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COMMENTARY

Can we predict success when failure is obscured?

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The CHA_2DS_2-VASc score was derived as a risk stratification tool for thromboembolism in patients with atrial fibrillation (AF), wherein patients with higher scores are predicted to have a greater risk of this severe AF complication. While derivation analysis produced encouraging results, numerous studies have since demonstrated that CHA_2DS_2-VASc alone has, at best, moderate predictive ability for incident cerebrovascular accident in AF patients [1, 2]. Indeed, there are numerous factors that interact with CHA_2DS_2-VASc, including AF burden and renal dysfunction, that provide a more comprehensive indication of thromboembolic risk stratification in AF [3, 4]. Despite these shortcomings, the CHA_2DS_2-VASc score has been incorporated into AF guideline statements and provides clinicians with a simple determinant of who may benefit from systemic anticoagulation [5].

The components of CHA_2DS_2-VASc (congestive heart failure, hypertension, advanced age, diabetes, prior stroke/thromboembolism, vascular disease, sex category) comprise many of the disease-modifying agents prevalent in patients with AF [6–9]. Because of this, it is natural to postulate that the CHA_2DS_2-VASc score may successfully predict other AF-associated outcomes. Indeed, the predictive ability of CHA_2DS_2-VASc has been evaluated for outcomes including mortality [10, 11], heart failure hospitalization [12], and ventricular arrhythmias [13], among others, in those with and without AF.

In this edition of the Journal of Interventional Cardiac Electrophysiology, Rordorf and colleagues attempt to extend to utility of CHA_2DS_2-VASc by assessing its ability to predict recurrent AF after cryoballoon ablation. Authors evaluated 3313 patients included in the 1STOP Clinical Service Project who underwent a first-time cryoballoon ablation for AF. The average duration of time of AF diagnosis prior to ablation was 51.6 months, and 26.3% of the cohort had persistent AF. Post-procedure monitoring included ECGs obtained at regularly scheduled intervals, and in response to symptoms. Only 4.7% of the patients had implantable devices capable of continuous rhythm monitoring. Recurrent AF was defined as any documented AF or atrial tachycardia > 30 s after the 90-day blanking period. By 3 years post-ablation, 72.5% of patients with CHA_2DS_2-VASc 0–1 and 65.9% of the patients with a CHA_2DS_2-VASc > 1 remained free from AF. Results demonstrate that patients with a CHA_2DS_2-VASc score > 1 had a greater rate of recurrent AF than patients with a score 0–1.

The authors should be congratulated on this multicenter collaborative effort, which adds to the data on factors that impact recurrent AF after ablation. In light of recent work that emphasizes the potential benefit of early rhythm control strategies, it is important to identify a vulnerable cohort of patients who are at high risk of recurrent AF after ablation [14, 15].

Despite the statistical significance between groups, readers of this manuscript should be aware that the absolute difference in the annual rate of recurrent AF between groups was low (CHA_2DS_2-VASc 0–1: 18.8% vs CHA_2DS_2-VASc > 1: 22.4%). As a result, the implications of these findings are unclear. Specifically, readers are left to determine whether a group at higher risk for recurrent AF would benefit from additional ablation targets to address arrhythmogenic substrate or non-pulmonary vein triggers, more comprehensive monitoring for recurrent AF, or longer duration of antiarrhythmic drug therapy following ablation. As there are no strong data to suggest that addition of additional lesion sets or aggressive management of

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asymptomatic AF following ablation improves outcomes, the clinical significance of these findings remains uncertain.

Furthermore, the results of the Rordorf's study are of particular interest when compared to those of Lohrmann and colleagues, also recently published in the Journal of Interventional Cardiac Electrophysiology [16]. Lohrmann investigated a similar clinical question as Rordorf, though with different follow-up methods. Specifically, Lohrmann's cohort consisted of 632 patients with a cardiac implantable electronic device (CIED) capable of continuous AF monitoring who underwent their first AF ablation following device implantation. Recurrent AF was defined as any period > 1 h of AF following the 90-day blanking period. Unsurprisingly, freedom from AF was much lower in Lohrmann's cohort of patients with continuous monitoring, ranging from 21.8 to 40.3% in CHA_2DS_2-VASc subgroups. While patients had a significant reduction in AF burden (~ 99%) regardless of CHA_2DS_2-VASc score, only patients with a CHA_2DS_2-VASc > 4 had a higher rate of recurrent AF after ablation [16]. Importantly, CHA_2DS_2-VASc had poor predictive ability for recurrent AF, with a c statistic of 0.53.

While differences in outcomes may be attributed to patient characteristics, the primary distinction between the two studies are the methods employed to detect recurrent AF. The juxtaposition of studies which answer a similar question using different forms AF monitoring invites the question of which should be used in clinical and research settings.

Society guidelines recommend that any AF > 30 s following ablation qualify as "recurrence," however, contemporary studies tell a more nuanced story [17]. Indeed, recent work indicates that lower AF burden is associated with improved AF outcomes [14, 15, 18]. In this setting, brief periods of recurrence may not be clinically relevant if the overall burden of AF is significantly reduced. Furthermore, if recurrent AF is defined by arbitrary thresholds—such as 30 s, 6 m, 1 h, or 23 h—the time frame chosen will be just as relevant to rates of recurrence as ablation or patient characteristics. To exemplify this, among a cohort of patients with CIEDs who underwent ablation with a median reduction in AF burden of > 99%, rates of recurrent AF ranged from 28.8 to 72.1% when "recurrence" was defined as > 6 m or > 23 h, respectively [19]. Therefore, one may question whether a patient with 6 m, or 23 h, has "failed" ablation if their overall burden has been reduced almost entirely [20].

Ultimately, the future definition of "recurrence" after AF ablation should be one that demonstrates impact on patient outcomes [21]. Indeed, determining a threshold of recurrent AF—either by time or burden—that is associated with symptoms or increased risk of stroke, would provide the most clinically relevant maker of "success" after ablation. However, the thresholds for these endpoints likely involve a combination of patient and arrhythmia characteristics that have yet to be derived. As the electrophysiology community continues to investigate AF ablation success, determining the most clinically relevant outcome measures will be of utmost importance. For now, studies such as Rordorf's provide important data that can hopefully be helpful to inform this future metric.

Data availability Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Declarations

Conflict of interest Rod S. Passman serves on advisory boards for Medtronic, Abbott, and Janssen, receives research support from Abbott, American Heart Association, National Institute of Health, and royalties from UpToDate; Northwestern University receives fellowship support from Medtronic.

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