Anesthesiology 2002; 96:352–6 

# *Older Age Is the Strongest Predictor of Postoperative Atrial Fibrillation*

*David Amar, M.D.,* Hao Zhang, M.D.,† Denis H. Y. Leung, Ph.D.,‡ Nancy Roistacher, M.D.,§ Alan H. Kadish, M.D.‖*

***Background:*** **Identification of patients vulnerable for atrial fibrillation (AF) after major thoracic surgery will allow targeting those most likely to benefit from prophylactic therapy. The goal of the current study was to evaluate the accuracy of easily available clinical characteristics for the prediction of this complication.**

***Methods:*** **Patients undergoing major elective thoracic surgery were chosen from an ongoing prospective database.**

***Results:*** **Postoperative in-hospital AF occurred in 79 (15%) of 527 patients Using cut-point methodology and logistic regression, the authors identified two preoperative risk factors independently associated with AF: age 60 yr or older ($P = 0.0007$) and heart rate 74 beats/min or greater on preadmission electrocardiogram ($P = 0.005$). The odds of developing AF increased by a factor of 2.5 (95% confidence interval, 1.7–3.4; $P < 0.0001$) between incremental age categories (< 60 yr, 60–69 yr, ≥ 70 yr) and by a factor of 2.3 (95% confidence interval, 1.4–3.8; $P < 0.0007$) between heart rate categories (< 74 beats/min, ≥ 74 beats/min). The combination of age 60 yr or older and preoperative heart rate 74 beats/min or greater predicted AF with a sensitivity of 73% and specificity of 57%. Maximum P-wave duration as measured from standard electrocardiogram did not differentiate patients who did or did not develop AF. Patients who developed AF had a higher incidence of postoperative pneumonia (14 *vs.* 4%; $P = 0.001$), acute respiratory failure (8 *vs.* 1.6%; $P = 0.01$), greater hospital stay (17 ± 17 *vs.* 10 ± 9 days; $P = 0.001$) and 30-day mortality (11 *vs.* 3%; $P = 0.001$) when compared with those who did not develop AF, respectively.**

***Conclusions:*** **Advanced age and preoperative heart rate identify patients at high risk for development of AF after thoracic surgery. Postoperative AF occurs more frequently in patients with greater postoperative morbidity and length of hospitalization.**

POSTOPERATIVE atrial arrhythmias, and atrial fibrillation and flutter (AF) specifically, are seen in 6.1% of elderly patients undergoing noncardiothoracic surgery and in 10–40% of patients after cardiothoracic operations.[1–4] The clinical symptoms, time of AF onset, and natural course of the arrhythmia are identical whether a patient has had cardiac, thoracic, or other surgery.[5] Patients with postoperative AF have an extended hospital stay with accompanying increased costs as well as greater risk of stroke.[1–6] As in AF unrelated to surgery, age 60 yr or older is consistently the only independent preoperative risk factor most strongly associated with postoperative AF.[1–7]

Beyond older age, however, our ability to further identify patients at greatest risk for postoperative AF is limited. Several studies examined whether the preoperative presence of a prolonged P-wave duration, as an indicator of intraatrial conduction delay, may select patients who are likely to develop postoperative AF. P-wave duration was measured from the standard preoperative electrocardiogram in some studies[8–10] or by using a computerized signal-averaging system, which allows recording of low-level cardiac signals, in other studies.[9–14] The latter technique is expensive, requires 20 min to perform, and is not widely available. Furthermore, there is controversy on how a prolonged signal-averaged P-wave duration is defined[12,14] and whether it predicts postoperative AF.[9,10] Ideally, having a risk stratification system based on clinical and routine preoperative tests to identify patients at risk for postoperative AF could limit the number of patients treated with prophylactic antiarrhythmic drugs. This study was designed to develop such a risk stratification system in a large population at risk for postoperative AF.

## Materials and Methods

The data used in this study were obtained from an ongoing prospective database of 527 of 743 patients who had major thoracic surgery beginning in October 1990 to September 1999 at Memorial Sloan-Kettering Cancer Center. After obtaining approval from the institutional review board at Memorial Sloan-Kettering and written informed consent, patients participated in consecutive trials focused on the study of postoperative AF.[1,10,15,16] All patients scheduled for thoracic surgery who met inclusion criteria were approached to enroll in the aforementioned studies subject to the availability of research staff. Excluded from this study were 216 patients receiving drugs such as class I and III antiarrhythmic drugs that may reduce the frequency of AF episodes. All 527 patients were in sinus rhythm. The preoperative heart rate was recorded from the preadmission electrocardiogram. History of smoking, hypertension, coronary artery disease, diabetes mellitus, and preoperative chemotherapy was recorded. Preoperative $\beta$ blockers were continued postoperatively to avoid withdrawal. No pa-

*Associate Professor of Anesthesiology, Weill Medical College of Cornell University. † Research Assistant, Department of Anesthesiology, ‡ Associate Attending Biostatistician, Department of Biostatistics and Epidemiology, § Associate Professor, Department of Medicine, Memorial Sloan-Kettering Cancer Center. ‖ Professor of Medicine, Director of Cardiac Electrophysiology, Northwestern University School of Medicine.

Received from the Departments of Anesthesiology and Critical Care Medicine, Biostatistics and Epidemiology, and Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York; Weill Medical College of Cornell University, New York, New York; and the Division of Cardiology, Northwestern University School of Medicine, Chicago, Illinois. Submitted for publication April 4, 2001. Accepted for publication September 26, 2001. Support was provided solely from institutional and/or departmental sources.

Address correspondence to Dr. Amar: Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, M-304, New York, New York 10021. Address electronic mail to: amard@mskcc.org. 

tient received prophylactic calcium channel blocker therapy to reduce AF risk. Patients who were taking calcium channel blockers for hypertension or coronary artery disease resumed taking these medications on the first postoperative day. The primary end point of the study was the new onset of AF within 30 days after surgery requiring intervention because of symptoms or hemodynamic compromise. AF was defined by an irregularly irregular cardiac rhythm other than sinus confirmed by 12-lead electrocardiogram.

The operations were performed using standard thoracotomy approaches designed to completely remove all neoplastic disease along with an ipsilateral mediastinal lymph node dissection. Intraoperative estimated blood loss was recorded. Postoperative pain relief was provided to all patients by continuous administration of either epidural opioid (usually fentanyl) administration (n = 252) or intravenous opioid (usually morphine) patient-controlled analgesia (n = 275). After an overnight stay in the postanesthesia care unit, patients were transferred to the thoracic surgical floor on the first postoperative day. Major postoperative cardiac or pulmonary complications were recorded throughout the hospital stay. A research nurse monitored patients for cardiac or pulmonary complications as outpatients for 30 days and queried patients about intercurrent hospitalizations or emergency department visits. An investigator reviewed these medical records.

Most patients (512 of 527; 97%) had a 12-lead electrocardiogram performed at our institution before surgery. P-wave duration was measured from simultaneous recording of the 12 standard leads by the MATRIX program software (Marquette Electronics, Inc., Milwaukee, WI). The MATRIX program simultaneously aligns the P-wave onset of all 12 leads. The computer-derived P-wave duration was then visually verified by two investigators, blinded to clinical end points, using the standard electrocardiogram recorded at a paper speed of 50 mm/s, amplification of 20 mm/mV, and filtration of 100 Hz. The longest P-wave duration in any of the 12 standard leads was then used as representative of the maximum P-wave duration. This analysis was performed in all but 15 patients who had their preoperative routine 12-lead electrocardiogram performed elsewhere; of these, two developed AF. The incidence of prolonged intraatrial conduction as measured by a P-wave duration greater than or equal to 120 ms from the standard electrocardiogram was recorded.[8]

Statistical analysis was performed with SAS version 6.12 software (SAS Institute, Inc., Cary, NC). To determine the difference of patient and operative characteristics between patients with and without AF, all variables were examined by univariate analysis (Student *t* test and Fisher exact test). All variables showing a univariate association ($P < 0.2$) with AF occurrence were entered into a stepwise logistic regression model. The final model showed the variables with independent influence on the incidence of AF. Once age and preoperative heart rate were found to be predictors of AF, cut-point analysis was used to find the optimal cutoff of these continuous variables. P values from the cut-point analysis were adjusted by the asymptotic method of Hilsenbeck and Clark.[17] The association between AF and hospital stay was examined by a Cox model with AF as a time-dependent covariate. A $P$ value $< 0.05$ was considered significant. Data are presented as mean ± SD unless otherwise indicated.

**Table 1. Patient Characteristics**

| | Atrial Fibrillation (n = 79) | No Atrial Fibrillation (n = 448) | *P* Value |
|---|---|---|---|
| Preoperative | | | |
| Age, yr | 68 ± 8 | 62 ± 11 | < 0.0001 |
| Weight, kg | 74 ± 15 | 75 ± 16 | 0.83 |
| Male (%) | 56 (71) | 269 (60) | 0.08 |
| Heart rate, bpm | 79 ± 13 | 75 ± 14 | 0.036 |
| P wave duration, ms | 106 ± 12 | 107 ± 12 | 0.49 |
| P wave duration ≥ 120 ms (%) | 17 (22) | 69 (16) | 0.20 |
| Smoking (%) | 49 (62) | 298 (67) | 0.52 |
| Hypertension (%) | 23 (29) | 104 (23) | 0.26 |
| Coronary artery disease (%) | 6 (8) | 29 (6) | 0.71 |
| Diabetes mellitus (%) | 3 (4) | 32 (7) | 0.27 |
| Chemotherapy (%) | 14 (18) | 88 (20) | 0.69 |
| Medication | | | |
| Ace-inhibitors (%) | 6 (8) | 40 (9) | 0.68 |
| Beta-blockers (%) | 8 (10) | 29 (6) | 0.24 |
| Ca-channel blockers (%) | 10 (13) | 47 (10) | 0.57 |
| Pulmonary function* | | | |
| $FEV_1$, % predicted | 76 ± 21 | 82 ± 22 | 0.13 |
| FVC % predicted | 89 ± 21 | 93 ± 20 | 0.27 |
| $FEV_1$/FVC % | 75 ± 17 | 80 ± 17 | 0.049 |
| DCO % predicted | 74 ± 21 | 82 ± 21 | 0.02 |
| Intraoperative | | | 0.14 |
| Lobectomy (%) | 33 (42) | 216 (48) | |
| Pneumonectomy (%) | 19 (22) | 83 (19) | |
| Extrapleural pneumonectomy (%) | 13 (15) | 40 (9) | |
| Esophagectomy (%) | 14 (12) | 109 (17) | |
| Estimated blood loss, L | 0.8 ± 1.1 | 0.6 ± 0.6 | 0.15 |
| Fluid replacement, L | 2.8 ± 3.2 | 2.6 ± 2.1 | 0.75 |
| Postoperative | | | |
| Pneumonia (%) | 11 (14) | 18 (4) | 0.001 |
| Acute respiratory failure (%) | 6 (7) | 7 (1.6) | 0.01 |

* Pulmonary functions studies were done in 431/527 (82%) patients.

FEV = forced expiratory volume; FVC = forced vital capacity; DCO = diffusing capacity of carbon monoxide.

## Results

Patient characteristics and surgical data are presented in table 1. A total of 79 of 527 patients (15%) developed AF within 30 days of surgery. AF occurred at a median of 69 h (94 ± 84 h) after surgery. The frequency of AF episodes by age is shown in figure 1, and that by heart rate is shown in figure 2. Patients with AF were older ($P < 0.0001$), had a greater preoperative heart rate ($P =$

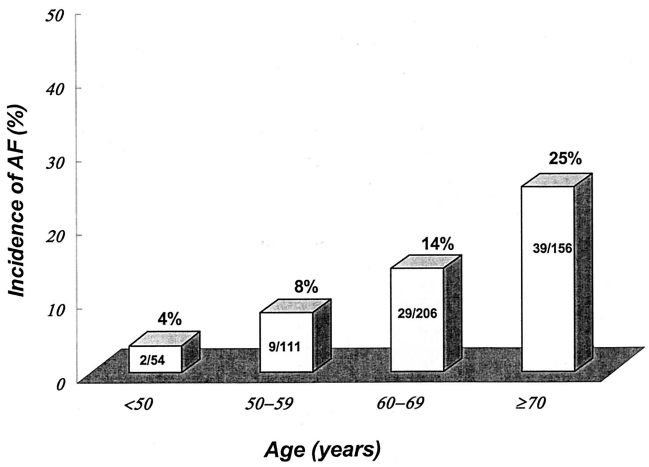


**Fig. 1. Incidence of postoperative atrial fibrillation based on analysis of four age groups.**

0.036), and reduced forced expiratory volume in 1 s/percent forced vital capacity ($P = 0.049$) and percent predicted diffusing capacity of carbon monoxide ($P = 0.02$; table 1). Using cut-point methodology, we found that patients age 60 yr or older ($P = 0.0007$) and preoperative heart rate 74 beats/min or greater ($P = 0.005$) defined subsets of patients with the greatest differences risk for AF. Maximum P-wave duration as measured from the preoperative standard electrocardiogram or a P-wave duration 120 ms or greater did not differentiate patients who did or did not develop AF (table 1). The use of postoperative epidural analgesia did not differ between patients who did or did not develop AF (38 of 79 [48%] *vs.* 210 of 448 [47%], respectively; $P > 0.9$). Postoperative complications such as pneumonia ($P = 0.001$) and acute respiratory failure ($P = 0.01$) occurred more frequently in patients who developed postoperative AF when compared with those who did not develop AF (table 1). In 15 of 79 patients (19%), AF onset was observed before (n = 4), simultaneously (n = 5), and

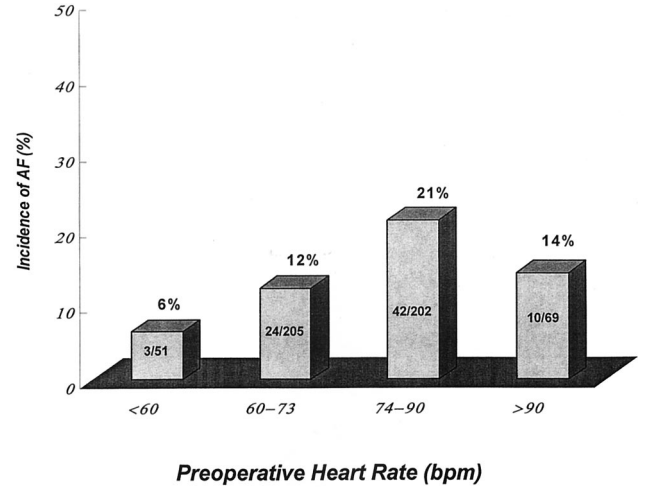


**Fig. 2. Incidence of postoperative atrial fibrillation in relation to preoperative heart rate.**

**Table 2. Multivariate Predictors of Atrial Fibrillation**

| Variable | OR (95% CI) | *P* Value |
|---|---|---|
| Preoperative | | |
| Age* | 2.5 (1.7–3.4) | < 0.0001 |
| Heart rate ≥ 74 beats/min | 2.3 (1.4–3.8) | < 0.0007 |
| Pre- and postoperative | | |
| Age* | 2.5 (1.7–3.4) | < 0.0001 |
| Heart rate ≥ 74 beats/min | 2.1 (1.3–3.5) | 0.0048 |
| Pneumonia and/or acute respiratory failure | 3.2 (1.5–6.7) | 0.0021 |

* Age groups included in this multivariate analysis were < 60 yr, 60–69 yr and ≥ 70 yr. When compared to patients < 60 yr those who were 60–69 yr were more likely to develop atrial fibrillation by a factor of 2.5. Similarly, patients ≥ 70 yr were more likely to develop atrial fibrillation by a factor of 2.5 when compared to patients 60–69 yr.

after (n = 6) the occurrence of pneumonia or acute respiratory failure, respectively. Patients who developed postoperative AF had a prolonged hospital stay (17 ± 17 *vs.* 10 ± 9 days; $P = 0.001$) and greater need for intensive care unit admission for any cause (24 *vs.* 4%; $P < 0.001$) when compared with those who did not develop AF. Although mortality within 30 days of surgery was greater among patients who developed AF (11 *vs.* 3%; $P = 0.001$), no patient appeared to die as a direct result of the arrhythmia.

*Multivariate Analysis*

A stepwise logistic regression analysis using the aforementioned cutoffs and all variables showing a univariate association with AF (table 1) identified age 60 yr or older and heart rate 74 beats/min or greater as the only independent predictors of AF development (table 2). The odds of developing AF increased by a factor of 2.5 (95% confidence interval, 1.7–3.4) between incremental age categories (< 60 yr, 60–69 yr, ≤ 70 yr) and by a factor of 2.3 (95% confidence interval, 1.4–3.8) in patients with a baseline heart rate 74 beats/min or greater. Age 60 yr or older predicted AF with a sensitivity of 87% and specificity of 35%. The combination of age 60 yr or older and heart rate 74 beats/min or greater had a sensitivity of 73% and specificity of 57% to predict AF. The addition of pneumonia or acute respiratory failure to the model did not significantly enhance the ability to predict AF occurrence.

When compared with younger (< 60 yr, n = 165) patients, older (≥ 60 yr, n = 362) patients had a higher incidence of postoperative AF (19 *vs.* 7%; $P < 0.0001$), a greater P-wave duration (109 ± 13 *vs.* 103 ± 11 ms; $P < 0.001$), a greater incidence of P-wave duration 120 ms or greater (23 *vs.* 4%; $P < 0.0001$), a slower heart rate (74 ± 13 *vs.* 81 ± 15 beats/min; $P < 0.0001$), a higher incidence of hypertension (29 *vs.* 14%; $P < 0.0001$) and coronary artery disease (8 *vs.* 3%; $P = 0.016$), and greater preoperative use of β blockers (9 *vs.* 2%; $P = 0.001$) and angiotensin-converting enzyme inhibitors (11 *vs.* 5%; $P = 0.03$), but not calcium channel blockers (12 *vs.* 7%;

$P = 0.1$). However, younger patients were more often treated with preoperative chemotherapy (29 *vs.* 15%; $P < 0.0001$).

## Discussion

The main findings of this study are that the incidence of postoperative AF is significantly higher in patients 60 yr and older, in those who have a greater preoperative heart rate (≥ 74 beats/min), and in those who develop postoperative pneumonia or acute respiratory failure. We found no association between mean maximum P-wave duration and AF occurrence. Advanced age alone was associated with AF occurrence and prolonged P-wave duration. Although patients who developed AF had a lower forced expiratory volume in 1 s/percent forced vital capacity and percent of predicted diffusing capacity of carbon monoxide than those who did not, the values were only mildly (70–80%) abnormal and did not predict AF on multivariate analysis. In-hospital morbidity and need for intensive care were greater among patients who developed postoperative AF, as was the overall length of hospitalization. In 11 of 79 patients (14%) who developed AF, arrhythmia onset occurred either simultaneously or shortly after the diagnosis of pneumonia or acute respiratory failure was made. Although we do not have data to identify with certainty the mechanism for the greater 30-day mortality among patients with AF, we believe that AF is a marker of poor cardiopulmonary reserve in patients who develop significant morbidity after thoracic surgery.[2]

To date, the only consistent clinical predictor of postoperative AF has been older age.[1–7] It is well known that aging causes degenerative changes in atrial anatomy that are accompanied by related changes in atrial physiology such as shorter effective refractoriness, longer SA and AV nodal conduction times, atrial stiffening, and splitting of the atrial excitation waveform caused by the pectinated trabeculae.[18,19] It is possible that unavoidable trauma to sympathovagal fibers originating from the deep or superficial cardiac plexus during surgery may be contributing to preexisting atrial electrical changes caused by aging, predisposing to AF. An association between older age and prolonged P-wave signal-averaged duration was recently demonstrated in a nonsurgical population.[20] In the current study, we also found that older age was associated with a prolonged maximum P-wave duration but observed only a small trend ($P = 0.2$) for patients with postoperative AF to have a prolonged (≥ 120 ms) maximum P-wave duration independent of age. In a study with a relatively small sample size, Hogue *et al.*[21] showed that patients who developed AF after cardiac surgery had a prolonged sinoatrial conduction time in response to surgery, perhaps reflecting some intraoperative damage to conduction fibers. The presence of known triggers such as atrial extrasystoles or sudden shifts in autonomic balance will facilitate AF generation and maintenance.[22] Our finding that a greater preoperative heart rate is independently associated with postoperative AF suggests that a lower vagal tone before surgery may be a contributing trigger of this arrhythmia. Heart rate has been proposed as a general indicator of autonomic balance,[23] and vagal withdrawal is common after thoracic surgery.[24] Taken together, the triad of age-related atrial changes, surgical autonomic denervation, and known arrhythmia triggers are all necessary to cause postoperative AF.

The role of the signal-averaged P-wave duration to predict postoperative AF remains controversial.[9] In our previous experience, a prolonged signal-averaged P-wave duration did not differentiate patients who developed AF after thoracic surgery.[10] Even among investigators who describe its usefulness as a predictor of postoperative AF, some proposed a cutoff point of greater than 140 ms and others one greater than 155 ms to indicate significant intraatrial conduction delay and, hence, increased risk for arrhythmia occurrence.[12,14] The latter group of investigators proposed a model for preoperative risk stratification of AF after coronary artery bypass surgery using advanced age (≥ 60 yr), prolonged signal-averaged P- wave duration (> 155 ms), and male sex as risk factors.[14] Patients with all three risk factors had a 58.8% chance of AF after coronary artery bypass surgery. Unfortunately, even with this model, one could only predict slightly better than 50% of those at high risk for AF. Moreover, the incremental benefit of the signal-averaged P-wave duration over advanced age alone was small. The likely multifactorial etiologies for postoperative AF partially explains why more than 60% of patients do not develop this complication after cardiothoracic surgery.[5] It also explains why our data and other clinical studies examining one mechanism, such as prolonged intraatrial conduction as determined by a prolonged P-wave duration by standard or signal-averaged electrocardiogram as a predictor of postoperative AF, have provided conflicting results.[9–14]

Another area of controversy has been whether to prophylactically treat patients against postoperative AF and whether to use rate control or rhythm control drugs.[25,26] Recent data suggest that once AF has occurred postoperatively, rhythm control drugs offer little advantage to a rate control strategy and intuitively may be associated with less risk of proarrhythmia.[27,28]

### *Limitations*

Because the primary end point of the study was the occurrence of symptomatic AF, it is probable that short-lived episodes of AF were underreported. Our study was designed to evaluate clinically significant dysrhythmias that are the focus of patients' complaints and physicians' therapeutic interventions. Therefore, our conclusions do

not apply to the occurrence of some transient and asymptomatic episodes of AF. In addition, our prospectively collected data was taken from a patient population in an ongoing database of consecutive trials but not necessarily from consecutive patients who had surgery at our institution during the study period. Nevertheless, this population of patients represents one of the more comprehensive and large prospective databases of patients undergoing major noncardiac thoracic surgery focused on the problem of postoperative AF.

In conclusion, postoperative AF is a frequent complication in elderly patients undergoing thoracic surgery that is commonly associated with hemodynamic compromise, a greater need for intensive care, and increased hospital stay. Therefore, in patients aged 60 yr or older with a preoperative heart rate 74 beats/min or greater undergoing major thoracic surgery, extended monitoring is recommended for the early diagnosis and prevention of potential sequelae of AF.

The authors thank James Tsang, M.S. (Database Administrator, Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, NY), for help with data analysis.

## References

1. Polanczyk CA, Goldman L, Marcantonio ER, Orav EJ, Lee TH: Supraventricular arrhythmia in patients having noncardiac surgery: Clinical correlates and effect on length of stay. Ann Intern Med 1998; 129:279–85

2. Amar D, Roistacher N, Burt M, Reinsel RA, Ginsberg RJ, Wilson RS: Clinical and echocardiographic correlates of symptomatic tachydysrhythmias after noncardiac thoracic surgery. Chest 1995; 108:349–54

3. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, Collins JJ, Cohn LH, Burstin HR: Predictors of atrial fibrillation after coronary artery surgery: Current trends and impact on hospital resources. Circulation 1996; 94:390–7

4. Mathew JP, Parks R, Savino JS, Friedman AS, Koch C, Mangano DT, Browner WS, for the Multicenter Study of Perioperative Ischemia Research Group: Atrial fibrillation following coronary artery bypass graft surgery: Predictors, outcomes, and resource utilization. JAMA 1996; 276:300–6

5. Cox JL: A perspective of postoperative atrial fibrillation in cardiac operations. Ann Thorac Surg 1993; 56:405–9

6. Cresswell LL, Schuessler RB, Rosenbloom M, Cox JL: Hazards of postoperative atrial arrhythmias. Ann Thorac Surg 1993; 56:539–49

7. Leitch JW, Thomson D, Baird DK, Harris PJ: The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. J Thoracic Cardiovasc Surg 1990; 100:338–42

8. Buxton AE, Josephson ME: The role of P-wave duration as a predictor of postoperative atrial arrhythmia. Chest 1981; 80:68–73

9. Frost L, Lund B, Pilegaard H, Christiansen EH: Re-evaluation of P-wave duration and morphology as predictors of atrial fibrillation and flutter after coronary artery bypass surgery. Eur Heart J 1996; 17:1065–71

10. Amar D, Roistacher N, Zhang H, Baum MS, Ginsburg I, Steinberg JS: Signal averaged P-wave duration does not predict atrial fibrillation after thoracic surgery. ANESTHESIOLOGY 1999; 91:16–23

11. Stafford PJ, Kolvekar S, Cooper J, Fothergill J, Schlindwein F, deBono DP, Spyt TJ, Garratt CJ: Signal averaged P-wave compared with standard electrocardiography or echocardiography for prediction of atrial fibrillation after coronary bypass grafting. Heart 1997; 77:417–22

12. Steinberg JS, Zelenkofske S, Wong SC, Gelernt M, Sciacca R, Menchavez E: Value of the P-wave signal-averaged ECG for predicting atrial fibrillation after cardiac surgery. Circulation 1993; 88:2618–22

13. Zaman AG, Alamgir F, Richens T, William R, Rothman MT, Mills PG: The role of signal averaged P-wave duration and serum magnesium as a combined predictor of atrial fibrillation after elective coronary artery bypass surgery. Heart 1997; 77:527–31

14. Zaman AG, Archbold RA, Helft G, Paul EA, Curzen NP, Mills PG: Atrial fibrillation after coronary artery bypass surgery: A model for preoperative risk stratification. Circulation 2000; 101:1403–8

15. Amar D, Burt ME, Bains MS, Leung DHY: Symptomatic tachydysrhythmias after esophagectomy: Incidence and outcome measures. Ann Thorac Surg 1996; 61:1506–9

16. Amar D, Roistacher N, Rusch VW, Leung DHY, Ginsburg I, Zhang H, Bains MS, Downey RJ, Korst RJ, Ginsberg RJ: Effects of diltiazem prophylaxis on the incidence and clinical outcome of atrial arrhythmias after thoracic surgery. J Thorac Cardiovasc Surg 2000; 120:790–8

17. Hilsenbeck SG, Clark GM: Practical p-value adjustment for optimally selected cutpoints. Stat Med 1996; 18:103–12

18. Davies MJ, Pomerance A: Pathology of atrial fibrillation in man. Br Heart J 1972; 34:520–5

19. Spach MS, Dolber PC: Relating extracellular potentials and their derivatives to anisotropic propagation at a microscopic level in human cardiac muscle: Evidence for electrical uncoupling of side-to-side fiber connections with increasing age. Circ Res 1986; 58:356–71

20. Babaev AA, Vloka ME, Sadurski R, Steinberg JS: Influence of age on atrial activation as measured by the P-wave signal-averaged electrocardiogram. Am J Cardiol 2000; 86:692–5

21. Hogue CW Jr, Filos KS, Schuessler RB, Sundt TM: Sinus nodal function and risk for atrial fibrillation after coronary artery bypass graft surgery. ANESTHESIOLOGY 2000; 92:1286–92

22. Falk RA: Atrial fibrillation. N Engl J Med 2001; 344:1067–78

23. Casadei B, Cochrane S, Johnston J, Conway J, Sleight P: Pitfalls in the interpretation of spectral analysis of the heart rate variability during exercise. Acta Physiol Scand 1995; 153:125–31

24. Amar D, Zhang H, Leung DHY, Ginsburg I: Effects of left and right pneumonectomy on time- and frequency-domain parameters of heart rate variability. Ann Noninvas Electrocardiol 1999; 4:325–32

25. Kowey PR: Atrial arrhythmias after cardiac surgery: Sisyphus revisited? J Am Coll Cardiol 1999; 34:348–50

26. Guarnieri T, Nolan S, Gottlieb SO, Dudek A, Lowry DR: Intravenous amiodarone for the prevention of atrial fibrillation after open heart surgery: The Amiodarone Reduction in Coronary Heart (ARCH) trial. J Am Coll Cardiol 1999; 34:343–7

27. Lee JK, Klein GJ, Yee R, Krahn AD, Zarnke KB, Simpson CS, Skanes A, Spindler B: Rate control versus conversion strategy in postoperative atrial fibrillation: A prospective, randomized pilot study. Am Heart J 2000; 140:871–7

28. VanderLugt JT, Mattioni T, Denker S, Torchiana D, Ahern T, Wakefield LK, Perry KT, Kowey PR, for the Ibutilide Investigators: Efficacy and safety of ibutilide fumarate for the conversion of atrial arrhythmias after cardiac surgery. Circulation 1999; 100:369–75