Pulmonary Vein Nonconduction
A False Indicator of Durable Pulmonary Vein Isolation*

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Durable isolation following pulmonary vein (PV) ablation may not be necessary for effective suppression of atrial fibrillation (AF) in certain patients with AF. However, most patients are thought to benefit from durable PV isolation, because PV reconnection seems to by and large underlie the mechanism of AF following catheter ablation (1). A recent study found that among patients undergoing ≥3 radiofrequency (RF) catheter ablations for AF, presence of durable isolation in all PVs was only noted in ~8% (2). It has been shown that in most cases, PV conduction recovery occurs rapidly, with as many as one-third of targeted PVs and four-fifths of those that recover electrical conduction reconnecting in as little as 30 min (3). Moreover, there still remains the possibility that conduction block may be observed despite presence of a conduction gap. Ranjan et al. (4) created a 2-dimensional model of the cardiac syncytium simulating RF ablation lines with gaps of varying lengths, conductivity, and orientation. The simulation model showed that with normal conductivity in the gaps and RF ablation lines oriented parallel to the direction of the conducting fibers, a maximum gap of 1.4 mm could exist while exhibiting conduction block. As the conductivity was decreased, the maximum gap length with conduction block increased exponentially, such that at 67% of normal tissue conductivity, the maximum gap length exhibiting conduction block increased to 4 mm. Subsequently, the authors examined the same phenomenon in a live canine model by intentionally creating transmural RF ablation lines with anatomic gap. The gap length was progressively decreased until there was conduction block. The ablation line was then analyzed using magnetic resonance imaging and correlated with histology. The authors similarly found that gaps ranging between 1.8 and 5.5 mm (median of 4.1 mm) could exist while displaying acute conduction block. More recently, Miller et al. (5) showed that although electrical PV isolation could be achieved frequently without completion of a circumferential RF ablation line, more than one-fourth of these “isolated” PVs exhibited dormant conduction via the unablated visible gaps in the ablation lesion set. These findings support the notion that reversible tissue injury may contribute to acute PV isolation that may not be necessarily durable.

In this issue of *JACC: Clinical Electrophysiology*, Baldinger et al. (6) report on the findings of a similar study conducted to characterize the relationship between PV excitability and acute entrance block in patients undergoing PV isolation as treatment for AF. This study provides several important insights. First, the findings reaffirm that entrance block can be achieved in ~60% of PVs despite a visible anatomic gap measuring >10 mm within the RF ablation circumferential lesion set, once again demonstrating that an anatomically continuous line of RF applications is not necessary to achieve conduction block. Second, they found that the initial loss of conduction commonly occurred when areas remote from the RF ablation line in the PVs lose excitability. That is, only approximately one-third of PVs remained excitable to pacing while exhibiting exit block despite the incompleteness of the ablation line, whereas approximately two-thirds showed loss of excitability even at sites remote
from the ablation line despite the presence of a visible gap. Hence, the latter may suggest an interconnection between the PVs and the left atrial tissue. Third, the majority of PVs (83%) that required an anatomically complete RF ablation line to yield entrance block remained excitable to pacing, suggesting that perhaps nonexcitability may contribute to the phenomenon of conduction block. Lastly, loss of excitability to pacing in PVs was more likely to occur if the anatomic gap was larger in the RF ablation line. The latter suggests tissue edema or stunning as a potential mechanism leading to acute PV isolation in such a scenario. The finding that the tissue within the visible ablation gap was in fact excitable indicates that such a gap will fail to serve as a permanent barrier to electrical conduc-
tion once the PV muscular sleeves regain conduction recovery. These observations unequivocally suggest that presence of acute PV entrance and exit block by itself is an insufficient endpoint of catheter ablation of AF. Furthermore, these findings also offer an explanation for the high rate of PV conduction re-
covery commonly observed despite achieving the acute endpoints of entrance and exit block at the time of PV isolation. As such, they are entirely consistent with the clinical experience and the published liter-
ature on the long-term outcomes of PV isolation and AF ablation. For instance, in the GAP-AF study (7), of those who underwent a “complete” PV isolation, up to 70% of patients and 57% of PVs exhibited PV reconnection at 3 months. Willems et al. (8) also discovered evidence of PV conduction recovery in 77% of patients and 43% of all PVs at 3 months post-ablation. Similarly, in the more contemporary EFFICAS I study (9), only 51% of PVs and 35% of patients exhibited complete PV isolation at 3 months post-catheter ablation by operators blinded to RF force sensing data. These findings further emphasize the role for improving the quality of RF applications delivered through novel technologies such as force sensing (9). Alternatively, strategies such as pacing along the PV isolation line to ensure nonexcitability seems necessary to maximize the long-term procedural efficacy (10). Another consideration may be to pharmacologically challenge patients intraprocedurally with an agent such as adenosine in an attempt to uncover presence of dormant conduction. In the recently published ADVICE (ADenosine Following Pulmonary Vein Isolation to Target Dormant Conduction Elimination) trial (11), administration of adenosine successfully unmasked dormant PV conduction in 53% of patients undergoing RF catheter ablation, which in turn was retargeted. Using such an approach, the authors demonstrated a greater incidence of freedom from atrial arrhythmias during long-term follow-up with an absolute risk reduction of 27% (hazard ratio: 0.44). But to the contrary, the outcomes from the UNDER-A
TP (UNmasking Dormant Electrical Reconnection by Adenosine TriPhosphate) trial (12) have in fact disputed these findings. That is, although adminis-
tration of adenosine in the latter study provided further identification of dormant PV conduction in approximately 28% of patients, nearly all of which (98%) were then retargeted, this did not translate into long-term improvements in freedom from atrial arrhythmias.

In summary, entrance and exit block can frequently occur in the presence of visible anatomic gaps within the RF ablation lesion set prior to completion of a circumferential PV ablation line. As such, conduction block alone should not be used as a steadfast indicator of durable PV isolation. Other confirmatory techniques such as administration of adenosine or pacing along the PV isolation lines may prove helpful in improving the procedural efficacy. Lastly, additional research is needed to enhance our understanding of durable PV isolation and optimal lesion formation to improve the long-term outcomes of catheter ablation of AF. The paper by Baldinger et al. (6) represents a great starting point.

REFERENCES
physiologic findings and long-term outcomes in patients undergoing third or more catheter abla-
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