Commentary

Rhythm is a dancer: the immediate management of postoperative atrial fibrillation following cardiac surgery

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Rhythm is something you either have or don't have, but when you have it, you have it all over——Elvis Presley

Post-operative atrial fibrillation (PoAF) complicates 30–50% of all adult cardiac surgery, with higher rates observed after valve and more complex surgery (1). Other identified patient risk factors include a past history of atrial fibrillation (AF) (2), older age (3), male gender (4) and hypertension (2). Occurrence of PoAF following cardiac surgery is associated with longer and more expensive hospital stay and increased frequency of adverse outcomes including increased in-hospital and long-term risk of stroke (5,6). In addition, patients with PoAF immediately following heart surgery, especially when present for more than 48 hours, have worse survival over the following years, even when accounting for age and comorbidity burden (5,7).

Many strategies to *prevent* PoAF have been studied, including preoperative administration of beta-blockers (8). calcium-channel blockers (9). magnesium (10,11) and amiodarone (12), amongst a plethora of others (13). However, these strategies are generally of low efficacy, fail to be effective outside of clinical trials (11), or are associated with a high incidence of drug side effects (12). Thus, no single optimal prevention regimen for PoAF has been derived (13).

There is some basic consensus on the optimal *treatment* strategy for patients who develop poAF in the postoperative period. There is agreement that control of ventricular rate is of symptomatic and morbidity benefit, based on several perioperative trials (14,15), and that beta-adrenergic and Ca-channel blockade are useful measures for ventricular rate control (16). The most contentious debate in the management of PoAF is whether control of ventricular heart rate is a sufficient end-point, or whether there is additional morbidity and mortality advantage to conversion to sinus rhythm. Thus far, guidance has come from the management of ambulatory AF, where several randomized trials have shown rate-control to be non-inferior to rhythm control strategy (17,18). The largest of those, the AFFIRM trial, revealed that in patients with ambulatory AF, focusing on restoring sinus rhythm offered no survival benefit but a higher rate of side effects, compared to a management approach focusing on controlling the heart rate (18). These studies have influenced current guidelines for management of AF following heart surgery, recommending beta-blockers as a first line treatment (19). However, the population experiencing PoAF after cardiac surgery has unique characteristics separating them from non-surgical patients with AF. These include hemodynamic instability in the postoperative period, and increased susceptibility to adverse hemodynamic side effects of rate and rhythm-restoring medications. Furthermore, delays in conversion to sinus rhythm might render a post-surgical patient susceptible to thromboembolic even when recent or ongoing postsurgical bleeding might limit anticoagulation options.

Thus the Cardiothoracic Surgical Trials Network (CTSN) performed a randomized AF-treatment trial, comparing a rate control strategy to a rhythm-control strategy in patients following cardiac surgery (20). The study included 2,109 patients undergoing elective coronary bypass or valve surgery without prior history of AF. As expected, 33% of these patients had PoAF following their surgery and were randomized to either rate-control treatment regimen targeting a resting heart rate of less than 100, or rhythm-control treatment regimen that included administration of amiodarone and cardioversion within 48 hours

for persistent PoAF with or without a rate-controlling regimen. Anticoagulation for 60 days was recommended for PoAF with duration of more than 48 hours. Both groups were followed for 60 days from randomization, with the total number of hospital days during follow-up as the primary outcome. Secondary outcomes included duration of hospitalization from randomization until therapeutic goals of PoAF management were met, readmission rate, time until stable rhythm without sustained PoAF, placement of permanent pacemaker and rates of death and adverse effects. The patients were also followed for timing of the onset and resolution of PoAF, and their rhythm at 30 and 60 day scheduled follow-ups

There was no difference in the primary outcome or other measurements of hospitalization between the two treatment groups. Although patients in the rhythm-control group achieved freedom from PoAF earlier, 92% of patients in the rhythm-control group and 90% in the rate control group were discharged without AF—clinically and statistically equivalent results. At 60 days, 98% of the rhythm-control group had achieved a stable rhythm without AF in the past 30 days, compared to 94% of the rate-control group. Of patients who experienced PoAF, 43% of both groups were discharged on warfarin. There were no differences in mortality or rates of adverse events between the two groups. In brief, rate control was equivalent to rhythm control.

Impressively, there was a high incidence of nonadherence to treatment assignment. Of the rate-control group, 27% of the rate-control group either received amiodarone or cardioversion. The nonadherence in the rate-controlling group was mostly for ineffectiveness, where rate-control could not be achieved with escalating doses of medication in a subset of the patients so rhythm-restoring strategy was applied. Similarly, 24% of the rhythm-control group did not complete the full dose of amiodarone and received rate-controlling medications. The most common reason for nonadherence in the rhythm-controlling group were side effects of amiodarone as judged by the treating clinician.

The authors ought to be complemented on their inclusion of a large number of patients representing the population currently undergoing cardiac surgery. The study should also be praised for a thorough follow up on the natural course of PoAF following cardiac surgery, with a high ratio of patients achieving the absence of PoAF within few days of its first occurrence, but a non-trivial recurrence of PoAF at 30 and 60-day follow-up. As the authors point out, they were underpowered to differentiate the individual rates of serious complications of PoAF between the two study arms but rather used hospitalization days as a surrogate marker of complications related to the arrhythmia or its treatment. Similarly they were only able to monitor for reoccurrence of PoAF after discharge by spot-checks via electrocardiograms at 30 and 60-day follow-up, so they were unable to quantify the overall AF burden in each patient group. It should also be pointed out that a more formal treatment protocol for medical management might have been beneficial to maximize separation for the two treatment arms, although this can be challenging to execute in a multicenter trial.

Based on the study findings, rhythm-control does not seem superior to rate-control strategy in the management of PoAF. Furthermore, the high rate of non-adherence to either protocol, speaks to the complexity in the management of this patient population following surgery. During this period of initial postoperative recovery, patients are especially vulnerable to both the hemodynamic effects of PoAF, and the side effects and toxicity of treatment regimens. Therefore, management of PoAF likely requires a individualized strategy, where the majority of patients can likely be managed with a rate-controlling mechanism, but the subset of patients that fail to respond or a more urgent restoration of sinus rhythm is required can receive rhythm-restoring therapy as well. The future might offer more targeted strategies offering a better prediction of effectiveness and toxicity of various treatment regiments. These could be based on preoperative and perioperative patient characteristics, biomarkers and even prediction of pharmacogenomic responses to therapy. To achieve this goal of personalized treatment of AF, studies such as this need to be powered for sub-group analyses.

Similarly, the study also calls for a prolonged follow-up of patients with PoAF following discharge for recurrence of PoAF and stroke. This might identify a subset of patients that has no benefit from continued treatment or may even suffer from continued drug treatment. Importantly, prolonged and more thorough follow-up might also identify characteristics of patients that suffer from long-term consequences of PoAF and might therefore benefit from a more aggressive treatment regimen, including prolonged anticoagulation. These strategies will hopefully serve to minimize the short-and long-term side effects of PoAF and improve the outcomes of cardiac surgery even further.

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Footnote

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