Atrial fibrillation after coronary bypass surgery – pathophysiology, resource utilisation and management strategies

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Abstract

Background

With an incidence rate of 30–50%, atrial fibrillation (AF) after bypass surgery continues to be one of the most common complications. The possibilities of haemodynamic instability and thromboembolism necessitate the initiation of antiarrhythmic and anticoagulant therapy. Despite early initiation of therapy, AF can increase post-bypass morbidity and mortality. It can also prolong intensive care unit and hospital stay and further increase resource utilisation. In this article we review the pathophysiology, risk factors, effect on resource utilisation, current prophylactic and therapeutic strategies, and risk-benefit assessment of anticoagulant therapy in post-bypass AF.

Methods

This is a review of the medical literature on post-bypass AF from January 1980 to March 2003. Relevant older references were also reviewed. Clinical and research studies on the mechanisms, pathophysiology, risk factors, complications, resource utilisation, prophylaxis and management were collected from the Medline, Embase, Cinhal and Sigle databases and reviewed.

Conclusion

AF significantly increases complications and resource utilisation after bypass surgery. Prophylactic therapy could significantly reduce the incidence of AF. In AF lasting more than 48 hours, anticoagulant or antiplatelet therapy based on individual risk assessment is recommended.

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Introduction

Though complication rates following cardiopulmonary bypass surgery have dropped significantly with modern perioperative care, post-bypass dysrhythmias, and atrial fibrillation (AF) in particular, continue to be one of the most common complications. With an incidence rate of 30–50% AF can result in haemodynamic instability, thromboembolic events, prolonged intensive care unit (ICU) and hospital stay, need for anticoagulation, antiarrhythmic therapy, and increased resource utilisation.

Materials and methods

This article consists of a review of the medical literature on post-bypass AF from January 1980 to March 2003. Relevant older references from studies were also reviewed. Clinical and research studies on the mechanisms, pathophysiology, risk factors, complications, resource utilisation, prophylaxis and management of post-bypass AF were collected from the Medline, Embase, Cinhal and Sigle databases and reviewed.

Pathophysiology and risk factors

Atrial contraction contributes 20–30% of the cardiac output. During episodes of AF there is loss of organised atrial contraction, and a rapid irregular ventricular rhythm occurs. The net result is a poorly emptying atrium with potential for thrombus formation in the atrial appendages, and a smaller ventricular end-diastolic volume leading to a low cardiac output state. Heart failure and thromboembolic complications resulting from AF are potential pitfalls during post-operative recovery. When a patient has had two or more episodes, AF is termed recurrent. Once terminated, recurrent AF is designated paroxysmal; when sustained for more than seven days, it is termed persistent; and when pharmacotherapy and cardioversion have failed, it is called permanent AF.

The precise mechanism of post-bypass AF is incompletely

Table 1. Significant risk factors identified by major studies on post-bypass atrial fibrillation

	Cresswell *et al.*[7]	Alamassi *et al.*[18]	Matthew *et al.*[21]	Aranki *et al.*[19]	Ducceschi *et al.*[26]	Zaman *et al.*[27]	Aytemir *et al.*[28]	Weber *et al.*[24]	Fuller *et al.*[22]	Hashimoto *et al.*[23]	Passman *et al.*[25]
Number of patients	3,983	3,855	2,417	570	150	105	53	214	1,666	800	152
Study type	RS	PS	PS	PS	PS	PS	PS	PS	PS	RS	RS
Demographic											
Age > 65 years	0.001	0.001	0.01	0.002	0.001	0.001		0.07	0.001	0.001	
Male sex	0.05		0.01	0.01					0.05		
Co-morbid conditions											
Hypertension		0.026		0.03							
Pre-op AF			0.01		0.007					0.0001	
COAD	0.001	0.001									
CCF			0.02								
Drug withdrawal											
Withdrawal of digoxin	0.001	0.001									
Withdrawal of beta blockers			0.01								
Withdrawal of ACE-inhibitors						0.02					
Investigation findings											
Right coronary disease					0.001		0.003				
Atrial enlargement					0.004		0.0001				
Impaired LV function								0.007			
Prolonged P-wave duration						0.04	0.001	0.0001			0.02
Operation technique/factors											
Pulmonary vein venting		0.0001				0.01					
Bicaval cannulation		0.0001				0.03					
Cross-clamp time											
Post-operative factors											
Post-op inotropes		0.0001									
Post-op atrial pacing						0.05					
Post-op IABP				0.03							
Ventilation > 24 hours				0.003							
Low serum magnesium						0.001					

Key: PS = prospective study; RS = retrospective study; ACE = angiotensin converting enzyme; ECG = electrocardiogram; IABP = intra-aortic balloon pump; COAD = chronic obstructive airways disease; CCF = congestive cardiac failure; LV = left ventricle
Note. Only p values after multivariate logistic regression analysis are included in the table

understood, and is still being investigated. In the predominantly elderly group of patients who undergo coronary bypass surgery, age-related structural changes such as atrial dilatation, hypertrophy, fibrosis and senile amyloidosis occur to varying degrees of severity in the atrium. This already heterogeneous myocardium, on being subjected to operative trauma and subsequent post-operative inflammation and oedema, becomes a tissue mosaic of differing refractory periods and conduction velocities susceptible to aberrant electrical activity, conduction and re-entry – the 'anisotropic' atrium.

Recent studies have shown that reversible electrical remodelling of the atrium, characterised by a shortening of the effective refractory period, occurs early during AF. The proposed mechanism is a reduction in inward calcium and outward potassium current densities due to a reduction in L-type calcium channels. This atrial electrical remodelling contributes to the maintenance and vulnerability to recurrent AF.[1-3]

Theory of multiple wavelets[4,5]

An anisotropic atrium fractionates a sinus or ectopic impulse into numerous daughter wavelets. Each wavelet traverses the atrium independently, depending on the refractory state of the adjoining myocardium. Multiple re-entry circuits are thus established, depending on the refractory period, conduction velocity and myocardial mass of different parts of the atria. The 'dispersion of refractoriness',[6,7] due to the heterogeneous nature of the susceptible atrium, is central to the initiation and perpetuation of AF.

Theory of unifocal/multifocal impulse formation and re-entry[8-10]

AF results from single or multiple, rapidly discharging, ectopic foci propagating in different directions and in turn giving rise to multiple re-entry circuits. The majority of the ectopic impulses are thought to originate in the pulmonary veins. Ectopic foci

also occur in the right atrium, and infrequently in the superior vena cava or coronary sinus. This mechanism seems to be more important in paroxysmal AF than in persistent AF.

Mapping studies have revealed three patterns of AF:[11] type I involves a single wave front propagating across the right atrium, type II involves one or two wave fronts, and type III is characterised by multiple wavelets criss-crossing the atrium.

In patients with an anisotropic atrium, AF may be triggered by post-operative pericarditis, autonomic imbalance, withdrawal of beta blockers, fluctuating electrolytes and blood gases. Two thirds of the post-bypass AF occurs on the second or third day: this correlates with the development of post-operative inflammatory pericarditis and the inflammatory infiltration of the myocardium[12] that increase the anisotropic nature of the atrium. The post-operative autonomic imbalance is believed to sensitise the myocardium to arrhythmogenic insults.[13-17] The electrophysiological characteristics of atrial cells, action potential duration, refractoriness and conduction speed are all modulated in opposing ways by vagal and sympathetic influences. High vagal tone favours macro re-entry, while increase in sympathetic tone favours abnormal automaticity and triggered activity. Fluctuations in autonomic tone, with a primary increase in adrenergic drive followed by a marked shift towards vagal predominance, have been noted just before the onset of AF in some patients.[13-17]

Independent predictors for post-bypass AF include age over 65 years,[6,7,12,17-25] pre-operative AF,[18,20,26] male sex[11,16,18,19] and post-operative withdrawal of beta blockers.[18] The risk of post-bypass AF increases by 20% for every 10-year increment in age above 65 years. The persistence of established aberrant pathways in chronic AF[21,23,26] leads to a recurrence of AF after surgery. Variations in ion channel expression, the effect of androgens on sympathetic tone and differences in the myocardial fibre orientation are the possible causes that predispose males to an increased incidence of post-coronary artery bypass grafting (CABG) atrial arrhythmias. Chronic beta blockade increases the sensitivity of the myocardium to sympathetic influence; withdrawal of beta blockers in the presence of high post-operative sympathetic tone can result in ectopic activity, triggering AF.[21] Other predictors identified include prolonged P-wave duration on signal-averaged echocardiography (SAECG),[24,25,27,28] especially in combination with poor left ventricular function,[21] right coronary artery disease[25,26] and atrial dilatation.[26,28]

The atrial wall is a highly trabeculated structure, and many of the trabeculae are discontinuous with the rest of the endocardial surface. Bicaval cannulation[18,27] and right superior pulmonary vein venting,[18,27] by producing new areas of discordance in an already anisotropic atrial myocardium, further increase the risk of AF after bypass surgery. The importance of cross-clamp time as a predictor has been debated, with some studies[13,15] failing to identify any relationship between the two, and others[19,21] demonstrating an increase in the incidence of AF with increasing cross-clamp time. In the series of Matthew and colleagues, the incidence of AF increased by 2.7% per hour increase in cross-clamp time.[21]

Due to the coronary anatomy (the blood supply to the atrium is relatively poor), instilled cardioplegia is mainly directed towards the ventricles and the atrium is less well protected. Atrial recovery from cardioplegic arrest occurs before ventricular recovery, and the gradually recovering atrial metabolic rate in the absence of perfusion, and with inadequate hypothermia, can result in ischaemic injury. This also partly explains the higher incidence of AF following combined valve and graft operations,[18,20] where the ischaemic period is longer. Myocardial dysfunction requiring supportive measures could be due to a compromised myocardium pre-operatively, poor myocardial preservation technique, intraoperative ischaemia or infarction, or could be a manifestation of myocardial stunning. The need for cardiovascular support with inotropes,[18] intra-aortic balloon pump (IABP),[19] atrial pacing,[27] or weaning off the bypass machine have all been associated with a high incidence of AF.

Post-operatively, hypokalaemia and hypomagnesaemia causing increased myocardial excitability and conduction abnormalities, hypertension causing increased afterload and myocardial strain, hypotension leading to myocardial ischaemia, fluid overload causing myocardial stretch injury, sensitive myocardium subjected to hypoxia and acid-base fluctuations, prolonged ventilation causing right heart strain, pyrexia and sepsis all increase the susceptibility of the atrium to AF.

Table 1 shows significant risk factors in post-bypass AF, as identified by major studies.

Effect of post-bypass AF on outcome and resource utilisation

AF after bypass surgery increases the morbidity, mortality and hospital resource utilisation.[6,18,19,21,23,30-33] Studies by Alamassi *et al.*[18] and Aranki *et al.*[19] revealed a two- to three-fold increase in perioperative myocardial infarction (MI), congestive cardiac failure (CCF) and stroke, intensive therapy unit (ITU) readmissions, hospital mortality and 60-day mortality. The incidence of post-operative stroke is three times higher and of reintubation is four times higher in patients going into AF after bypass surgery. The mean ITU and hospital stay were 3.6 and 10 days in the AF group compared to two and seven days in the non-AF group.

To reduce the risk of atrial thrombus formation and embolisation, anticoagulation is advised in cases of AF not responding to treatment within 24–48 hours. However, anticoagulation in itself has the inherent risk of bleeding complications and further readmission for optimisation of anticoagulation. In addition, direct current cardioversion after pharmacological loading of antiarrhythmics requires pre-procedure trans-oesophageal echocardiography, anaesthesia and utilisation of theatre resources. Matthew *et al.*,[21] Veledar *et al.*,[31] Hravnak *et al.*,[33] Kowey *et al.*[30] and Aranki *et al.*[19] estimated the overall increase in the cost of treating post-bypass AF at $1,616, $5,413, $6,356, $7,867 and $10,055 respectively per patient.

Table 2 shows outcome and resource utilisation post-bypass in patients with AF, compared to those seen in patients in sinus rhythm.

Table 2. Outcome and resource utilisation post-bypass, atrial fibrillation versus sinus rhythm

	Cresswell *et al.*[7]	Alamassi *et al.*[18]	Matthew *et al.*[21]	Aranki *et al.*[19]	Hashimoto *et al.*[23]	Hravnak *et al.*[33]	Kowey *et al.*[30]	Veledar *et al.*[31]	Kim *et al.*[32]
Post-operative MI		7.4% *vs.* 3.36%		5% *vs.* 3%					
Post-operative CCF		4.5% *vs.* 1.4%	10% *vs.* 7%	5% *vs.* 2%					
Post-operative stroke		5.26% *vs.* 2.44%	7% *vs.* 2%	3.7% *vs.* 1%					
Duration of ICU stay in days	2.3 days more than patients in SR	3.6 *vs.* 2 days	3 *vs.* 2.5 days						
Readmission to ICU		13% *vs.* 3.9%	11% *vs.* 8%	9% *vs.* 2%					
Reintubation rate		10.59% *vs.* 2.95%		12% *vs.* 3%					
Total length of stay in days	3.4 days more than patients in SR	10 *vs.* 7 days	12.8 *vs.* 10.2 days	15.3 *vs.* 9.4 days	9.8+/-5.7 *vs.* 8.3+/-3.5 days		10 *vs.* 7 days		1.5 days more than patients in SR
Hospital mortality			5.95% *vs.* 2.95%						
60-day mortality			9.36% *vs.* 4.17%						
Additional cost per patient in AF			$1,616	$10,055		$6,356	$7,867	$5,413	

Key: AF = atrial fibrillation; SR = sinus rhythm; CCF = congestive cardiac failure; MI = myocardial infarction; ICU = intensive care unit

Table 3. Results of meta-analysis of prophylactic measures against atrial fibrillation post-CABG

Prophylaxis *vs.* placebo or no treatment	Total number of studies	Total number of patients	Prophylactic efficacy: odds ratio (95% confidence interval)	Length of stay: odds ratio (95% confidence interval)	Adverse reaction: odds ratio (95% confidence interval)
Digoxin	24	507	0.97 (0.62–1.49)	Not assessed	Not assessed
Verapamil	24	432	0.91 (0.57–1.46)	Not assessed	Not assessed
Beta blockers	27	3,840	0.39 (0.28–0.52)	Not assessed	Not assessed
Sotalol	8	1,294	0.35 (0.26–0.49)	-0.13 (-0.33–0.07)	9.7% (0.086–19.3)
Amiodarone	9	1,384	0.48 (0.37–0.61)	-0.18 (-0.38–0.02)	1.95% (-0.48–4.38)
Right atrial pacing	10	581	0.68 (0.39–1.19)	Not assessed	Not assessed
Left atrial pacing	10	148	0.57 (0.28–1.16)	Not assessed	Not assessed
Biatrial pacing	10	744	0.46 (0.30–0.71)	-1.54 (-2.85–0.24)	Not assessed

Key: CABG = coronary artery bypass grafting

Prophylactic therapy

Given the high incidence and resource utilisation due to post-bypass AF, prophylactic therapy is strongly recommended in high-risk cases. Beta blockers, sotalol, amiodarone and biatrial pacing significantly reduce the incidence of post-bypass AF.[12,34-45] Meta-analysis of studies using sotalol versus placebo and amiodarone versus placebo have revealed no significant difference in the effect on length of hospitalisation or adverse drug reaction between the two.[42] Studies using digoxin alone, verapamil, diltiazem, procainamide, propafenone or flecainide have failed to reduce the incidence of AF significantly.[42] A limited number of studies have shown magnesium sulphate[46,47] and triiodothyronine (in patients with impaired LV function)[48] to reduce the episodes and severity of post-bypass AF.

Table 3 shows the results of a meta-analysis of prophylactic measures against AF post-CABG.

Therapeutic strategies

The key issues in deciding the therapeutic approach are haemodynamic stability, symptoms (palpitations, fatigue, dyspnoea, light-headedness, generally feeling unwell), ventricular rate, left ventricular function and thromboembolic risk. Therapy is focused on maintaining haemodynamic stability, achieving ventricular rate control and early conversion to sinus rhythm without affecting ventricular function (most antiarrhythmics have a negative inotropic effect).[40,49-51]

Digoxin, because of its mild inotropic effect, is useful in

Table 4. Risk assessment for anticoagulation in atrial fibrillation post-CABG

High stroke risk

Clinical criteria
- ≥ 75 years
- Recurrent paroxysmal atrial fibrillation
- Previous stroke/TIA
- Congestive cardiac failure
- Hypertension
- Diabetes mellitus
- Thyrotoxicosis
- Previous thromboembolism
- Prosthetic valves
- Rheumatic valve disease

Echocardiographic criteria
- Left atrial enlargement
- Left ventricular dyskinesia/poor function
- Cardiomyopathy/valvular heart disease/intracardiac thrombus

Contraindications to anticoagulation

Major
- History of GI/GU/intracranial haemorrhage
- Coagulation disorders
- Complications after previous anticoagulation therapy
- Recurrent falls
- Unsupervised dementia
- Unexplained anaemia
- Excessive alcohol intake
- Doubtful drug/clinic compliance

Minor
- BP > 180/110 mmHg
- Other illnesses needing regular steroid/NSAID usage

Key: TIA = transient ischaemic attack; GI = gastrointestinal; GU = genitourinary; NSAID = non-steroidal anti-inflammatory drug

achieving rapid ventricular rate control in the unstable patient. If the patient is haemodynamically stable, the choice of drug should be based on the ventricular function. Amiodarone (a class III antiarrhythmic) is the most widely used drug for rate control and conversion to sinus rhythm, in patients with good or poor ventricular function. In cases of good ventricular function, sotalol, a beta blocker with class III effect, can be used for conversion to sinus rhythm. Class Ia (e.g. quinidine, procainamide) and class Ic (e.g. propafenone) drugs and another class III drug, ibutilide, have been used in cases that do not respond to amiodarone or sotalol. However, the risk of torsades de pointes with quinidine and ibutilide has precluded their routine use in post-bypass AF.

Immediate DC (direct current) cardioversion is indicated in patients who are haemodynamically unstable or symptomatic. In patients who are stable, the choice is either DC cardioversion after 24–48 hours of pharmacotherapy, or elective out-patient cardioversion if they fail to cardiovert after 3–4 weeks of anticoagulation and antiarrhythmia therapy.[49-51]

In persistent AF, the aims of treatment are to optimise ventricular rate control and anticoagulation. In the absence of contraindications, and with good ventricular function, beta blockers are the drug of choice for rate control. However, digoxin should be used as a first-line drug in cases of poor ventricular function. Specific data to guide us on anticoagulation in post-bypass AF are lacking. Suggested guidelines are based on studies of risk-benefit evaluation of anticoagulation or antiplatelet therapy on non-surgical patients. Depending on the stroke risk, oral anticoagulation aimed at achieving an international normalised ratio (INR) between 2–3 or antiplatelet agents should be considered for AF lasting for more than 48 hours.[49-51] Anticoagulation should be considered in patients of 75 years or older and patients with risk factors for stroke, while antiplatelet agents may prove useful in younger patients, subgroups in whom anticoagulation is contraindicated, and in patients with low risk for stroke.[52-55]

Table 4 gives a guide to risk assessment for anticoagulation AF post-CABG.

Key messages

- Independent predictors for post-bypass AF include age over 65 years, male gender, pre-operative AF and withdrawal of beta blocker
- AF after bypass surgery increases the morbidity and hospital resource utilisation
- Prophylactic possibilities in high-risk cases include beta blockers, sotalol, amiodarone and biatrial pacing

Conclusion

AF, the most common complication after bypass surgery, increases post-operative morbidity and resource utilisation. The predictors of AF include a variety of risk factors, many of which are unmodifiable and some of which are inherent to the surgery. Increasing age, male sex, pre-operative AF, perioperative beta blocker withdrawal, prolonged P-wave duration on signal-averaged ECG, superior pulmonary vein venting and bicaval cannulation are some of the significant predictors of post-bypass AF.

Identifying patients at risk and modifying post-operative outcome by prophylactic therapy or the early initiation of treatment for conversion to sinus rhythm or rate control, reduces patient morbidity and resource utilisation, with significant cost savings.

The choice of prophylaxis includes beta blockers, sotalol, amiodarone and biatrial pacing. The aim of pharmacotherapy and cardioversion is to restore haemodynamic stability and to achieve early conversion to sinus rhythm and ventricular rate control without compromising ventricular function. In AF lasting more than 48 hours despite therapy, oral anticoagulation or antiplatelet agents, based on judicious individual risk-benefit assessment, is recommended.

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