.128
Chronic lung diseases (%)	90(14.6)	82(28.5)	43(35.8)	**<0.001**
Peripheral arterial disease (%)	50(8.1)	21(7.3)	15(12.5)	0.207
Renal fail dialysis (%)	29(4.7)	13(4.5)	9(7.5)	0.399
Last creatinine level (mean ± SD)	1.4±1.9	1.4±1.4	1.6±2.0	0.541
Dyslipidemia (%)	362(58.8)	186(64.6)	58(48.3)	**0.009**
Endocarditis (%)	68(11.0)	37(12.9)	20(16.7)	0.210

Immunosuppressive therapy (%)	71(11.5)	28(9.7)	17(14.2)	0.422
Hemoglobin (mean ± SD)	12.6±2.3	12.7±2.5	12.9±2.3	0.564
Preoperative hematocrit (mean ± SD)	37.3±5.6	37.3±5.4	38.0±6.1	0.384
Previous cardiac intervention (%)	237(38.5)	119(41.3)	49(40.8)	0.685
Prior MI (%)	75(12.2)	62(21.5)	19(15.8)	**0.001**
Angina (%)	160(26.0)	89(30.9)	31(25.8)	0.279
Heart failure within 2 weeks (%)	403(65.4)	184(63.9)	68(56.7)	0.188
Doctor experience level (%)				**0.028**
Level ≥200 patients	323(52.4)	128(44.4)	58(48.3)	-
Level 100-200 patients	75(12.2)	61(21.2)	21(17.5)	-
Level 50-100 patients	137(22.2)	61(21.2)	23(19.2)	-
Level <50 patients	81(13.2)	38(13.2)	18(15.0)	-
Cardiac arrhythmia (%)	140(22.7)	83(28.8)	24(20.0)	0.073
Diseased vessels (%)	117(19.0)	81(28.1)	23(19.2)	**0.006**
Emergent/urgent status (%)	315(51.1)	106(36.8)	52(43.3)	**<0.001**
Procedure type (%)				**0.014**
AV replacement	396(64.3)	186(64.6)	71(59.2)	-
MV repair	92(14.9)	33(11.5)	9(7.5)	-
MV replacement only	128(20.8)	69(24.0)	40(33.3)	-
Cardioplegia use (%)	609(98.9)	279(96.9)	115(95.8)	**0.032**

*** C**ategorical variables are summarized as counts (percentage); quantitative variables are presented either as mean plus or minus standard deviation, or median (interquartile range), as appropriate.

Table 2. Association of smoking with postoperative stay days in hospital and total ICU hours by age, race and gender.

Outcomes	Never smoker (n = 616)	Former smoker (n = 288)	Current smoker (n = 120)	Former smoker		Current smoker	
				Crude *p*	Adjusted *p**	Crude *p*	Adjusted *p**
Postoperative stay days in hospital (median(Q1, Q3))	7.0(5.0, 9.0)	7.0(5.0, 10.0)	6.0(5.0, 8.0)	0.72	1.00	0.93	0.96
Age < 55 years	6.0(5.0, 7.0)	7.0(4.0, 10.0)	6.0(5.0, 7.0)	0.99	1.00	1.00	1.00
Age 55-69 years	6.0(5.0, 9.0)	6.0(5.0, 8.5)	7.0(5.0, 8.0)	1.00	1.00	1.00	1.00
Age ≥ 70 years	8.0(6.0, 11.0)	8.0(5.0, 12.0)	6.5(5.0, 23.0)	1.00	1.00	1.00	1.00
Race - White	6.0(5.0, 9.0)	7.0(5.0, 9.0)	6.0(5.0, 8.0)	0.98	0.97	0.99	0.99
Race - Black	7.0(5.0, 10.0)	7.5(5.0, 11.0)	6.5(6.0, 10.0)	1.00	0.92	1.00	1.00
Gender - Male	6.0(5.0, 9.0)	6.0(5.0, 10.0)	6.0(5.0, 9.0)	0.98	0.99	0.96	0.70
Gender - Female	7.0(5.0, 10.0)	7.0(6.0, 9.0)	6.0(5.0, 8.0)	1.00	1.00	0.39	0.65
Total ICU hours (median(Q1, Q3))	46.5(24.6, 90.5)	47.4(25.0, 91.6)	48.8(24.8, 72.9)	0.88	0.99	0.89	0.93
Age < 55 years	41.6(23.7, 55.0)	45.0(23.2, 73.2)	30.0(23.2, 70.3)	1.00	1.00	1.00	1.00
Age 55-69 years	45.8(24.0, 93.2)	44.2(26.0, 79.3)	62.3(26.8, 97.5)	1.00	1.00	1.00	1.00
Age ≥ 70 years	66.9(28.3, 100)	52.1(26.5, 100)	58.7(26.0, 120)	0.78	0.96	0.80	0.74
Race - White	46.0(24.2, 90.5)	47.2(25.0, 90.1)	46.6(24.0, 73.0)	0.99	1.00	0.97	1.00
Race - Black	49.5(28.0, 90.5)	50.6(26.9, 94.5)	62.9(26.6, 71.5)	1.00	1.00	1.00	1.00
Gender - Male	46.3(24.6, 87.1)	46.0(25.0, 90.9)	49.7(24.3, 73.0)	1.00	1.00	1.00	1.00
Gender - Female	47.0(24.7, 94.9)	49.5(26.4, 94.0)	45.6(25.0, 72.2)	1.000	1.00	0.92	0.97

***** Adjusted by age, race, gender, family history of premature CAD, hypertension, obesity, dyslipidemia, prior MI, surgeon's experience in heart valve surgery, diseased vessels, emergent/urgent status, procedure type, and cardioplegia use.

Table 3. Association of smoking with postoperative in-hospital events, 30-day mortality and 30-day re-admission, by age, race and gender.

Outcomes	Never smoker (n = 616)	Former smoker (n = 288)	Current smoker (n = 120)	Former smoker Crude OR	Former smoker Adjusted OR*	Current smoker Crude OR	Current smoker Adjusted OR*
Postoperative in-hospital events	311(50.5)	165(57.3)	59(49.2)	1.32(0.99,1.74)	1.14(0.84,1.54)	0.95(0.64,1.40)	1.15(0.75,1.75)
Age < 55 years	61(34.3)	24(47.1)	25(41.0)	1.56(0.92,2.67)	1.61(0.84,3.07)	1.24(0.71,2.17)	1.22(0.66,2.25)
Age 55-69 years	104(51.0)	63(54.3)	24(53.3)	1.27(0.95,1.71)	1.08(0.67,1.75)	1.26(0.80,1.99)	1.10(0.56,2.16)
Age ≥ 70 years	146(62.4)	78(64.5)	10(71.4)	1.04(0.68,1.58)	0.99(0.62,1.59)	1.28(0.53,3.10)	1.28(0.38,4.32)
Race - White	258(53.1)	142(57.3)	42(48.8)	1.18(0.87,1.61)	1.06(0.76,1.48)	0.84(0.53,1.34)	1.06(0.65,1.74)
Race - Black	53(40.8)	23(57.5)	17(50.0)	1.95(0.95,3.99)	1.56(0.74,3.31)	1.45(0.68,3.09)	1.41(0.64,3.12)
Gender - Male	166(51.9)	99(56.6)	41(50.6)	1.21(0.83,1.75)	1.00(0.67,1.48)	0.95(0.58,1.55)	1.11(0.66,1.86)
Gender - Female	145(49.0)	66(58.4)	18(46.2)	1.46(0.94,2.27)	1.36(0.86,2.16)	0.89(0.46,1.74)	1.18(0.58,2.41)
30-day mortality	16(2.6)	15(5.2)	6(5.0)	**2.06(1.01,4.23)**	1.99(1.00,3.98)	1.97(0.76,5.15)	**3.22(1.26,8.28)**
Age < 55 years	1(0.6)	1(2.0)	1(1.6)	0.88(0.14,5.44)	3.02(0.37,25.0)	1.02(0.16,6.68)	2.95(0.37,23.7)
Age 55-69 years	8(3.9)	3(2.6)	2(4.4)	1.48(0.59,3.73)	0.80(0.24,2.64)	2.62(0.97,7.08)	1.42(0.35,5.78)
Age ≥ 70 years	7(3.0)	11(9.1)	3(21.4)	**2.49(1.03,6.01)**	**3.36(1.33,8.51)**	**6.68(1.74,25.7)**	**8.76(2.01,38.1)**
Race - White	12(2.5)	14(5.7)	5(5.8)	**2.35(1.08,5.09)**	**2.41(1.13,5.12)**	2.56(0.91,7.21)	**4.04(1.42,11.5)**
Race - Black	4(3.1)	1(2.5)	1(2.9)	1.07(0.16,7.15)	0.80(0.13,4.96)	1.26(0.19,8.49)	1.71(0.27,10.9)
Gender - Male	5(1.6)	9(5.1)	4(4.9)	**3.27(1.12,9.53)**	**3.15(1.13,8.78)**	3.33(0.93,11.9)	**4.85(1.41,16.7)**
Gender - Female	11(3.7)	6(5.3)	2(5.1)	1.50(0.56,4.04)	1.37(0.53,3.55)	1.66(0.40,6.88)	2.35(0.55,9.95)
30-day re-admission	44(7.1)	16(5.6)	9(7.5)	0.77(0.42,1.38)	0.89(0.48,1.65)	1.05(0.50,2.22)	0.98(0.45,2.15)
Age < 55 years	15(8.4)	4(7.8)	6(9.8)	0.85(0.30,2.42)	1.14(0.38,3.40)	1.44(0.57,3.64)	1.26(0.48,3.29)
Age 55-69 years	12(5.9)	5(4.3)	3(6.7)	0.81(0.45,1.46)	0.86(0.31,2.35)	0.82(0.30,2.23)	1.13(0.33,3.84)

Age ≥ 70 years	17(7.3)	7(5.8)	0(0.0)	0.77(0.33,1.84)	0.86(0.36,2.06)	0.47(0.07,3.43)	0.44(0.03,7.64)
Race - White	32(6.6)	10(4.0)	6(7.0)	0.62(0.30,1.26)	0.67(0.33,1.34)	1.13(0.47,2.72)	1.04(0.43,2.50)
Race - Black	12(9.2)	6(15.0)	3(8.8)	1.79(0.64,5.01)	2.06(0.73,5.79)	1.05(0.30,3.73)	1.09(0.31,3.81)
Gender - Male	27(8.4)	11(6.3)	6(7.4)	0.75(0.37,1.53)	0.92(0.45,1.87)	0.92(0.38,2.25)	0.96(0.39,2.33)
Gender - Female	17(5.7)	5(4.4)	3(7.7)	0.81(0.30,2.22)	0.92(0.36,2.40)	1.53(0.46,5.14)	1.27(0.38,4.24)

***** Adjusted by age, race, gender, family history of premature CAD, hypertension, obesity, dyslipidemia, prior MI, surgeon's experience in heart valve surgery, diseased vessels, emergent/urgent status, procedure type, and cardioplegia use.