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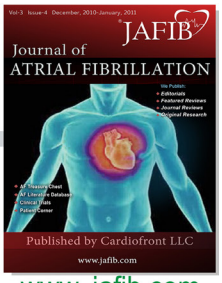

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Atrail Fibrillation after Carfiac Surgery: Benign or Deserving of Prophylaxis

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Abstract

New onset atrial fibrillation (AF) is the commonest complication after cardiac surgery affecting around 30% of coronary artery bypass graft (CABG) patients, up to 50% of valve surgery patients and as many as 60% of those undergoing combined valve and CABG operations. After cardiac transplantation where the native pulmonary veins are electrically separated from the donor heart atria the incidence is only 11%.

Introduction

New onset atrial fibrillation (AF) is the commonest complication after cardiac surgery affecting around 30% of coronary artery bypass graft (CABG) patients, up to 50% of valve surgery patients and as many as 60% of those undergoing combined valve and CABG operations.[1] After cardiac transplantation where the native pulmonary veins are electrically separated from the donor heart atria the incidence is only 11%.[2] Onset is typically within 6 days of operation with 15-20% of episodes spontaneously converting to sinus rhythm within 2 hours. Whilst patients are warned of the possibility of AF the sudden onset of palpitations, breathlessness or chest pain with hypotension, invariably causes anxiety. Re-admission to hospital is common when AF begins after discharge.

Most surgeons regard transient AF as a benign event, easily managed and with little impact on the eventual outcome. Recourse to the literature suggests otherwise. For any individual AF doubles the risk of stroke, myocardial infarction or renal failure and increases overall mortality by 10%.[3] Loss of atrial contraction together with a rapid ventricular rate lowers cardiac output by 20-30% or more in the presence of a significant post operative pericardial effusion. Whilst low risk patients with good left ventricular function tolerate this insult, those with poor left ventricular function, pre-existing heart failure and renal or respiratory impairment may deteriorate rapidly requiring re-admission to the intensive care unit. An intra-aortic balloon pump is less effective with a rapid irregular heart rate and cardioversion may cause ventricular fibrillation or heart block in a hypoxic patient. Even uncomplicated AF adds 3-4 days extra hospital stay with associated costs.[4]

Irrespective of the risks and economic consequences by no means all surgical centres employ routine AF prophylaxis nor do they attempt intra-operative AF ablation for those with the chronic dysrhythmia. As a result some patients are discharged from hospital without restoring sinus rhythm. How important is persistent AF in the long term after cardiac surgery? In 1999 my group showed that both AF and paced rhythm had an important negative effect on left ventricular reverse remodeling after aortic valve replacement5. For patients in sinus rhythm there is a 20-30% fall in left ventricular mass index over the first post operative year

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caused by regression of hypertrophy. In the succeeding 3-5 years there is a further 10% reduction through resolution of interstitial fibrosis. Chronic AF compromises reverse remodeling resulting in persistent left ventricular hypertrophy and a more spherical left ventricular cavity. Does this adverse physiology influence outcome? In a large series of carefully anticoagulated mechanical valve replacement patients we found 92% of those discharged from hospital in sinus rhythm to remain in sinus rhythm at 10-15 years later.[6] Similarly all patients operated whilst in AF remained in AF long term with important adverse consequences for survival. After isolated aortic valve replacement 10 year mortality was 64% for AF patients but only 19% for those in sinus rhythm ($p<0.001$). Following aortic valve replacement with CABG, the equivalent mortality was 83% versus 21% ($p <0.001$) and for aortic with mitral valve replacement 80% versus 18% ($p <0.001$). Whilst these remarkable differences partially reflect more advanced cardiac pathology at the time of operation, the adverse long term effects on ventricular remodeling must also contribute to the poor outcome.

Many different factors are known to contribute to the development of post-operative AF [Table 1]. In this Journal Reddy et al. report a retrospective analysis which identified left atrial volume index (LAVI) as a sensitive marker for new onset AF (44% incidence) after aortic valve replacement with or without CABG. An LAVI of >46cc/m2 predicted post-operative AF with a sensitivity of 92% and specificity of 77%.[7] Also predictive were age, greater severity of aortic stenosis (valve area) and raised left atrial pressure. In a prospective study, Osranek et al. had already shown left atrial volume to correlate with risk of AF after cardiac surgery.[8] Roshanali et al. have shown another echocardiographic parameter, prolonged atrial electro-mechanical interval through left atrial conduction delay to have even greater sensitivity (100%) and specificity (95%) than LAVI.[9] Increased left atrial size is a feature of mitral valve disease but also of chronic aortic valve disease and systemic hypertension where increased left ventricular afterload and increased left atrial wall tension cause left atrial enlargement. Left atrial volume correlates with the severity of aortic stenosis.[10] In long standing aortic stenosis with very poor left ventricular function and raised pulmonary artery pressure, the tricuspid valve becomes regurgitant and the right atrium also enlarges. This is the situation with many patients who present for aortic valve replacement with established AF and a dilated remodeled left ventricle which is unlikely to recover significantly after valve replacement.[5]

It is only worth predicting post operative AF if effective prophylaxis can ensure prevention. This objective has been the subject of research efforts for the last 30 years.[11] Atrial stretch activates extracellular signal-related kinase cascade to stimulate atrial fibrosis.[12] In turn this increases dispersion of the atrial effective refractory period pre-disposing to atrial dysrhythmias. Electrical remodelling occurs such that repolarisation is accelerated whilst the atrial action potential duration and refractory period are shortened.[13] This results in the disruption of the normal de-polarisation/re-polarisation cycle of atrial cells and sets the stage for atrial fibrillation. Even after a short period of AF atrial contractile function is impaired by electrophysiologic remodelling.[14] After about 5 days contractile function is abolished due to a reduction in L-type calcium currents. After restoration of sinus rhythm recovery is delayed.[15] In the meantime mural thrombus may develop predisposing to thrombo-embolic events.

Suggested mechanisms for AF must attempt to explain the delayed onset after surgery. There are two plausible hypotheses. First is the time frame of the systemic inflammatory response after cardiopulmonary bypass or surgery itself in the case of off-pump CABG.[16] Polymorphism in the -1749/C Interleukin 6 (IL-6) promoter gene plays a part in modulating the inflammatory response to surgery and high levels of IL-6 and C-Reactive protein have been linked to development of AF in both surgical and non-surgical patients.[17] Prospective randomised trials of intravenous corticosteroids or anti-inflammatory agents have reported a significant reduction in post operative AF.[1] Secondly, atrial distention may occur during mobilisation of interstitial fluid accumulated during cardiopulmonary bypass. Stretch activated ion channels in atrial myocardium can promote AF and would provide the link between atrial size and AF in the 2-6 day time frame.[18] Translocation of fluid from extra-vascular to vascular compartments may reduce serum potassium and magnesium levels, thus providing the setting for dysrhythmia. Magnesium is a co-factor of NA-K adenosine triphos-

Table 1 Risk factors for atrial fibrillation after cardiac surgery

Pre-operative:	**Advanced age** **Left atrial enlargement** **Previous AF** **Renal failure** **Male gender** **Hypertension/LV hypertrophy** **Congestive heart failure** **Chronic obstructive pulmonary disease** **Obesity (BSA) and metabolic syndrome** **Right coronary artery disease** **Withdrawal of beta-blocker or ACE-I**
Intra-operative:	Bicaval cannulation Pulmonary vein venting Aortic cross clamp time Cardiopulmonary bypass time Systemic hypothermia Type of operation
Post-operative:	Systemic inflammatory response Red cell transfusion Respiratory compromise (hypoxia) Fluid overload/electrolyte imbalance Renal impairment

phatase which regulates the myocardial transmembrane sodium and potassium gradients. In one randomised study magnesium infusion was found to be superior to Amiodarone for cardioversion to sinus rhythm.[19] Intraoperative venting through the pulmonary veins may act as a trigger for AF.[20]

Straightforward post operative pain and anxiety cause hightened sympathetic tone which may promote the onset of AF. The European Association for Cardiothoracic Surgery guidelines for AF prophylaxis recommend beta blockers for all patients unless contra-indicated by comorbid conditions when Amiodarone is suggested.[21] The American Heart Association recommends pre-operative or early post-operative beta blockers for patients undergoing CABG.[22] Intravenous administration is well tolerated after surgery and superior to oral use because of absorption issues following cardiopulmonary bypass. The non-selective beta-adrenergic receptor blocker Sotalol also blocks the delayed rectifier K+ channel and prolongs the refractory period and QT interval.[23] It has been shown to provide more effective prophylaxis in randomised trials. Amiodarone at low dose (<3,000 mg) used in intravenous and oral combination provides effect prophylaxis for all patients but specifically in high risk CABG patients with poor left ventricular function.[24-25] This last group are particularly at risk for peri-operative stroke. Digoxin does not offer prophylactic benefit.26

When AF occurs every effort should be made to restore sinus rhythm before hospital discharge. Spontaneous correction occurs in many low risk patients particularly in response to management of electrolyte imbalance or hypoxia. Immediate electrical cardioversion is required when AF causes profound hemodynamic compromise in high risk patients. A belief that rate control and anti-coagulation prove satisfactory in the long term must be challenged given the mortality differences for valve replacement patients.[6] After discharge a sinus rhythm AF is unusual in the long term given the physiological benefits of the surgery.

References

1. Kaireviciate D, Aidietis A, Lip GYH. Atrial fibrillation following cardiac surgery: clinical features and preventative strategies. Eur Heart J 2009; 39:410-425.
2. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg 1993; 56:539-549.
3. Almassi GH, Schowalter T, Nicolosi AC, Aggarval A, Moritz TE, Henderson Wg, Tarazi R, Shroyer L, Sethi GK, Grover FL, Hammermeister KE. Atrial fibrillation after cardiac surgery. A major morbid event? Ann Surg 1997; 226:501-513.
4. Auer J, Weber T, Berent R, Ng CK, Lamm G, Eber E. Postoperative atrial fibrillation independently predicts prolongation of hospital stay after cardiac surgery. J Cardiovasc Surg (Torino) 2005; 46:583-588.
5. Jin XY, Pillai R, Westaby S. Medium term determinants of left ventricular mass index after stentless aortic valve replacement. Ann Thorac Surg 1999; 67:411-416.
6. Schulenberg R, Antonitsis P, Stoebel A, Westaby S. Chron ic atrial fibrillation is associated with reduced survival after aortic and double valve replacement. Ann Thorac Surg 2010; 89(3):738-44.
7. Reddy YM, Satpathy R, Shen X et al. Left atrial volume and post operative atrial fibrillation after aortic valve replacement. J Atr Fib 2011.
8. Osranek M, Fatema K, Qaddoura F, Al-Saileek A, barnes ME, Bailey KR, Gersh BJ, Tsang TS, Zehr KJ, Seward JB. Left atrial volume predicts the risk of atrial fibrillation after cardiac surgery: a prospective study. J Am Coll Cardiol 2006; 48(4):779-86.
9. Roshanali F, Mandegar MH, Yousefinia MA, Rayatzadeh H, Alaeddini F, Amouzadeh F. Prediction of atrial fibrillation via atrial electromechanical interval after coronary artery bypass grafting. Circulation 2007; 116:2012-2017.
10. Dalsgaard M, Egstrup K, Wachtell K, Gerdts E, Cramariuc D, Kjaergaard J, Hassager C. Left atrial volume in patients with asymptomatic aortic valve stenosis (the Simvastatin and Exetimibe

in Aortic Stenosis study). Am J Cardiol 2008; 101(7):1030-4.
11. Kailasam R, Palin CA, Hogue CW. Atrial fibrillation after cardiac surgery: An evidence-based approach to prevention. Semin Cardiothorac Vasc Anesth 2005; 9:77-85.
12. Goette A, Staack T, Röcken C, Arndt M, Geller JC, Huth C, Ansorge S, Klein HU, Lendeckel U. Increased expression of extracellular signal-regulated kinase and angiotensin-converting enzyme in human atria during atrial fibrillation. J Am Coll Cardiol 2000; 35(6):1669-77.
13. Allessie MA, Boyden PA, Camm AJ et al. Pathophysiology and prevention of atrial fibrillation. Circulation 2001; 103:769-777.
14. Wijffels MC, Kirchhof CJ, Dorland R et al. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. Circulation 1995; 92:1954-1968.
15. Schotten U, Duytschaever M, Ausma J et al. Electrical and contractile remodelling during the first days of atrial fibrillation go hand in hand. Circulation 2003; 107:1433-1439.
16. Palin CA, Kailasam R, Hogue CW. Atrial fibrillation after cardiac surgery: pathophysiology and treatment. Semin Cardiothorac Vasc Anesth 2004; 8:175-183.
17. Gaudino M, Andreotti F, Zamparelli R et al. The -174G/C interleukin-6 polymorphism influences postoperative interleukin-6 levels and postoperative atrial fibrillation. Is atrial fibrillation an inflammatory complication? Circulation 2003; 108:195-199.
18. Franz MR, Cima R, Wang D et al. Electrophysiological effects of myocardial stretch and mechanical determinants of stretch-activated arrhythmias. Circulation 1992; 86:968-978.
19. Moran JL, Gallagher J, Peake SL et al. Parental magnesium sulphate versus Amiodarone in the terapy of atrial tachyarrhythmias: A prospective, randomised study. Crit Care Med 1995; 23:1816-1824.
20. Mathew JP, Fontes ML, Tudor IC, et al: A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA 2004; 291:1720-1729.
21. Dunning J, Treasure T, Versteegh M, Nashef SAM, on behalf of the EACTS Audit Guidelines Committee. Guidelines for the prevention and management of de novo atrial fibrillation after cardiac and thoracic surgery. Eur J Cardiothorac Surg 2006; 30:852-872.
22. Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, Gott JP, Herrmann HC, Marlow RA, Nugent WC, O'Connor GT, Orszulak TA, Rieselbach RE, Winters WL, Yusuf S, Gibbons RJ, Alpert JS, Eagle KA, Garson A Jr, Gregoratos G, Russel RO, Smith SC Jr. Acc/AHA guidelines for coronary artery bypass graft surgery: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee to revise the 1991 guidelines for coronary artery bypass graft surgery). J Am Coll Cardiol 1999; 34:1262-1347.
23. Patel A, Dunning J. Is soltalol more effective than standard beta-blockers for prophylaxis of atrial fibrillation during cardiac surgery? Interact Cardiovasc Thorac Surg 2005; 4:147-150.
24. White CM, Caron MF, Kalus JS, Rose H, Song J, Reddy P, Gallagher R, Kluger J. Intravenous plus oral Amiodarone, atrial septal pacing, or both strategies to prevent post-cardiothoracic surgery atrial fibrillation: the Atrial Fibrillation Supression Trial II (AFIST II). Circulation 2003;108(Suppl 11):11-200-11-206.
25. Budeus M, Hennersdorf M, Perings S, Röhlen S, Schnitzler S, Felix O, Reimert K, Feindt P, Gams E, Lehmann N, Wieneke H, Sack S, Erbel R, Perings C. Amiodarone prophylaxis for atrial fibrillation of high-risk patients after coronary artery bypass grafting: a prospective, double-blinded, placebo-controlled, randomized study. Eur Heart J 2006; 27:1584-1591.
26. Kowey PR, Taylor JE, Rials SJ, Marinchak RA. Meta-analysis of the effectiveness of prophylactic drug therapy in preventing supraventricular arrhythmia early after coronary artery bypass grafting. Am J Cardiol 1992; 69:963-965.
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