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EDITORIAL COMMENT

Atrial Fibrillation Ablation and the ABC-Death Score

Beyond Rhythm Outcomes*

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Catheter ablation of atrial fibrillation (AF) is increasingly being performed worldwide with the advancements in the ablation technology and understanding of the pathophysiology of AF. Catheter ablation has shown high procedural success rates and sinus rhythm maintenance rates, especially for paroxysmal AF. Recently, catheter ablation has been reported to improve not only the rhythm outcomes but also mortality. The CASTLE-AF (Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation) trial showed that catheter ablation reduces all-cause mortality and hospitalizations for heart failure along with reducing the AF burden and improving the left ventricular ejection fraction (LVEF).[1] The CABANA (Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial, which was the largest randomized trial of catheter ablation vs antiarrhythmic drug therapy for AF, showed no significant difference in the primary composite endpoint of death, disabling strokes, serious bleeding, and cardiac arrest.[2] However, a subgroup analysis in a cohort with heart failure, most of whom had a preserved LVEF, showed that ablation reduced the primary composite endpoint.[3] Another subanalysis of the CABANA trial showed that the relative benefit of ablation was greatest for those younger than 65 years, decreased for those age 65 to 75 years, and importantly, may be harmful for those older than 75 years.[4]

Even if ablation reduces the AF burden and subsequent cardiovascular events, it is critically important for clinicians to recognize that some patients will still experience such events after ablation as demonstrated in numerous studies. The number of patients post-AF ablation is increasing in our clinical practice, making it important to stratify the high-risk patients for cardiovascular events who require close follow-up and additional treatment, given the limited health care resources. However, there are few data on risk stratification scores for predicting the risk of death or cardiovascular events after AF ablation.

In this issue of *JACC: Asia*, Wang et al[5] have reported that a preablation biomarker-based ABC-death score could be a better option for discriminating AF patients with a high mortality risk undergoing AF ablation, especially regarding the cardiac mortality risk. The ABC-death score consists of the age, heart failure, and 3 biomarkers including the N-terminal pro-B-type natriuretic peptide, cardiac troponin T measured by high sensitivity assays, and growth differentiation factor (GDF)-15. The score was originally developed by Hijazi et al[6] for predicting the risk of death in anticoagulated patients with nonvalvular AF. In comparison with the original research, Wang et al[5] investigated the utility of the ABC-death score in patients undergoing AF ablation. The investigators enrolled nonvalvular AF patients undergoing catheter ablation between 2013 and 2019 from the Chinese Atrial Fibrillation Registry. The mean age was 59.8 years, and only 4.6% of those had heart failure before ablation. Importantly, approximately 80% of patients discontinued their anticoagulation therapy for at least 1 year after AF ablation. During a median follow-up period of 4.0 years, 119 patients died of all causes, with 49 dying from cardiac causes. Elevated levels of cardiac troponin T measured by high sensitivity

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assays, N-terminal pro-B-type natriuretic peptide, and GDF-15 before AF ablation were independently related to an increased risk of all-cause mortality and cardiac mortality. The incidence rates of all-cause mortality and cardiac mortality stratified by the ABC-death score were 0.43%, 1.62%, and 3.16%/person-year, and 0.12%, 0.86%, and 2.23%/person-year in the low, intermediate, and high-risk groups, respectively.

In the cohort of postablation patients, the majority of whom had discontinued anticoagulation therapy and would have had a reduced AF burden, the ABC score was associated with mortality. That indicates that the score reflected the integrated severity of AF comorbidities such as hypertension, diabetes, coronary artery disease, and heart failure, or the severity of atrial cardiomyopathies associated with the development of AF.[7,8]

Aging is easily assumed to be associated with mortality, partly because of the increased number of comorbidities and development of aging-associated atrial and ventricular cardiomyopathy. A recent atrial biopsy study in patients undergoing AF ablation demonstrated that a decrease in the myocyte nuclear density, a surrogate of the myocardial cell number, is strongly associated with aging.[8] Invasive catheter ablation in elderly patients may worsen their atrial cardiomyopathy and atrial function, which could explain the low or unclear benefit of ablation in the elderly compared with the medical therapy.[4] Heart failure is a progressive disease, and pre-existing heart failure will increase mortality. Some patients often fail to recover their systolic left ventricular function even when maintained in sinus rhythm.[9] There is also no clear evidence that AF ablation improves the left ventricular diastolic function; however, a retrospective study showed that AF ablation reduces heart failure rehospitalizations in patients with heart failure associated with a preserved LVEF.[10]

The troponin level presumably helps discriminate patients with underlying heart diseases, such as severe coronary artery disease, dilated cardiomyopathy, and hypertrophic cardiomyopathy. An elevated troponin level is also associated with cardiac amyloidosis,[11] which has a strong association with the development of AF. Recently, amyloid deposition is also identified in atrial biopsy samples obtained from patients undergoing AF ablation.[8] The B-type natriuretic peptide level may have helped discriminate patients with a volume overload irrespective of the left ventricular systolic function. On the other hand, it is difficult at this time to clearly explain how GDF-15, a marker of inflammation and oxidative stress, is associated with mortality. GDF-15 may be an integrative quantitative indicator of the severity of various comorbidities associated with the mortality risk from AF.[12]

With the advent of aging societies around the world, the number of elderly patients undergoing catheter ablation of AF is expected to increase, and the number of patients with heart failure or many comorbidities will also increase. The ABC-death score is expected to be useful in stratifying patients at a high mortality risk in our clinical practice; however, further clinical studies are warranted to verify its validity. It is now time to consider mortality and cardiovascular outcomes, not just rhythm outcomes.

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