EDITORIAL COMMENT

Postoperative Atrial Fibrillation and Mortality: Do the Risks Merit Changes in Clinical Practice?

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Atrial fibrillation (AF), the most common sustained cardiac rhythm disturbance, is estimated to afflict more than 2 million people in the U.S. (1). The incidence of AF is highly age dependent, roughly doubling with each successive decade of age in both men and women from 3 and 2 cases, respectively, per 1,000 person-years from ages 55 to 64 years to 38 and 31 cases per 1,000 person-years from ages 85 to 94 (2). The prevalence of AF has increased in recent years; from 1968 to 1989, the prevalence of AF in Framingham Heart Study subjects 65 to 84 years of age rose from 3.2% in men and 2.8% in women to 9.1% and 4.7%, respectively (3). During the last two decades of the 20th century, the number of hospital discharges with a diagnosis of AF increased more than twofold (4). In addition, a recent National Center for Health Statistics death certificate review revealed an increase in deaths with a diagnosis of AF; from 1980 to 1998, the number of decedents with AF tripled (5). It is likely that with the aging of the U.S. population and advances in awareness of the consequences of AF and the widespread use of improved methods of arrhythmia detection, the number of people with a diagnosis of AF will continue to grow (6). In light of these trends, AF has been referred to as an emerging epidemic (7).

Although AF was recognized long ago as a hazard for stroke in patients with rheumatic heart disease, the magnitude of the cardiovascular risk of nonrheumatic AF in the general population was not appreciated until results from the Framingham Heart Study indicate an association of AF with mortality (8). Atrial Fibrillation is now widely recognized as a risk factor for stroke and other thromboembolic complications and for heart failure (HF), leading to a substantial disease burden and medical costs (1). In addition, AF is associated with increased mortality. In the Framingham Heart Study, AF was associated with a 1.5-fold increase in risk for death from all causes in men and 1.9-fold increase in women (10).

Whereas the hazards due to chronic AF are well established, the prognostic implications of AF after cardiac surgery are less certain. AF is common after heart surgery, especially in the elderly. Its reported postoperative incidence in recent studies varies from about 20% to 50% (6). Until recently, the prevailing opinion was that postoperative AF is transient and that its prognosis is mostly benign. That opinion, however, is changing. In a series of nearly 4,000 patients undergoing cardiac surgery, Creswell et al. (11) reported a 31.9% incidence of atrial arrhythmias, the most common being AF. In that series, postoperative AF was associated with increased risk for stroke, prolonged length of hospital stay, and the occurrence of ventricular tachycardia or fibrillation.

In this issue of the Journal, Villareal et al. (12) at the Texas Heart Institute report an association of postoperative AF with increased risk for short-term and long-term adverse outcomes in patients undergoing coronary bypass surgery. In this large case series, drawn from 6,477 patients undergoing a first coronary bypass, the incidence of postoperative AF was 16%. Patients with postoperative AF were sicker than those who did not develop this arrhythmia; risk factors for its occurrence included advanced age, hypertension, congestive HF, a history of previous peripheral vascular or cerebrovascular disease, chronic obstructive lung disease, more diseased coronary arteries, obesity, and the need for an intra-aortic balloon pump. In the short term, patients with AF were at increased risk for stroke and death, and they also had longer and more complicated hospital stays. In the long term, patients with AF were at increased risk for death (relative risk 1.5; 95% confidence interval 1.3 to 1.8). Other predictors of increased mortality risk were advance age, congestive HF, history of previous peripheral vascular or cerebrovascular disease, diabetes, renal insufficiency, the number of diseased coronary arteries, and the use of an intra-aortic balloon pump. Thus, many of the risk factors that predicted the occurrence of postoperative AF also predicted long-term mortality (12). These intertwined threads illustrate the complexity in distinguishing the intrinsic hazards due to postoperative AF from the risks related to its etiologic factors, and they underscore the inherent challenge of establishing an independent contribution of AF to mortality.

In assessing the prognostic importance of transient AF in the postoperative setting, an independent relation is credible if mechanisms for a direct adverse effect can be postulated. Plausible mechanisms for direct harm due to AF are HF and recurrent AF with attendant thromboembolic sequelae. The links between AF and HF are well established. Animal experiments and case reports indicate that AF with rapid ventricular response can predispose to dilated cardiomyop-
therapy or anticoagulation could have reduced mortality in patients with postoperative AF cannot be determined.

RESIDUAL CONFUNDING

Third, we must consider residual confounding as an explanation for the reported 50% higher mortality risk associated with postoperative AF. In the multivariable analyses, numerous risk factors were adjusted for, but the adequacy of the adjustment was limited to the variables entered into the model. Some key determinants of both AF risk and outcome were not entered in the multivariable model. Two examples are the failure to adjust for AF status upon discharge or for the presence and severity of valvular heart disease. Inadequate adjustment for risk factors also may have contributed to residual confounding. Specifically, in the multivariable analyses, age was entered as >65 years versus younger, yet the relationship of age to risk of AF and to mortality is so powerful that the categorical variable used to capture its effect may be insufficient. In addition, as in any cohort study, the analyses can only adjust for measured covariates and not for risk factors that were not measured. In an attempt to address the problem of incomplete accounting for covariates, the authors conducted a subgroup analysis in which AF cases and controls were matched on as many variables as possible. Unfortunately, fewer than 20% of AF cases are represented in this matched-set analysis. The AF subgroup selected for this analysis was not representative of the far-larger AF sample from which it was drawn. The 195 AF patients in the matched analysis differed from the overall AF sample with regard to multiple traits including age (66 vs. 68 years), gender (18% vs. 27% women), and prevalence of previous myocardial infarction (9% vs. 17%), cerebrovascular disease (1% vs. 8%), peripheral vascular disease (12% vs. 28%), and diabetes (3% vs. 11%). Despite attempts to account for confounding, it remains distinctly possible that AF was associated with mortality because it occurs in sicker patients and the contention that postoperative AF is an independent predictor of mortality is incompletely substantiated.

Is the finding of increased mortality in patients with AF sufficient evidence to change current clinical practice? For example, are the results of this study so compelling that we should recommend perioperative antiarrhythmic therapy as a means to prevent postoperative AF and thereby reduce mortality? Or, does this report provide sufficient indication of mechanism of harm that, even if postoperative AF is transient, prolonged anticoagulation is necessary? In considering the answer to these questions, we must be cognizant of the fact that observational data can establish an association between a risk factor and an outcome and determine the magnitude of the associated risk, but they cannot establish causation. In the absence of evidence to support a causal pathway linking AF with mortality, there are insufficient grounds to recommend changes in current clinical practice guidelines. In light of the considerable risk
for morbidity and mortality associated with postoperative AF, widespread adoption of proven prevention strategies is warranted, including prophylactic treatment with beta-blocking agents, unless contraindicated (6). In addition, anticoagulation for patients with persistent or recurrent postoperative AF, as in patients with nonsurgical AF, is indicated. A recent large clinical trial in patients with nonsurgical AF suggested superiority of a strategy of rate control plus anticoagulation to one of rhythm control (17). Compared with rhythm control, the rate control plus anticoagulation strategy resulted in lower mortality in older patients and those with coronary disease. Whether or not the benefits of rate control and anticoagulation extend to coronary artery bypass patients with postoperative AF remains to be determined.

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REFERENCES