Atrial fibrillation occurs in 5-40% patients after coronary artery bypass graft surgery. Atrial fibrillation increases mortality and morbidity in the post-operative period. We sought to conduct a comprehensive review of literature focusing on pathophysiology, risk factors, prevention and treatment of post coronary artery bypass graft atrial fibrillation.

**Key words:** AF, AF post CABG, atrial fibrillation post open heart, CABG

**PATHOPHYSIOLOGICAL MECHANISMS**

The precise mechanism of post-CABG AF is still being investigated. The following pathophysiological factors play an important role: atrial factors (age-related structural changes such as atrial dilatation, hypertrophy, fibrosis and senile amyloidosis), postoperative inflammation (making the myocardium a tissue mosaic of differing refractory periods and conduction velocities susceptible to aberrant electrical activity, conduction and re-entry - the ‘anisotropic’ atrium,[11,12] pericarditis,[13] electrical remodeling (shortening of the effective refractory period),[14-16] autonomic imbalance (over activation of the sympathetic nervous system in response to stress, increased vagal tone,[17-20] atrial incision, perioperative ischemia,[21] alterations in atrial oxidative...
stress increased expression of the gap-junctional protein connexin 40, inflammatory mediators and leucocytosis after extracorporeal circulation. Some theories proposed for AF in general are ‘Theory of Multiple Wavelets’ and ‘Theory of Unifocal/ Multifocal Impulse Formation and Re-entry’. However, it is unclear if these theories hold good for post-CABG AF.

**RISK FACTORS**

Many risk factors have been investigated in the past; however, we will focus on those found consistently in multivariate analyses in major trials.

**Preoperative**

Advanced age; male gender; genetic predisposition assessed by the interleukin-6 promoter gene variant; history of CHF or AF; chronic obstructive pulmonary disease, chronic renal insufficiency, diabetes mellitus, rheumatic heart disease, previous cardiac surgery, metabolic syndrome, obesity; absence or withdrawal of beta-blocker or ACE inhibitor treatment, high pre-op Brain Natriuretic Peptide, severe proximal right coronary artery stenosis, mitral valve disease, increased left atrial size, decreased left ventricular ejection fraction, left atrial volume index ≥ 75 mL/m², preoperative increase in P wave duration on surface (>116 ms) or on signal averaged (>140 ms) EKG and blood transfusion before surgery.

Age is consistently the independent factor most strongly associated with POAF. For every decade there is a 75% increase in the odds of developing POAF and based on age alone, anyone older than 70 years is considered to be at high risk for developing AF. Age-associated changes in the atria such as dilatation, muscle atrophy, and decreased conduction may explain the strong association. Concomitant valvular heart disease is also associated with postoperative atrial tachyarrhythmias. It is unclear whether this is because of the additional complexity of the required surgical procedure or the valvular disease itself. Neither the degree of ischemia nor the extent of coronary artery disease is a consistent predictor of postoperative atrial tachyarrhythmias.

When beta-blocker was continued or started postoperatively, POAF risk was significantly reduced by 51–68%. The use of adrenergic drugs is an independent risk factor for AF post-CABG.

**Intraoperative**

Prolonged mechanical ventilation, atrial ischemia, hypokalemia, hypomagnesemia. There is conflicting data whether increased aortic cross-clamp and cardiopulmonary bypass time increase POAF.

**Postoperative**

A study of the Atrial Fibrillation Suppression Trial II (AFIST) showed that patients who developed postoperative AF received 1.3 L more fluid than those without postoperative AF over 5 postoperative days. Net fluid balance on postoperative day 2 was an independent predictor of post-CTS AF among amiodarone-naive patients (OR 6.4; 95% CI 1.4 to 29.1) which is noteworthy since most post-CTS AF occurs on this day.

Characteristics that have not been identified consistently as independent risk factors include hypertension, left ventricular dysfunction, angina pectoris, and noncardiac illnesses.

**PREVENTION**

**Beta-blocker**

Since the autonomic nervous system plays a major role in the pathophysiology of post-CABG AF, beta blockers have been widely studied in its prevention. In one study beta-blockers had the greatest magnitude of effect across 28 trials (4,074 patients) with an odds ratio (OR) of 0.35, 95% CI 0.26-0.49. In another meta-analysis of 24 trials limited to patients with ejection fraction >30% undergoing CABG, prophylactic beta-blockers were associated with protection against supraventricular tachycardia with an OR of 0.28, 95%CI 0.21-0.36.

**Sotalol**

In a meta-analysis of 14 trials including 2,583 patients that compared beta-blocker or placebo, sotalol was found to be more effective in reducing POAF than beta-blocker or placebo. Therefore, it seems to offer significant additional protection over standard beta-blockers.

**Amiodarone**

In a randomized trial including 124 patients undergoing a complex cardiac surgery, amiodarone administered orally at least 1 week preoperatively significantly reduced the incidence of POAF, from 53% in the placebo group to 25% in the treated group (P = 0.003). In the Amiodarone Reduction in Coronary Heart (ARCH) trial, postoperative intravenous administration of amiodarone was associated with a lower incidence of POAF (35%) compared with the placebo arm (47%) (P = 0.01).

**Atrial pacing**

Prophylactic pacing has been investigated in a number of trials. Meta-analyses of these clinical trials have consistently...
shown that single- or dual-site atrial pacing significantly reduces the risk of new-onset POAF.[59,60] In a randomized trial, biatrial overdrive pacing in patients undergoing CAGB was shown to be more effective in preventing POAF than single-site atrial pacing (12.5% vs. 36%).[61] However, this trial included a small number of patients and had significant limitations. Major adverse effect is potential proarrhythmic effect.

**Calcium channel blockers**

A recent meta-analysis showed that calcium-channel blockers reduce supra-ventricular tachyarrhythmia risk (OR 0.62; 95% CI 0.41-0.93).[62] However, in some studies, the perioperative use of these drugs was associated with an increased incidence of AV block and low output syndrome, due to their negative chronotropic and inotropic effect. In patients undergoing CAGB, diltiazem reduced post-CAGB AF incidence by 50–74% compared with placebo.[63]

**Magnesium**

A meta-analysis concluded that magnesium administration was effective for reducing POAF with a similar efficacy to common antiarrhythmic drugs.[64] Meta-analyses have shown magnesium to reduce POAF risk by 23–36%,[64,65] However, the studies included in these analyses included a small number of patients, and the design varied among the different studies, thus limiting the interpretation of the results.

Statins- The prospective randomized study Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery (ARMYDA-3) has demonstrated that treatment with Atorvastatin 40 mg/day started 7 days before elective cardiac surgery under cardiopulmonary bypass and continued in the postoperative period significantly reduces the incidence of POAF by 61%,[66] Statins have been shown to reduce inflammation in patients with coronary artery disease; and thus the theoretical benefit to decrease postoperative inflammation as a potential cause of POAF. When the theory examined was found to be useful in the prevention of POAF.

**N-3 polyunsaturated fatty acids**

In a randomized controlled trial of 160 patients undergoing elective CAGB, PUFAs supplementation significantly reduced the incidence of POAF by 65% versus control, an effect similar to that obtained with beta-blockers, sotalol, or amiodarone (OR 0.35; 95% CI 0.16-0.76). [67] The modulation of cardiac connexin was probably the contributing mechanism to the antiarrhythmic effects of fish oil supplementation. Furthermore, in the general population, consumption of fish, inducing high plasma PUFA concentration, has been associated with a lower incidence of AF in a 12-year follow-up study.[68]

**Anti-inflammatory agents**

In a randomised controlled trial the authors concluded that nonsteroidal anti-inflammatory medications are effective in significantly reducing the incidence of AF after CAGB. However, the risk versus benefit ratio of such prophylactic strategy remains uncertain, given their nephrotoxicity.[69] In another multicenter trial hydrocortisone proved beneficial in reducing the incidence of POAF in the first 84 hours.[70]

**TREATMENT**

Before initiating the treatment of AF, underlying medical comorbidities like electrolyte imbalance, hypoxia, COPD should be treated.[71] AF has been associated with physiological stress, drugs, pulmonary embolism, chronic lung disease, hyperthyroidism, caffeine, infectious processes, and various metabolic disturbances. AF has also been linked with obesity, and this phenomenon seems to be mediated by left atrial dilation.

The treatment of post-CAGB AF includes use of drugs and electrical cardioversion. Drugs can target to achieve rate control or rhythm control [Table 1]. According to a study

| Table 1: Dosage, advantages, and side effects of drugs used for treatment of POAF |
|-------------------------|-------------------------------|-----------------|-------------------|
| **Drugs** | **Adult dosage** | **Advantages** | **Side effects** |
| Esmolol | 500 μg/kg over 1 min then 0.05–0.2 mg/kg/min | Short-acting effect and short duration | Might worsen congestive heart failure; can cause bronchospasm, hypotension; AVB |
| Atenolol | 1–5 mg IV over 5 min repeat after 10 min then 50–100 mg b.i.d. PO | Rapid onset of rate control (IV) | |
| Metoprolol | 1–5 mg IV over 2 min then 50–100 mg b.i.d. PO | Rapid onset of rate control (IV) | Nausea, AVB moderate effect in POAF |
| Digoxin | 0.25–1.0 mg IV then 0.125–0.5 mg/day PO | Can be used in heart failure | Might worsen congestive heart failure, AVB |
| Verapamil | 2.5–10 mg IV over 2 min then 80–120 mg/day b.i.d. PO | Short-acting effect | |
| Amiodarone | 2.5–5 mg/kg IV over 20 min then 15 mg/kg or 1.2 g over 24 h | Can be used in patients with severe LV dysfunction | Thyroid and hepatic dysfunction, torsades de pointes, pulmonary fibrosis, photosensitivity, bradycardia |
| Procainamide | 10–15 mg/kg IV up to 50 mg/min | Therapeutic levels quickly achieved | Hypotension, fever, accumulates in renal failure, can worsen heart failure; requires drug level monitoring |
| Ibutilide | 1 mg IV over 10 min, can repeat after 10 min if no effect | Easy to use | Torsades de pointes more frequent than amiodarone and procainamide |

IV = Intravenous; LV = Left ventricular; AVB = Atroventricular block; b.i.d. = Twice daily; PO = By mouth
AF score that can predict POAF is in order, and further research is required as to how to interpret these criteria and use them to utilize the available prevention and treatment modalities.

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CONCLUSIONS AND RECOMMENDATIONS

POAF is a burden to our health care system and increases ICU stay. We do have multiple modalities which range from the conservative medical approach to invasive biatrial pacing, so it would be worthwhile to be able to predict the occurrence of POAF. Many recent studies have tried to find predictors of POAF.[80, 81] Developing a practical and simple

Thromboembolism prevention: AF after CABG poses an increased risk of cerebrovascular accidents in the form of stroke;[75,76] however, using anticoagulants in the post-operative period can lead to increased risk of bleeding and cardiac tamponade.[77] The risks might far outweigh the benefits especially in patients with advanced age, previous history of bleeding and uncontrolled hypertension.[61] Anticoagulants can be used for prolonged and/or frequent episodes of AF and is recommended by the American College of Chest Physicians in patients with history of stroke and transient ischemic attacks (30 days after the return of sinus rhythm).[78] Anticoagulation should be considered in patients 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.[79]
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