Potential Use of Statins in Reducing Atrial Fibrillation After Off-Pump Coronary Artery Bypass Grafting Surgery

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Atrial fibrillation (AF) is a common complication after cardiac surgery and has important implications.¹ Postoperative AF leads to prolonged hospital stay and increases hospitalization costs.² Although the pathophysiology is not fully understood, the causes are likely multifactorial, including atrial myocyte alterations or atrial myocarditis, operative trauma, enhanced sympathetic nervous system activity, ischemic injury to the atria, atrial distension from fluid overload, chemical stimulation, and pericarditis.³ Above all, several clinical studies suggest that inflammation might play a pivotal role in the pathogenesis of postoperative AF.⁴

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In this regard, it has been generally accepted that cardiopulmonary bypass (CPB) inclusive of cardioplegic arrest is associated with the development of postoperative AF,⁵ which may be related to inadequate protection during CPB, inflammatory response after CPB itself, need for atrial cannulation, electrolyte and volume shifts during CPB, myocardial damage from cross-clamping of the aorta, and adverse effects of cardioplegia.

In the surgical treatment of coronary artery disease, the off-pump coronary artery bypass grafting (CABG) procedure has recently emerged as an alternative to conventional on-pump CABG. Considering that off-pump CABG is associated with a significant reduction in the systemic inflammatory response and in the release of markers of myocardial necrosis compared with conventional on-pump CABG,^{6,7} myocardial revascularization of the beating heart is expected to be associated with a reduction in the incidence of postoperative AF. However, the evidence from both observational and randomized studies is still conflicting.⁵ Moreover, results from a previous study show that the incidence of postoperative AF after CABG is still high, even when a beating heart technique is used.⁸

Although there has been a great deal of interest in preventing postoperative AF pharmacologically, including amiodarone, β -blocker agents, and sotalol, several patients still experience AF despite prophylactic therapy. Furthermore, patients with deteriorated left ventricular function, chronic obstructive pulmonary disease, and renal failure are frequently excluded from the use of drugs as prophylaxis for AF. These patients are the ones most affected by AF and would benefit from other preventive treatment.

Apart from antiarrhythmic drugs, lipid-lowering agents

have been suggested to have a beneficial effect in patients prone to developing AF.^{9,10} Beyond their lipid-lowering actions, statins have been shown to have pleiotropic effects, including improvement of endothelial dysfunction, increased nitric oxide bioavailability, antioxidant properties, inhibition of inflammatory responses, stabilization of atherosclerotic plaques, and antithrombotic properties.¹¹ To date, the ability of statins to reduce the occurrence of postoperative AF in patients undergoing cardiac surgery has been evaluated in several observational and prospective randomized studies.^{11,12} The reviewed data suggest that statins may possess antiarrhythmic properties that reduce the propensity for AF,^{9,10} although the underlying mechanisms for the beneficial effects of statins on postoperative AF are not completely understood.

In this issue of the Journal, Kinoshita et al describe the ability of preoperative statin therapy to reduce the incidence of AF after off-pump CABG in Japanese patients.¹³ Although this was not a randomized study, propensity score-matched analysis between the statin group and the no-statin group was performed to eliminate selection and treatment bias as much as possible. In their study, 195 patients in the statin group received any commercially available statin, including atorvastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin, and fluvastatin. The rate of postoperative AF was significantly lower in the statin group than in the no-statin group (14.4% vs 24.6%, $P=0.01$), which was highly comparable with a previous report on atorvastatin alone.¹² With regard to the mechanism of the beneficial effect of statins, the postoperative level of C-reactive protein, as a marker of systemic inflammation, tended to be lower in the statin group than in the no-statin group. Although previous studies have demonstrated the preventive effect of statins, particularly atorvastatin in contrast to pravastatin,¹⁴ an overall beneficial effect was found in Kinoshita et al's study performed with every variety of statins. Additionally, their study is the first to reveal the beneficial effects of statins on postoperative AF in Japanese patients. AF has significant genetic heterogeneity and racial variation in its prevalence, and the effects of statins have ethnic differences, so evaluation of the effects of statins on postoperative AF in Japanese patients undergoing off-pump CABG is important.^{15,16}

In the light of the importance of postoperative AF to patient outcome, there has been a great deal of interest in preventing this complication pharmacologically. Multiple mechanisms, however, may be responsible for the protective influence of preoperative statin therapy on the development

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of postoperative AF.

In conclusion, statin therapy is a low-cost, low-risk preventive AF strategy, and all cardiac surgery patients may benefit from such a prophylactic regimen. Further investigations are required to establish statin administration as standard preoperative management for cardiac surgery, including off-pump CABG.

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