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Incidence, severity and perioperative risk factors for atrial fibrillation following pulmonary resection

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Abstract

OBJECTIVES: Postoperative atrial fibrillation (PAF) occurs commonly following pulmonary resection. Our aims were to quantify the incidence and severity of PAF using the Thoracic Morbidity & Mortality classification system, and identify risk factors for PAF.

METHODS: All consecutive patients undergoing pulmonary resection at a single centre (January 2008 - April 2010) were enrolled. PAF was defined as postoperative, electrocardiographically documented and requiring initiation of pharmacological therapy. Univariate and multivariate analyses of risk factors associated with the development of PAF were conducted.

RESULTS: The incidence of PAF was 11.8% ($n = 43$) of 363 pulmonary resections (open: $n = 173$; 47.7%; video-assisted: $n = 177$; 48.8%; converted: $n = 13$; 3.6%): sublobar ($n = 93$; 25.6%), lobectomy ($n = 237$; 65.3%), bilobectomy ($n = 7$; 1.9%) and pneumonectomy ($n = 24$; 6.6%). Twenty-eight cases (65.1%) were uncomplicated/transient, and 15 cases (34.9%) were complicated/persistent PAF, defined as lasting for >7 days (40.0%), requiring cardioversion (13.3%), vasopressors (33.3%), in-hospital use of anticoagulants (46.7%) and/or anticoagulants on discharge (26.7%). Patients with PAF had increased mean lengths of hospital stay (10.5 days vs 6.9 days; $P = 0.04$). Peak onset of PAF occurred 2.5 (standard deviation (SD) ± 1.3) days after pulmonary resection, lasting for 1.8 ± 2.8 (mean, ±SD) days. Multivariate analysis identified (relative risk; 95% confidence interval): age ≥70 years (2.3; 1.1–5.1), history of angioplasty/stents/angina (4.0; 1.4–11.3), thoracotomy (3.6; 1.4–9.3), conversion to open thoracotomy (16.5; 2.2–124.0) and extent of surgery/stage (7.1; 1.0–49.4) as predictors of PAF.

CONCLUSIONS: While the majority of PAF is uncomplicated and transient, one-third of cases lead to persistence or major intervention. Age, coronary artery disease and extent of surgery/stage increase the risk of PAF following pulmonary resection. Identifying patients with elevated risk may lead to targeted prophylaxis to reduce the incidence of PAF.

Keywords: Atrial fibrillation, Flutter • Lung cancer surgery • Statistics, risk analysis/modelling • Epidemiology

INTRODUCTION

Postoperative atrial fibrillation (PAF) has remained one of the most common complications that occur following non-cardiac thoracic surgery. Although it is difficult to determine the true incidence of PAF due to various methodologies used to identify its occurrence, reported rates have varied between 4 and 37% [1–3]. The occurrence of PAF is associated with significant morbidity, such as increased risk of stroke, atrial thrombosis and systemic embolization, postoperative mortality and significant increases in hospital length of stay (LOS) and costs [1, 4]. Accordingly, several prophylactic antiarrhythmic drug treatments have been proposed in an attempt to reduce the incidence of PAF [5–7].

In addition, a number of efforts have been made at identifying risk factors for PAF [1, 8–13]. Risk factors of PAF have included increasing age, male sex, pre-existing history of ischaemic heart disease, valvular heart disease, congestive heart failure, peripheral vascular disease, intrapericardial dissection, increasing extent of pulmonary resection, intraoperative blood transfusions, postoperative electrolyte imbalance and hypoxia [1, 8–12]. A definite causative relationship between PAF development and preoperative and intraoperative risk factors has not yet been firmly established. Moreover, past studies have not used a standardized and validated definition of PAF; nor have previous studies attempted to stratify the severity of disease burden associated with PAF.

In accordance with the Clavien–Dindo classification system of adverse events [14], we have developed a standardized system to identify both the presence and severity of Thoracic Morbidity & Mortality (TM&M) [14, 15]. The TM&M classification system was implemented at The Ottawa Hospital in January 2008 and is a

prospective database documenting all complications and their severity for all thoracic surgical procedures. The TM&M database is created to prospectively record postoperative adverse event information, and it provided an essential platform for the current study as the onset of PAF most commonly occurs in the first 7 days following pulmonary resection. Thus, using the TM&M classification system, our objectives were to quantify the incidence and severity of PAF and identify preoperative and intraoperative risk factors for PAF following pulmonary resection.

MATERIALS AND METHODS

Study population

A retrospective review of the prospectively collected TM&M database was conducted. All consecutive patients who underwent pulmonary resection for benign or malignant disease by the Ottawa Hospital's Division of Thoracic Surgery between January 2008 and April 2010 were considered for inclusion into this study. Among the 371 patients initially identified, 4 patients were excluded because they did not undergo formal preoperative assessment. Of the remaining 367 patients, 13 more were excluded due to a history of AF. If a patient underwent multiple separate pulmonary resections during the study period, data were collected and analysed for each surgery separately. Data were collected on patient demographics, medical history, surgical history, active medications, neoadjuvant chemotherapy and/or radiotherapy, preoperative cardiopulmonary functional testing, operative details and postoperative adverse events. Data on PAF characteristics and hospital LOS were also recorded. This study was approved by the Ottawa Hospital Research Ethics Board.

Classification of postoperative adverse events, and definition and monitoring of PAF

The incidence and severity of PAF were classified prospectively during the study period using the TM&M classification system, which grades adverse events on a severity scale from Grade I to V based on the effort required to treat the event [14].

PAF was defined as uncomplicated/transient (≤7 days) or complicated/persistent (>7 days) electrocardiographically documented PAF requiring initiation of pharmacological therapy (Grade II). PAF was considered complicated/persistent if it lasted for >7 days and/or if the patient required: (i) cardioversion or vasopressors (Grade III); (ii) intensive care unit (ICU) admission (Grade IV); (iii) in-hospital use of anticoagulants and/or (iv) the patient was discharged on amiodarone, diltiazem, digoxin or anticoagulants. During the postoperative period, clinical examination of patients was performed daily until hospital discharge and electrocardiogram (ECG) monitoring was performed daily or when required by clinical examination.

Statistical analysis

Summary statistics for continuous variables were recorded as medians and means, and analysed using Student's *t*-test; categorical data were summarized as frequencies and percentages, and comparisons between the two groups were performed with the Pearson χ^2 test or Fisher exact test. A *P*-value of <0.05 was considered statistically significant. Stepwise logistic regression analysis was used to determine independent correlates for both PAF and complicated/persistent PAF development. A two-sided *P*-value of <0.05 was considered statistically significant for inclusion into the multivariate model. Discrimination and calibration of the model were assessed using the *C*-statistic and the Hosmer–Lemeshow goodness of fit test. Data collection was performed using paper case-report forms, data entry was performed using Excel (Microsoft, Redmond, WA, USA) and data analyses were conducted using the IBM SPSS Statistics Version 20® software (SPSS, Chicago, IL, USA).

Table 1: Patient demographics, medical history and preoperative evaluation

	–PAF (*n* = 320) (%)	+PAF (*n* = 43) (%)	*P*-value
Patient characteristics			
Age			0.01
≤69	205 (64)	19 (44)	
≥70	115 (36)	24 (56)	
Sex			0.45
Male	149 (47)	19 (44)	
Female	171 (53)	24 (56)	
Body mass index median	26.2	26.3	0.85
Past medical history			
Cardiac risk factors			
Angioplasty/stents/ angina	22 (7)	9 (21)	0.01*
Myocardial infarction	21 (7)	4 (9)	0.51
Cerebrovascular disease	16 (5)	2 (5)	0.64
Peripheral vascular disease	24 (8)	2 (5)	0.50
Valvular disease	15 (5)	3 (7)	0.52
Other risk factors			
Diabetes mellitus	35 (11)	7 (16)	0.30
Previous cancer	125 (39)	14 (33)	0.41
Previous cardiac surgery	18 (6)	4 (9)	0.34
Previous thoracic surgery	17 (5)	1 (2)	0.40
Preoperative chemotherapy	7 (2)	3 (7)	0.07
Preoperative radiation therapy	3 (1)	1 (2)	0.41
Lung function tests			
$FEV_{1\ predicted,\ median,\ \%}$	82.0	82.5	0.70
$FVC_{predicted,\ median,\ \%}$	89.0	83.0	0.21
$FEV_1/FVC\%$	70.0	69.0	0.51
$DLCO_{predicted,\ median,\ \%}$	78.0	83.0	0.06
Echocardiographic variables	(*n* = 258)	(*n* = 33)	
Left systolic dysfunction	13 (5)	6 (18)	<0.05*
Left diastolic dysfunction	23 (9)	6 (18)	0.09
Left atrial enlargement	12 (5)	3 (9)	0.28
Left ventricular hypertrophy	6 (2)	2 (6)	0.2
Pulmonary hypertension	11 (4)	1 (3)	0.60
Atrial septal defect	3 (1)	2 (6)	0.04*
Valvular pathology	23 (9)	5 (15)	0.25
Diagnosis			0.74
Benign	12 (8)	1 (2)	
Malignant NSCLC	244 (76)	35 (81)	
Other malignant	64 (20)	7 (16)	

% DLCO: diffusing capacity of the lung for carbon monoxide; % NSCLC: non-small-cell lung cancer.

RESULTS

Baseline features and outcomes

During the study period, a total of 354 patients underwent 363 pulmonary resections. A total of 195 (53.7%) patients were female and 139 (38.3%) patients were over the age of 70. Disease diagnoses included primary lung cancer (*n* = 279; 76.9%), pulmonary metastasis (*n* = 71; 19.6%) and benign lung disease (*n* = 13; 3.6%). A comparison of preoperative risk factors in patients with and those without PAF is presented in Tables 1 and 2.

Overall incidence of PAF was 11.8% (*n* = 43), including 28 cases (65.1%) of uncomplicated/transient PAF and 15 cases (34.9%) of complicated/persistent PAF. Approximately one-quarter (23.3%) of patients with PAF experienced PAF during the first 24 h. The peak onset of PAF occurred 2.5 (standard deviation (SD) ± 1.3) days after pulmonary resection, lasting for a mean duration of 1.8 (SD ± 2.8) days. Sixteen patients (37.2%) developed PAF after Day 3. Five patients (11.6%) had PAF after Day 5.

Operative characteristics

The types of procedures performed were sublobar resection (*n* = 93; 25.6%), lobectomy (*n* = 237; 65.3%), bilobectomy/extended lobectomy (*n* = 7; 1.9%) and pneumonectomy (*n* = 24; 6.6%). The majority of the operations were approached through open thoracotomy (*n* = 173; 47.7%). A comparison of operative characteristics, intraoperative complications and pathological staging in patients with and without PAF is presented in Tables 3 and 4.

The comparison of PAF occurring in total number of patients operated on for malignant non-small-cell lung cancer (NSCLC) or other lung diseases revealed a trend towards more frequent PAF in patients with malignant NSCLC (data not shown).

Table 2: Patient demographics, medical history and preoperative evaluation

	–PAF (*n* = 320) (%)	Uncomplicated/transient PAF (*n* = 28) (%)	*P*-value	Complicated/persistent PAF (*n* = 15) (%)	*P*-value
Patient characteristics					
Age			0.01*		0.40
≤69	205 (64)	11 (39)		8 (53)	
≥70	115 (36)	17 (61)		7 (47)	
Sex					0.31
Male	149 (47)	18	0.18	6 (40)	
Female	171 (53)	10		9 (60)	
Body mass index median	26.2	25.8	0.49	28.2	0.38
Past medical history					
Cardiac risk factors					
Angioplasty/stents/angina	22 (7)	5 (18)	0.24	11 (73)	0.02*
Myocardial infarction	21 (7)	1 (4)	0.46	3 (20)	0.08
Cerebrovascular disease	16 (5)	1 (4)	0.45	0 (0)	0.77
Peripheral vascular disease	24 (8)	0 (0)	0.12	2 (13)	0.33
Valvular disease	15 (5)	3 (11)	0.17	0 (0)	0.50
Other risk factors					
Diabetes mellitus	35 (11)	4 (14)	0.39	3 (20)	0.23
Previous cancer	125 (39)	9 (32)	0.31	5 (33)	0.66
Previous cardiac surgery	18 (6)	2 (7)	0.49	2 (13)	0.22
Previous thoracic surgery	17 (5)	0 (0)	0.23	1 (7)	0.57
Preoperative chemotherapy	7 (2)	0 (0)	0.55	3 (20)	0.01*
Preoperative radiation therapy	3 (1)	0 (0)	0.77	1 (7)	0.17
Lung function tests					
$FEV_{1\ predicted,\ median,\ \%}$	82.0	82.5	0.39	82.0	0.74
$FVC_{predicted,\ median,\ \%}$	89.0	83.5	0.47	91.0	0.84
FEV_1/FVC%	70.0	69.0	0.64	70.0	0.52
$DLCO_{predicted,\ median,\ \%}$	78.0	83.5	0.05*	83.0	0.18
Echocardiographic variables	(*n* = 258)	(*n* = 21)		*n* = 12	
Left systolic dysfunction	13 (5)	3 (14)	0.11	3 (25)	0.03*
Left diastolic dysfunction	23 (9)	4 (19)	0.13	2 (17)	0.31
Left atrial enlargement	12 (5)	1 (5)	0.65	2 (17)	0.12
Left ventricular hypertrophy	6 (2)	2 (10)	0.12	0 (0)	0.76
Pulmonary hypertension	11 (4)	1 (5)	0.62	0 (0)	0.60
Atrial septal defect	3 (1)	1 (5)	0.27	1 (8)	0.17
Valvular pathology	23 (9)	1 (5)	0.44	4 (33)	0.02*
Diagnosis			0.52		0.92
Benign	12 (8)	1 (4)		0 (0)	
Malignant NSCLC	244 (76)	23 (82)		12 (80)	
Other malignant	64 (20)	4 (14)		3 (20)	

% DLCO: diffusing capacity of the lung for carbon monoxide; % FEV1: forced expiratory volume in 1 s; % FVC: forced vital capacity; % PAF: postoperative atrial fibrillation; % NSCLC: non-small-cell lung cancer.

Table 3: Operative characteristics, intraoperative complications, pathological staging and hospital LOS

	–PAF (*n* = 320) (%)	+PAF (*n* = 43) (%)	*P*-value
Approach			<0.05
Thoracoscopy	167 (52)	9 (21)	
Thoracotomy	143 (45)	30 (70)	
Converted	10 (3)	4 (9)	
Procedure performed			
Sublobar resection	89 (28)	4 (9)	<0.05
Lobectomy	213 (67)	30 (70)	0.41
Right upper lobectomy	80 (38)	8 (27)	0.25
Right middle lobectomy	16 (8)	0 (0)	0.12
Right lower lobectomy	32 (15)	7 (23)	0.18
Left upper lobectomy	54 (25)	10 (33)	0.35
Left lower lobectomy	31 (15)	5 (17)	0.76
Bilobectomy/extended lobectomy	7 (2)	0 (0)	0.33
Pneumonectomy	15 (5)	9 (21)	<0.05
Left	11 (73)	4 (44)	0.16
Right	4 (27)	5 (56)	0.16
Unresectable	2 (1)	0 (0)	0.60
Intraoperative complications	18 (6)	7 (16)	0.02
Bleeding	7 (2)	4 (9)	0.01*
Hypotension	3 (1)	2 (5)	0.05*
Hypoxaemia	2 (1)	0 (0)	0.60
Open/close	4 (1)	0 (0)	0.46
AJCC 7th edition 2009 stage	*n* = 239	*n* = 35	0.01
IA/IB	151 (63)	16 (46)	0.05
IIA/IIB	56 (23)	11 (31)	0.30
IIIA/IIIB	28 (12)	4 (11)	0.96
IV	4 (2)	4 (11)	<0.05
Hospital LOS, mean, days	6.9	10.5	0.04

% PAF: postoperative atrial fibrillation; LOS: length of stay.

Similarly, the comparison of PAF occurring in total number of patients operated on for malignant NSCLC or other lung diseases revealed a trend towards more frequent PAF in patients who underwent pneumonectomy.

Univariate analysis to identify risk factors associated with PAF following pulmonary resection

Univariate predictors of PAF are outlined in Table 5. Predictors that are associated with PAF include (odds ratio; 95% confidence interval): age ≥70 (2.3; 1.2–4.3), cardiac history positive for: angioplasty/stents/angina (3.6; 1.5–8.4), left systolic dysfunction (4.2; 1.5–11.9) and atrial septal defect (5.5; 0.9–34.1); surgical approach: open thoracotomy (3.9; 1.8–8.5) and thoracoscopic surgery converted to open thoracotomy (7.4; 1.9–28.3); increasing extent of pulmonary resection: pneumonectomy (13.4; 3.6–48.9); presence of intraoperative complications, such as bleeding (4.6; 1.3–16.3) and hypotension (5.2; 0.8–31.8), and higher American Joint Committee on Cancer (AJCC) 7th edition 2009 stage: IV (7.6; 1.8–31.9).

Risk factors identified by univariate subanalysis for complicated/persistent PAF were similar to those described above. Age ≥70 years, however, did not prove to be a significant risk factor for complicated/persistent PAF upon univariate analysis (data not shown).

Multivariate analysis to identify risk factors associated with PAF following pulmonary resection

Stepwise logistic regression analysis was used to determine independent correlates of PAF using the variables listed in Table 6. Significant predictors of PAF in multivariate analysis included (relative risk; 95% confidence interval): age ≥70 years (2.3; 1.1–5.1), history of angioplasty/stents/angina (4.0; 1.4–11.3), thoracotomy (3.6; 1.4–9.3), conversion to open thoracotomy (16.5; 2.2–124.0) and higher AJCC 7th edition 2009 stage (7.1; 1.0–49.4). The presence of intraoperative complications was not a significant predictor for PAF development upon multivariate analysis. The final model had a *C*-statistic of 0.81, Hosmer–Lemeshow χ^2 value of 2.9 and *P*-value of 0.89 (Table 6).

Multivariate subanalysis of risk factors identified for complicated/persistent PAF were similar to those described above (data not shown). Increasing age, thoracotomy and the presence of intraoperative complications were not significant predictors for complicated/persistent PAF development upon multivariate analysis.

Clinical course, management, and sequelae of PAF

The majority of PAF in this series were uncomplicated/transient in nature and were managed with pharmacological therapy alone (Grade II) (Table 7). Uncomplicated/transient PAF was successfully managed with pharmacological therapy: 96.4% (*n* = 27) cases were treated with a beta-blocking agent such as metoprolol and 21.4% (*n* = 4) were treated with digoxin. Two cases (7.1%) required in-hospital treatment with amiodarone. A total of 19 cases (67.9%) with uncomplicated/transient PAF were discharged from hospital on metoprolol.

Complicated PAF was persistent in 6 cases (40.0%), required cardioversion (Grade III) in 2 cases (13.3%) and vasopressors haemodynamic support with ICU admission (Grade IV) in 5 cases (33.3%). With respect to anticoagulation for complicated/persistent PAF, 7 patients (46.7%) were started on anticoagulants in hospital due to increased risk of stroke following cardiology assessment, and 4 patients (26.7%) continued anticoagulation on discharge from hospital. Two cases (4.7%) displayed persistent PAF on discharge from hospital.

Patients with PAF had increased mean hospital LOS (10.5 days vs 6.9 days; *P* = 0.04) (Table 2). Approximately 11.6% (*n* = 5) of patients with PAF required hospital readmission following initial discharge in comparison with 7.2% (*n* = 23) in the control group (*P* = 0.31); an additional 11.6% (*n* = 5) required admission to the ICU for management; no patients in the control group were admitted to the ICU for management (*P* < 0.05).

Approximately 20% (*n* = 3) of patients with complicated/persistent PAF required hospital readmission following initial discharge; an additional 33.3% (*n* = 5) required admission to the ICU for management (data not shown).

PAF was associated with a greater incidence of additional postoperative complications in comparison with the control group: 1.58 per patient vs 0.48 per patient (*P* < 0.05), respectively (data not shown). There was 1 death (1.5%) reported in the PAF group, and 4 deaths (2.6%) in the control group (*P* = 0.47) (data not shown).

DISCUSSION

Despite ongoing efforts to decrease its occurrence, PAF remains the most common cardiac complication in patients following

Table 4: Operative characteristics, intraoperative complications, pathological staging and hospital LOS

	–PAF (*n* = 320) (%)	Uncomplicated/transient PAF (*n* = 28) (%)	*P*-value	Complicated/persistent PAF (*n* = 15) (%)	*P*-value
Approach			0.02*		<0.05
Thoracoscopy	167 (52)	7 (25)		2 (13)	
Thoracotomy	143 (45)	19 (68)		11 (73)	
Converted	10 (3)	2 (7)		2 (13)	
Procedure performed					
Sublobar resection	89 (28)	3 (11)	0.05	1 (7)	0.07
Lobectomy	213 (67)	20 (40)	0.38	10 (67)	0.99
Right upper lobectomy	80 (38)	6 (30)	0.50	3 (30)	0.63
Right middle lobectomy	16 (8)	0 (0)	0.20	0 (0)	0.37
Right lower lobectomy	32 (15)	6 (30)	0.08	1 (10)	0.66
Left upper lobectomy	54 (25)	5 (25)	0.92	4 (40)	0.30
Left lower lobectomy	31 (15)	3 (15)	0.95	2 (20)	0.63
Bilobectomy/extended lobectomy	7 (2)	0 (0)	0.63	0 (0)	0.33
Pneumonectomy	15 (5)	5 (18)	0.02	4 (27)	0.01
Left	11 (73)	3 (60)	0.32	1 (25)	0.08
Right	4 (27)	2 (40)	0.57	3 (75)	0.08
Unresectable	2 (1)	0 (0)	0.67	0 (0)	0.76
Intraoperative complications	18 (6)	3 (11)	0.23	4 (27)	0.01
Bleeding	7 (2)	1 (4)	0.50	3 (20)	0.01
Hypotension	3 (1)	1 (4)	0.29	1 (7)	0.17
Hypoxaemia	2 (1)	0 (0)	0.85	0 (0)	0.91
Open/close	4 (1)	0 (0)	0.71	0 (0)	0.83
AJCC 7th edition 2009 stage	*n* = 239	*n* = 23	0.28	*n* = 12	<0.05
IA/IB	151 (63)	11 (48)	0.11	5 (42)	0.13
IIA/IIB	56 (23)	9 (39)	0.08	2 (17)	0.59
IIIA/IIIB	28 (12)	2 (9)	0.49	2 (17)	0.61
IV	4 (2)	1 (4)	0.37	3 (25)	<0.05
Hospital LOS, mean, days	6.9	6.7	0.92	17.7	<0.05

% PAF: postoperative atrial fibrillation; LOS: length of stay.

pulmonary resection [7]. The incidence of PAF in our study was 11.8% and was lower in comparison with other published reports [8, 13, 16]. This difference in incidence rates can be explained by the absence of a uniform definition of PAF, the oversight of its sometimes transient nature and the various methodologies used to record its occurrence. In the present study, a standardized definition of PAF was applied requiring electrocardiographic evidence, initiation of pharmacological therapy, and prospective monitoring and documentation of PAF using the TM&M classification system. The TM&M classification system facilitates monitoring, reporting and evaluation of surgical adverse events, and has recently been evaluated for its inter-rater agreement [17].

Several risk factors have been identified for the development of PAF [1, 8–13]. In the current study, age ≥70 years, history of angioplasty/stents/angina, open thoracotomy surgical approach, conversion and higher AJCC 7th edition 2009 stage/extent of surgery were significantly associated with PAF development on multivariate analysis. First, when preoperative risk factors are taken into account, increasing age has been the most consistent predictor of PAF due to age-related structural changes in atrial connective tissue, dilatation and irregular anisotropic conduction [12, 18].

Secondly, higher AJCC 7th edition 2009 stage/increasing extent of pulmonary resection was associated with a significantly higher incidence of PAF compared with lesser resections. It has been suggested that the removal of one lung can increase the cardiac function with ventricular dilatation, increased right-heart pressure and transient pulmonary hypertension [19]. Laterality of pneumonectomy has also been linked with higher incidence of PAF development [16]. Laterality of pneumonectomy was not a significant predictor of PAF development in our data. Of note, however, patients who underwent pneumonectomy represented a small proportion of the total patient population in the current study, limiting the comparison.

Thirdly, in contrast to results of previously reported studies [20], this study revealed a significantly higher incidence of PAF following open thoracotomy compared with the minimally invasive surgical approach; suggesting that incision-related effects may be responsible for the pathogenesis of PAF in high-risk patients.

Fourthly, the presence, extent and severity of coronary artery disease have not been a consistent predictor of PAF in the literature. The current study did, however, identify previous percutaneous transluminal coronary angioplasty and stent placement and pre-existing history of angina to be associated with an increased risk of PAF development.

Significant risk factors for complicated/persistent PAF identified on multivariate analysis were similar to those found in the overall PAF population, including: conversion to open thoracotomy, cardiac history positive for: angina, angioplasty and coronary artery stenting, and higher AJCC 7th edition 2009 stage/extent of pulmonary resection. Increasing age did not prove to be a significant risk factor for complicated/persistent PAF development. Due to the small sample size of the dependent variable, however, these results should be interpreted with caution.

The most common time for onset of PAF is during the first 24 h following major thoracic surgery [21]. Approximately one-quarter (23.3%) of our patients with PAF experienced PAF during the first

Table 5: Results of univariate analysis to identify preoperative and intraoperative risk factors associated with PAF after pulmonary resection

Variable	Odds ratio	95% CI lower	95% CI upper	*P*-value
Demographics				
Age				0.01
≤69	1.0			
≥70	2.3	1.2	4.3	0.01
Medical history				
Angioplasty/stents/angina	3.6	1.5	8.4	0.01
Echocardiographic variables				
Left systolic dysfunction	4.2	1.5	11.9	<0.05
Atrial septal defect	5.5	0.9	34.1	0.04
Surgical approach				<0.05
Thoracoscopy	1.0			
Thoracotomy	3.9	1.8	8.5	<0.05
Converted	7.4	1.9	28.3	0.05
Procedure performed				<0.05
Sublobar resection	1.0			
Lobectomy	3.2	1.1	9.4	0.68
Pneumonectomy	13.4	3.6	48.9	<0.05
Intraoperative complications	3.3	1.3	8.3	0.02
Bleeding	4.6	1.3	16.3	0.01
Hypotension	5.2	0.8	31.8	0.05
AJCC 7th edition 2009 stage				<0.05
IA/IB	1.0			
IIA/IIB	1.5	0.7	3.2	0.30
IIIA/IIIB	1.0	0.3	3.0	0.96
IV	7.6	1.8	31.9	<0.05

Table 6: Results of multivariate analysis to identify preoperative and intraoperative risk factors associated with PAF after pulmonary resection

Variable	Relative risk	95% CI lower	95% CI upper	*P*-value
Demographics				
Age				
≤69	1.0			
≥70	2.3	1.1	5.1	0.04
Medical history				
Angioplasty/stents/angina	4.0	1.4	11.3	0.01
Surgical approach				<0.05
Thoracoscopy	1.0			
Thoracotomy	3.7	1.5	9.3	0.01
Converted	16.5	2.2	124.0	0.01
Intraoperative complications	1.1	0.3	4.6	0.90
AJCC 7th edition 2009 stage				0.12
IA/IB	1.0			
IIA/IIB	2.0	0.8	4.9	0.12
IIIA/IIIB	1.0	0.3	3.7	0.95
IV	7.1	1.0	49.4	0.05

C-statistic, 0.81; Hosmer–Lemeshow goodness of fit test, $P = 0.89$.

Table 7: Atrial fibrillation characteristics

Characteristic	+PAF (*n* = 43) (%)	Uncomplicated/ transient +PAF (*n* = 28) (%)	Complicated/ persistent +PAF (*n* = 15) (%)
Paroxysmal	37 (86.0)	28 (100)	9 (60.0)
Persistent	6 (14.0)	0 (0)	6 (40.0)
Cardioversion	2 (4.7)	0 (0)	2 (13.3)
Vasopressors	5 (11.6)	0 (0)	5 (33.3)
Anticoagulants in hospital	7 (16.3)	0 (0)	7 (46.7)
Metoprolol in hospital	41 (95.3)	27 (96.4)	14 (93.3)
Amiodarone in hospital	8 (18.6)	2 (7.1)	6 (40.0)
Diltiazem in hospital	2 (4.7)	0 (0)	2 (13.3)
Digoxin in hospital	19 (44.2)	6 (21.4)	13 (86.7)
Anticoagulants on discharge	4 (9.3)	0 (0)	4 (26.7)
Metoprolol on discharge	32 (74.4)	19 (67.9)	13 (86.7)
Amiodarone on discharge	2 (4.7)	0 (0)	2 (13.3)
Diltiazem on discharge	0 (0)	0 (0)	0 (0)
Digoxin on discharge	10 (23.3)	0 (0)	10 (66.7)
Discharge with PAF	2 (4.7)	0 (0)	2 (13.3)
LOS >5 days	29 (67.4)	16 (57.1)	13 (86.7)

% PAF: postoperative atrial fibrillation; LOS: length of stay.

24 h with a peak incidence on postoperative Day 2. The majority of our patients (37.2%), however, developed PAF after Day 3. These data suggest that extended ECG monitoring should be performed in higher risk patients for timely diagnosis and prevention of additional complications of PAF.

In addition to increased morbidity and mortality, previous studies have found that PAF is associated with increased hospital LOS [1, 4, 10, 13]. Consistent with these findings, the current study found PAF to be associated with prolonged hospital LOS in the majority of patients (67%). We were also able to document the rate of PAF readmission and its significant association with a greater complication rate.

Professional opinions remain at odds whether PAF should be treated with beta-blockers that reduce the adrenergic response or with calcium-channel blockers that decrease the pulmonary hypertensive response [22]. Medications most commonly used to treat PAF in our series included beta-blockers such as metoprolol (95.4%) and digoxin (46.5%). The safety and efficacy of other pharmacological therapies for PAF prophylaxis have also been studied. In high-risk patients, only amiodarone and diltiazem have been shown to provide effective prophylaxis against AF [5–7, 18, 23]. Amiodarone and diltiazem, however, were not commonly used in this study for management of PAF as beta-blockers were found to successfully control the rhythm disturbance in the majority of cases. Moreover, it is not our standard of care to use prophylactic antiarrhythmic treatment.

This study has several limitations. Perioperative imbalances in serum electrolytes have been associated with the development of PAF [24]. Data on perioperative potassium and magnesium levels were not collected in this study, nor were data on volemia, hypoxia, anemia and hypothermia, all of which have been associated with increased sympathetic activity and PAF [24]. Although

our patients were selected from a prospective database, it remained a retrospective review, and is subject to limitations attributed to retrospective studies, including difficulties in controlling bias and confounders and establishing cause and effect relationships. Small sample size of the dependent variable and the use of a single institution may limit the generalizability of our results to other institutions as well.

There were several strengths of this study. First, a frequent postoperative complication after pulmonary resection was explored and our findings are similar to those of previously published studies. Secondly, we believe that the reported incidence of PAF was accurate as routine ECG monitoring was employed in all patients, untreated transient PAF was not included in the analysis, and a standardized and validated definition of PAF was used. Thirdly, while the majority of PAF cases were classified as uncomplicated/transient and were well-controlled with minimal intervention in this study, complicated/persistent PAF accounted for 34.9% of cases warranting further discussion. Preoperative risk stratification may be used (i) to better inform the surgical patient of the risk of PAF development; (ii) for patient selection for whom prophylactic drug therapy might be most safe and beneficial; (iii) to improve standard therapeutic regimens and ultimately (iv) to develop criteria for patient selection for future randomized controlled trials.

In summary, patient- and procedure-related risk factors of PAF development following pulmonary resection were identified. The TM&M classification system further quantified the incidence and severity of disease burden from PAF. Severity stratification and accurate prediction of PAF following pulmonary resection may lead to more aggressive prophylaxis of specific populations that may reduce the incidence of PAF.

Conflict of interest: none declared.

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