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Atrial tachyarrhythmia recurrence after cryoballoon ablation: does thickness imply failure?

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Pulmonary vein reconnection remains the Achilles' heel of catheter ablation of atrial fibrillation (AF). Whether the index procedure is performed with radiofrequency energy, cryoablation [1], or pulsed field ablation [2], pulmonary vein reconnection is observed in more than half of patients after pulmonary vein isolation (PVI) and is associated with an increased risk of AF recurrence [3]. Among several mechanistic determinants of reconnection, gaps in ablation lines and lack of lesion transmuralty appear to be key. The electrophysiological assessment of ablation lesion transmuralty is complicated by the fact that non-transmural lesions are sometimes undetectable at endocardial mapping: in a previous series of patients undergoing endo-epicardial mapping and ablation of AF, in 3 patients (20% of the study patients with evidence of pulmonary vein reconnection), epicardial pulmonary vein connection could be demonstrated despite endocardial bidirectional PVI [4]. Although greater wall thickness appears to be associated with increased odds of local reconnection after radiofrequency ablation [5], less is known for patients undergoing cryoballoon ablation.

In the current issue of the *Journal of Interventional Cardiac Electrophysiology*, Bai and colleagues add novel insights to this topic, by systematically assessing the association of pulmonary vein antrum thickness and risk of recurrent atrial tachyarrhythmias (AT) in a cohort of patients undergoing cryoablation of paroxysmal AF [6]. This retrospective, observational study included 364 patients undergoing a first-procedure cryoballoon PVI using the second-generation Arctic Front Advance™ device (Medtronic, MN, USA) at a single institution in China between 2018 and 2022. Each subject underwent a pre-ablation computed tomography (CT) reconstruction of the left atrium (LA), with measurements of both the indexed LA volume (LAVI) and wall thickness in 16 segments of the pulmonary vein antrum using a semiautomatic method. The primary endpoint of recurrent AT, as ascertained using intermittent monitoring with a 3-month blanking period, occurred in 22.5% of the study population during a median follow-up of 19 (12–28) months. In multivariable Cox analysis, the mean (left and right) antral LA wall thickness (LAWT) was found to be linked to AT recurrence (HR, 3.657 per 1-mm increase; 95% CI, 2.319–5.765; $p < 0.001$), with a stronger association than CT-derived LAVI, a well-known predictor of arrhythmia recurrence after AF ablation (area under the receiver operating characteristic curve [AUC] for LAWT, 0.737; AUC for LAVI, 0.573; $p < 0.001$ for the comparison of AUCs). Furthermore, the inclusion of LAWT improved discrimination and reclassification (two measures of performance) of the model for predicting AT recurrence as compared to a model including clinical (age, sex, BMI, nt-proBNP, early recurrence), procedural (right superior pulmonary vein nadir temperature), and imaging (LAVI) variables without LAWT. As corollary findings, pulmonary veins with thicker antral LAWT needed longer time to achieve electrical isolation at index procedure, and among the 23 patients undergoing a redo procedure during follow-up, reconnected antral segments (as assessed by electroanatomical voltage mapping) were thicker than non-reconnected segments (1.96 ± 0.78 mm vs. 1.69 ± 0.56 mm, $p = 0.011$). Finally, the

reported technique for LAWТ measurement was found to have an acceptable interobserver agreement (interobserver correlation coefficient, 0.814, $p < 0.001$).

The results of this study should be interpreted in light of some limitations. First, this was a retrospective study. Therefore, we cannot yet speculate on the need to titrate the duration of cryoenergy applications according to pre-procedural CT-derived LAWТ to optimize results of PVI, and this hypothesis will require dedicated, prospective testing. Second, only patients with paroxysmal AF undergoing PVI were included, and the association between LAWТ and clinical outcomes after cryoballoon ablation in persistent AF is currently unknown. Third, the relationship between LA posterior wall thickness and outcomes of PVI plus posterior wall isolation using cryoballoon ablation — a common procedural strategy in persistent AF patients — remains unknown. Fourth, an outdated technology was used in the study, second-generation cryoballoons being now substituted by fourth-generation devices from the same constructor.

Bai and colleagues should be credited for having shed some light on the importance of studying atrial anatomy prior to cryoballoon ablation. Besides identifying pulmonary venous return anatomical variants and excluding LA appendage thrombus, the possibility to measure LAWТ and the prognostic importance of this parameter may reinforce the common practice of performing a pre-procedural CT scan. Currently available softwares allow to derive three-dimensional LA wall thickness maps from CT scans; these maps may then be integrated into electroanatomical mapping systems and have already been prospectively used to titrate radiofrequency energy delivery during AF ablation [7], by adapting the regional target ablation index [8] to local wall thickness, underscoring the importance of producing trans-mural lesions to achieve persistent pulmonary vein isolation and address subepicardial atrial arrhythmogenic structures, such as the septopulmonary bundle and Bachmann's bundle [9]. Whether preprocedural CT-based LAWТ measurements may complement time to pulmonary vein isolation for adapting the duration of cryoenergy deliveries among patients undergoing cryoballoon PVI will need adequate prospective validation. Furthermore, future studies should elucidate whether the distribution and amount of atrial epicardial fat, which can be measured by CT scans, may be combined with LAWТ for improving prediction of ablation success and tailoring cryoenergy applications.

Intracardiac echocardiography (ICE) has already been used to obtain intraprocedural real-time measurements of LA wall thickness by advancing the ultrasound catheter into the LA. These measurements were validated against CT and have been used to tailor regional ablation index values during radiofrequency AF ablation [10]. Whether the use of ICE-based LAWТ measurements may be of prognostic value in patients undergoing cryoballoon PVI is still unknown and should be the subject of future research, also considering that the quality of ICE images is continuously improving through updates of ICE technology, which currently allows 4-dimensional acquisitions. The use of ICE may also reduce exposure to ionizing radiations, an important limitation of CT.

In summary, the authors should be credited for having reinforced the concept that preprocedural LA imaging using CT may have greater value than simple procedural planning before cryoballoon PVI. LAWТ measurement may improve prognostication and refine the discussion on the expected efficacy of cryoablation. Future research efforts should try to prospectively use LAWТ together with time to isolation to tailor cryoenergy deliveries according to patients' anatomy.

Data availability: The data that support the findings of this study are available on request from the corresponding author, PC.

Declarations:

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Consent to participate: Not applicable.

Competing interests: The authors declare no competing interests.

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