Response to Letter Regarding Article, “Ablation of Persistent Atrial Fibrillation Targeting Low-Voltage Areas With Selective Activation Characteristics”

We thank Bartoletti et al for their comments on our novel approach for ablation of persistent atrial fibrillation (AF) targeting selective atrial low-voltage sites. Here we provide answers to their comments:

1. Left atrial substrate characterization using bipolar voltage mapping has been mostly performed in sinus rhythm (SR). However, only a single study compared high-density voltage maps of the left atrium during SR in patients (1) without history of AF versus (2) patients with paroxysmal AF versus (3) persistent AF; versus long-persistent AF.2 In this study, the authors report in patients without history of AF; bipolar voltage values during SR that exceed >2.5 mV at all left atrial sites.2 In contrast, the bipolar voltages during SR were significantly reduced in patients with history of AF.2 Atrial arrhythmias develop at slow-conduction sites with increased myocardial fibrosis.3 Yet, these regions are not completely fibrotic or electrically silent. To our knowledge, no sharp cutoff value for low voltage has been found that includes all proarrhythmic sites and excludes normal tissue. During substrate mapping of scar-related ventricular tachycardias, the bipolar voltage threshold on 3-dimensional maps is set between 0.1 and 1.5 mV to identify slow conduction channels responsible for the arrhythmia. Our current work suggests a relationship between AF drivers and regions with slow conduction and reduced bipolar voltage.1

Recent data from our group1 and from Yang et al4 revealed atrial slow-conduction sites with fractionated/delayed activity localized to areas displaying bipolar voltages ≤1.0 mV3 and 1.3 mV4 in SR. Importantly, ablation of these slow-conduction sites within 1.3 mV areas in SR is associated with favorable arrhythmia freedom rates.3,4 Therefore, studies using the voltage <0.5 mV in SR as the low-voltage threshold have certainly identified and targeted an important proportion of the diseased atrial tissue; however the fixed threshold of 0.5 mV in SR does not reflect all proarrhythmic atrial tissue.

In our study,1 18 (22%) patients maintained SR after electric cardioversion 10 weeks earlier and were not inducible for sustained (>6 min) AF. Therefore, voltage mapping was done in SR in these 18 patients. In contrast to the statement of Bartoletti et al, the extent of low-voltage areas ≤1.0 mV during SR was limited in these patients (5% of left atrial surface area), and the pulmonary vein isolation–only (PVI-only) strategy was associated with high arrhythmia freedom rate (78%) off antiarrhythmic drugs after 13-month follow-up. Therefore, choosing the threshold of 1.0 mV in SR did not add patients with significant low-voltage substrate to the study cohort nor contribute to overestimation of low-voltage substrate, but did identify patients with a history of persistent AF and lack of atrial low-voltage substrate who benefit from a PVI-only approach.

In AF, reduced bipolar voltage (<0.5 mV) may result from increased fibrosis or functional tissue refractoriness, which would display normal voltage during regular rhythms. However, low voltage in AF may also reflect arrhythmogenic sites that display rapid activity with slow conduction phenomena that may only be observed during rapid rhythms (as AF) and overlooked during slow regular rhythms (sinus or paced rhythms). We, therefore, chose a combined voltage- and activation-based approach to identify potential AF drivers and ablation target sites. The current work demonstrates the colocalization of AF drivers (and AF termination sites) with repetitive rotational activity (displaying electric activity with AF cycle length coverage >70% on multiple consecutive electrodes of the spiral-like mapping catheter) to low-voltage areas <0.5 mV in AF. The voltage threshold of 0.5 mV in AF (using the 20-pole spiral-like AFocus HD catheter, SJM) was chosen because (1) slow conduction isthmuses of localized reentrant circuits in atrial tachycardia display these low-voltage values and (2) atrial-delayed enhanced areas on high-resolution magnetic resonance imaging displayed bipolar voltages <0.5 mV in AF.6

2. As mentioned in the methods section, the historical control group underwent ablation by the same experienced operators and same ablation technologies (75% of patients in both the study group and control group were ablated using contact force–enabled catheters). Therefore, the outcome difference between the groups is not related to the type of technology/ablation catheter used.

We agree that randomized prospective studies are necessary to evaluate the added value of any novel ablation strategy.1 Therefore, we have initiated the prospective multicenter study PVI versus PVI plus Selective Ablation of Low Voltage Areas for Persistent AF (SOLVE-AF), comparing the novel low voltage–based ablation approach to a PVI-only approach for persistent AF.

Disclosures

None.

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