






Preoperative personalization of atrial fibrillation ablation strategy to prevent esophageal injury: Impact of changes in esophageal position

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Abstract

Introduction: Due to changes in esophageal position, preoperative assessment of the esophageal location may not mitigate the risk of esophageal injury in catheter ablation for atrial fibrillation (AF). This study aimed to assess esophageal motion and its impact on AF ablation strategies.

Methods and Results: Ninety-seven AF patients underwent two computed tomography (CT) scans. The area at risk of esophageal injury (AAR) was defined as the left atrial surface ≤ 3 mm from the esophagus. On CT1, ablation lines were drawn blinded to the esophageal location to create three ablation sets: individual pulmonary vein isolation (PVI), wide antral circumferential ablation (WACA), and WACA with linear ablation (WACA + L). Thereafter, ablation lines for WACA and WACA + L were personalized to avoid the AAR. Rigid registration was performed to align CT1 onto CT2, and the relationship between ablation lines and the AAR on CT2 was analyzed. The esophagus moved by 3.6 [2.7 to 5.5] mm. The AAR on CT2 was 8.6 ± 3.3 cm², with 77% overlapping that on CT1. High body mass index was associated with the AAR mismatch (standardized β 0.382, $p < .001$). Without personalization, AARs on ablation lines for individual PVI, WACA, and WACA + L were 0 [0–0.4], 0.8 [0.5–1.2], and 1.7 [1.2–2.0] cm². Despite the esophageal position change, the personalization of ablation lines for WACA and WACA + L reduced the AAR on lines to 0 [0–0.5] and 0.7 [0.3–1.0] cm² ($p < .001$ for both).

Conclusion: The personalization of ablation lines based on a preoperative CT reduced ablation to the AAR despite changes in esophageal position.

KEYWORDS

atrial fibrillation, catheter ablation, collateral damage, computed tomography, esophagus

1 | INTRODUCTION

Collateral damage is one of the critical issues in catheter ablation for atrial fibrillation (AF). In particular, the esophagus may be injured as it locates close to several ablation lines. This can lead to severe complications, including atrial-esophageal and pericardial-esophageal fistulas. Although these serious complications are rare, up to 20% of patients may experience less severe symptoms, including odynophagia, dysphagia, chest discomfort, gastric reflux, gastroparesis, or dysmotility.¹ Recent reports using acute postablation magnetic resonance imaging have shown that esophageal injury is quite common, observed up to 43% of the patients undergoing catheter ablation for AF with thermal methods.² Some perioperative attempts have been made to avoid esophageal injuries,^{3–8} but no definite method to protect the esophagus has been established. One promising idea to prevent esophageal injury is to avoid ablation to the area near the esophagus. However, although the esophageal course relative to the left atrium (LA) has been commonly assessed by computed tomography (CT) or esophagography, it has been difficult to measure the actual distance between the LA and the esophagus. Moreover, since the esophagus is a mobile structure,^{9,10} it is unclear whether the LA-esophagus distance measured preoperatively remains a valid indicator of esophageal position at the time of the ablation procedure.

In the present study, we introduced a method to automatically map the LA-esophagus distance from CT images, allowing for the visualization of the area at risk of esophageal injury (AAR) over the LA surface. We applied this method to serial CT scans performed before AF ablation at different time points in patients undergoing multiple procedures. The study aimed to quantify the esophageal position change and its impact on personalized AF ablation strategies based on a preoperative assessment of the AAR.

2 | METHODS

2.1 | Study population

We retrospectively included 106 AF patients who underwent two contrast-enhanced CT studies before two serial ablation procedures at Bordeaux university hospital from January 2017 to July 2020. Among them, we excluded nine patients in whom the quality of CT images was insufficient for the accurate segmentation of the LA or the esophagus. Consequently, we analyzed 97 patients in the present study. The Institutional Ethics Committee approved the study, and all patients gave informed consent.

2.2 | CT image acquisition

Contrast-enhanced cardiac CT scans were performed with a dual-source CT system (Siemens Force, Siemens Medical Systems) 1–3 days before the ablation procedure. Images were acquired at end-systole using prospective electrocardiogram-triggering to assess the LA at its maximal volume. The delay was set in percentage of the RR interval during sinus rhythm and ms during AF. The tube voltage and current were adapted to patient morphology. Images were acquired using a biphasic injection protocol: 1 ml/kg of iomeprol 350 mg/ml at the rate of 5 ml/s, followed by a 1 ml/kg flush of saline at the same rate. Bolus tracking or test bolus methods were applied to trigger the acquisition at the time of maximal enhancement in the ascending aorta. An additional CT acquisition at the venous phase was also added for the ruling out of thrombus, CT being the first-line method for this indication in our center. Thus, no trans-esophageal echocardiography was performed between the CT scan and the procedure.

2.3 | CT image analysis

Image processing was performed using the MUSIC software (IHU Liryc, Université de Bordeaux, Bordeaux & INRIA) and Python programming language (Python Software Foundation, <https://www.python.org/>). The LA segmentation was performed using a fully automated artificial intelligence model priorly trained, validated, and tested on a separate database of 550 cardiac CT scans acquired in patients undergoing AF ablation, and with available expert segmentation.¹¹ Details on the model and its performance are provided as supplemental methods. The esophagus segmentation was performed using a semi-automated method, with regions of interest being manually drawn on some slices and then interpolated. These segmentations were used to compute three-dimensional meshes at high and uniform density (>85 000 triangles per LA mesh).¹² Surface-to-surface distance was computed from the LA endocardial surface mesh to the esophagus surface mesh, and the distance was color-coded on the LA surface. On these distance maps, the AAR was defined as the LA surface with a distance ≤ 3 mm from the esophagus.¹³

2.4 | Assessment of changes in esophageal position between CT scans

A scheme of the proposed pipeline is shown in Figure 1. We arbitrarily assumed the first CT (CT1) as the preoperative

esophagus position and the second CT (CT2) as the intraoperative esophagus position. The LA mesh corresponding to CT1 was rigidly (i.e., translation and rotation) registered to the LA mesh corresponding to CT2 using an Iterative Closest Point algorithm. Thereafter, the same transformation was also applied to the esophageal mesh from CT1. This allowed us to display both the AAR from CT1 and that from CT2 on the same LA mesh derived from CT2. The AAR mismatch between CT1 and CT2 was computed as a surface area (cm^2) and as the percentage of the total AAR on CT2. This AAR mismatch included only the AAR on CT2, which was not observed in CT1 (and not the other way around), that is, the intraoperative AAR, which was not detected in the preoperative CT scan. In addition to changes in AAR on the LA surface, changes in esophageal position were also directly measured between esophageal meshes. It was computed as the mean pairwise point to point Euclidean distance between the two surface meshes and expressed in mm (Figure S1). A large esophageal position change was defined as the median displacement of the esophagus >10 mm.

2.5 | Assessment of personalized and non-personalized ablation strategies

To analyze the impact of changes in esophageal position on personalized ablation strategies, experienced electrophysiologists manually drew different sets of ablation lines onto the LA mesh derived from CT1. First, conventional ablation lines were delineated on the LA surface to simulate different ablation strategies: (1) individual pulmonary vein isolation (PVI) mimicking one-shot ablation such as cryoballoon ablation; (2) wide antral circumferential ablation (WACA); and (3) WACA with additional linear ablation consist of the roof line, floor line, and mitral isthmus line (WACA + L). These ablation lines were firstly delineated based solely on the LA anatomy and blinded from the esophagus position. Thereafter, personalized ablation lines were drawn to avoid the AAR as much as possible. These personalized strategies were only delineated for WACA and WACA + L because the room for optimizing individual PVI lines was considered negligible. To mimic ablated lesions delivered in the clinic, the width of ablation lines was set to 5 mm for WACA and WACA + L

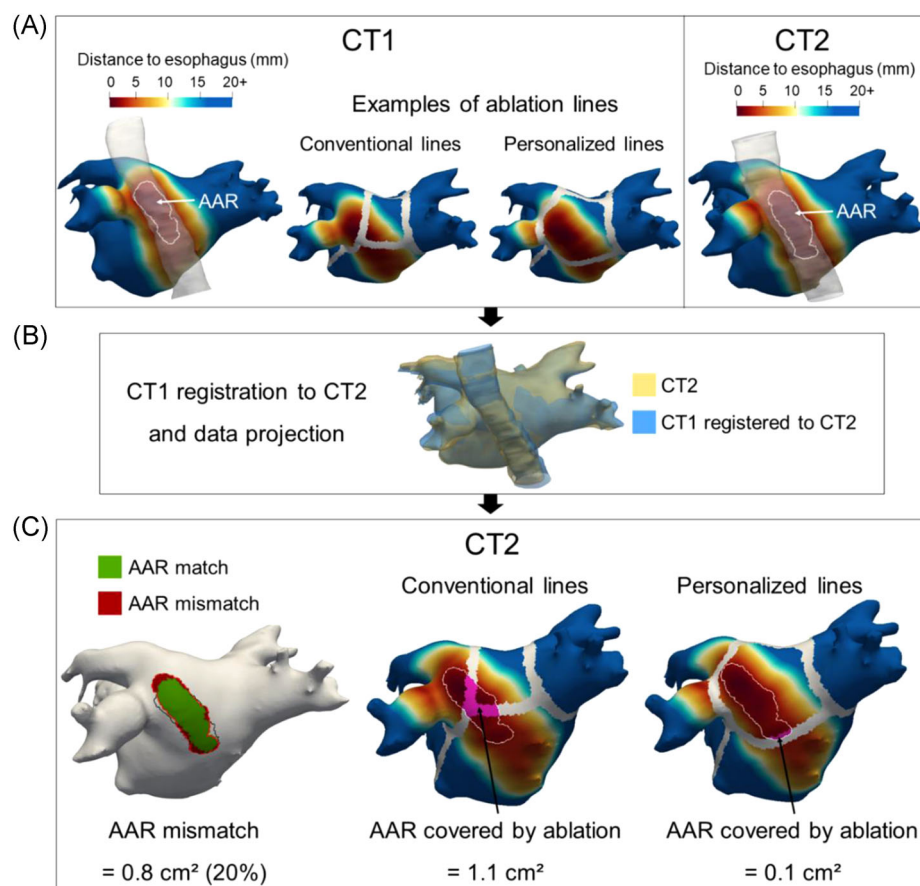


FIGURE 1 The assessment of the area at risk of esophageal injury (AAR) and the impact of personalized ablation. (A) The left atrium (LA) and esophagus surface meshes were obtained from computed tomography (CT). Colors on the LA surface indicate the distance to the esophagus. The AAR, defined as the LA surface ≤ 3 mm from the esophagus, is enclosed by a white contour. In the first CT (CT1), ablation lines were both delineated without the information of the AAR (conventional lines) and designed to avoid the AAR (personalized lines). (B) The LA from CT1 was registered to that from the second CT (CT2). (C) The AAR and ablation lines from CT1 were projected onto the LA surface of CT2. We assessed the AAR mismatch and the AAR covered by ablation lines

strategies and increased to 8 mm when drawing individual PVI to reproduce the expected impact of cryoballoon ablation. Both conventional and personalized ablation lines were projected onto the LA surface mesh of CT2. Finally, changes in the AAR covered by ablation lines with respect to CT1 were assessed.

2.6 | Spatial distribution of the AAR

To study the most common location of the AAR across the population, all LA geometries were registered on a single LA template corresponding to a patient with average LA shape and size. Registration was performed using a similarity transformation (rotation, translation, and isotropic scaling). Furthermore, centroids of conventional ablation lines for WACA were used as two landmarks to enhance good registration. After registration, all AARs were projected onto the LA template, and the prevalence of AARs across the study population (as assessed on CT1) was color-coded on each point of the LA template.

2.7 | Statistical analysis

The Shapiro–Wilk test of normality was used to assess whether quantitative data conformed to the normal distribution. Continuous data are expressed as mean \pm standard deviation when following a normal distribution and as median [interquartile range Q1–Q3] otherwise. Categorical data are expressed as numbers (%). Differences in variables between two settings were assessed using a parametric test (paired Student's *t*-test) or a nonparametric test (Wilcoxon signed-rank test) depending on data normality. Differences in variables among multiple settings were assessed using repeated-measures analysis of variance. If significant differences were observed, posthoc tests with Bonferroni-adjusted pairwise comparisons were performed. Linear regression analysis was performed to identify determinants of the AAR and its changes. All variables with $p < .050$ in univariable analysis were included in the multivariable analysis. We considered $p < .050$ as statistically significant.

3 | RESULTS

3.1 | Baseline patient characteristics

Baseline patient characteristics are summarized in Table 1. The mean age was 64 [55–70] years, and 63% of patients had nonparoxysmal AF. The left ventricular ejection fraction was $57 \pm 11\%$, and the LA volume was 146 [121–178] ml. A left common pulmonary vein was observed in 9% of patients.

3.2 | Determinants of the AAR

The AAR on CT1 was $9.4 \pm 3.6 \text{ cm}^2$. The distribution of the AAR over the LA posterior wall in the study population is shown in Figure 2.

TABLE 1 Baseline patient characteristics

	n = 97
Age, years	64 [55–70]
Gender, male	77 (76%)
Body mass index, kg/m ²	28 \pm 4
Nonparoxysmal AF	64 (63%)
Previous ablation	41 (41%)
Previous cardiac surgery	7 (7%)
Structural heart disease	33 (33%)
Congestive heart failure	20 (20%)
Hypertension	46 (46%)
Diabetes mellitus	7 (7%)
Stroke/transient ischemic attack	11 (11%)
Vascular disease	13 (13%)
Pulmonary disease	5 (5%)
CHA2DS2-Vasc score	2 [1–3]
Left ventricular ejection fraction, %	57 \pm 11
Left atrial volume, ml	146 [121–178]
Left common pulmonary vein	9 (9%)
Antiarrhythmic drugs	70 (69%)

Note: Data are presented as mean \pm SD, median [interquartile range Q1–Q3], or number (%) of patients.

Abbreviation: AF, atrial fibrillation.

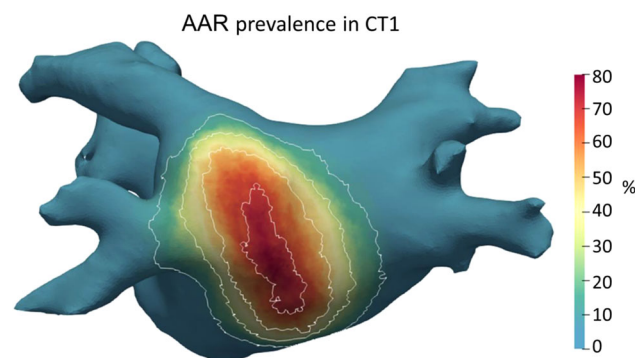


FIGURE 2 Spatial distribution of the area at risk of esophageal injury (AAR) in the study population. The prevalence of AAR in CT1 across the population, expressed in % of the total population, is color-coded from blue to red. Iso-percentage lines at 10%, 30%, 50%, and 70% are additionally displayed. CT1, the first computed tomography

The AAR was distributed predominantly on the left-inferior area of the posterior wall. The determinants of the AAR are summarized in Table 2. In univariable analysis, a large AAR was related to the female gender, low body mass index (BMI), history of stroke/transient ischemic attack, and high LA volume. In multivariable analysis, female gender (standardized β -0.178 , $p = .036$), low BMI (standardized β -0.304 , $p = .001$), and high LA volume (standardized β 0.507 ,

TABLE 2 Determinants of the area at risk of esophageal injury (AAR)

	Univariable		Multivariable	
	β	<i>p</i>	β	<i>p</i>
Age, years	-.071	.490		
Gender, male	-.204	.045	-.178	.036
Body mass index, kg/m ²	-.208	.041	-.304	.001
Nonparoxysmal AF	-.006	.957		
Previous ablation	-.057	.582		
Previous cardiac surgery	-.039	.703		
Structural heart disease	.025	.806		
Congestive heart failure	.007	.946		
Hypertension	-.164	.109		
Diabetes mellitus	-.139	.175		
Stroke/transient ischemic attack	.249	.014	.157	.067
Vascular disease	-.164	.108		
Pulmonary disease	-.050	.625		
CHA2DS2-Vasc score	.018	.859		
Left ventricular ejection fraction, %	-.105	.313		
Left atrial volume, ml	.452	<.001	.507	<.001
Left pulmonary vein common tract	-.040	.699		
Antiarrhythmic drugs	.018	.864		

Abbreviation: AF, atrial fibrillation.

$p < .001$) were independent correlates of the large AAR. The relationship between LA dilatation and the AAR is illustrated in Figure 3.

3.3 | Changes in esophageal position and AAR

The delay between CT1 and CT2 was 405 ± 258 days. On CT1, the esophageal position was left in 62 patients (64%), middle in 25 patients (26%), and right in 10 patients (10%). On CT2, the esophageal position was left in 67 patients (69%), middle in 23 patients (24%), and right in 7 patients (7%). The median distance of the esophageal position change between two CTs was 3.6 [2.7–5.5] mm. A large esophageal position change was observed in four patients (4%).

The AAR on CT2 was 8.6 ± 3.3 cm². The AAR mismatch between two CTs was 1.9 ± 1.3 cm² (i.e., $23 \pm 17\%$ of the AAR on CT2). In univariable analysis, the only characteristic related to the large AAR mismatch was high BMI (standardized β .382, $p < .001$; Table 3). CT1 imaging was performed during sinus rhythm in 36 patients (37%) and AF rhythm in 61 patients (63%), whereas CT2 imaging was performed during sinus rhythm in 64 patients (66%) and AF rhythm in 33 patients (34%). A different rhythm between the two CTs was observed in 32 patients (33%). In these, the AAR mismatch between CTs was similar to that observed in the remaining subjects (1.8 ± 1.4 cm² vs. 1.9 ± 1.3 cm², $p = .655$).

3.4 | Impact of the esophageal position change on personalized ablation strategies

The total area of conventional lines for individual PVI, WACA, and WACA + L was 15.0 ± 2.2 , 9.6 ± 1.7 , and 14.2 ± 1.8 cm², respectively. The total area of personalized lines for WACA and WACA + L was 9.6 ± 1.6 and 14.8 ± 1.8 cm², respectively. The AAR covered by these ablation lines is summarized in Figure 4. The AAR covered by ablation lines for individual PVI was minimal and did not change after projection on CT2 ($0 [0-0.2]$ cm² on CT1 vs. $0 [0-0.4]$ cm² on CT2,

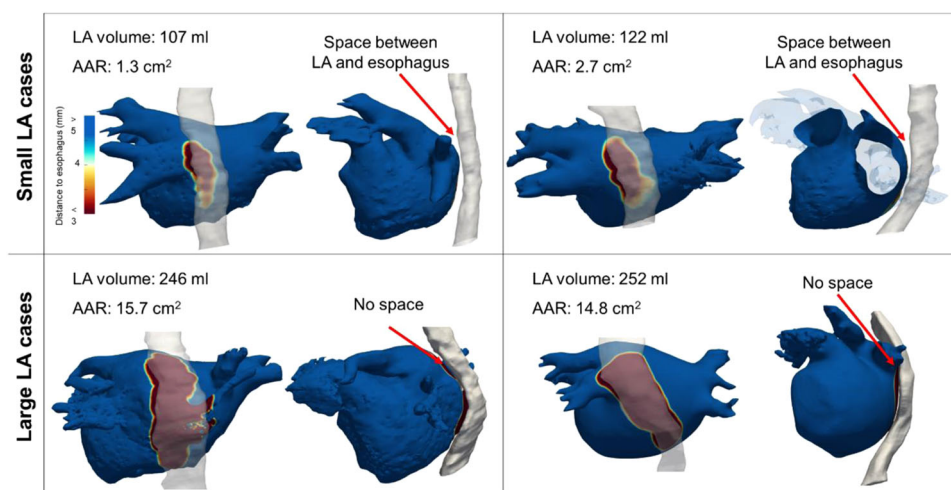


FIGURE 3 Impact of the left atrium (LA) volume on the area at risk of esophageal injury (AAR). The space between the LA and esophagus present in cases with low LA volume leads to a smaller AAR (upper panel). In contrast, the posterior extension of the LA eliminates such a space and consequently increases the AAR in cases with high LA volume (lower panel)

TABLE 3 Determinants of the mismatch of the area at risk of esophageal injury (AAR) between computed tomography studies

	Univariable	
	β	<i>p</i>
Age, years	.111	.283
Gender, male	-.117	.255
Body mass index, kg/m ²	.382	<.001
Nonparoxysmal AF	.067	.517
Previous ablation	-.040	.700
Previous cardiac surgery	.142	.166
Structural heart disease	.167	.103
Congestive heart failure	.146	.152
Hypertension	.159	.121
Diabetes mellitus	.107	.298
Stroke/transient ischemic attack	-.019	.857
Vascular disease	.144	.159
Pulmonary disease	-.027	.791
CHA2DS2-Vasc	.170	.095
Left ventricular ejection fraction, %	.056	.590
Left atrial volume, ml	-.070	.495
Left pulmonary vein common tract	.144	.158
Antiarrhythmic drugs	.130	.205

Abbreviation: AF, atrial fibrillation.

$p = .442$). The AARs covered by conventional ablation lines for WACA and WACA + L were more significant; however, the personalized strategy significantly reduced the AAR covered by ablation lines for both WACA (0.9 [0.4–1.3] cm² with conventional lines vs. 0 [0–0.1] cm² with personalized lines, $p < .001$) and WACA + L (1.7 [1.1–2.2] cm² with conventional lines vs. 0.6 [0.3–0.9] cm² with personalized lines, $p < .001$). More importantly, despite changes in esophageal position between two CTs, the personalized strategy on CT1 remained beneficial after projection on CT2, with a 75 ± 36% reduction of the AAR covered by ablation lines for WACA (0.8 [0.5–1.2] cm² with conventional lines vs. 0 [0–0.5] cm² with personalized lines, $p < .001$), and a 53 ± 34% reduction for WACA + L (1.7 [1.2–2.0] cm² with conventional lines vs. 0.7 [0.3–1.0] cm² with personalized lines, $p < .001$). Examples of AARs covered by conventional versus personalized ablation lines are shown in Figure 5.

4 | DISCUSSION

This study is, to our knowledge, the first to consistently quantify the esophageal position change between different time points and its impact on personalized ablation strategy. The main findings are as follows: first, in patients with AF undergoing catheter ablation, female gender, low BMI, and high LA volume are independently

associated with a larger AAR. Second, changes in esophageal position between two distant time points remain moderate, with 77% of the AAR correctly predicted by prior imaging. Third, the large esophageal position change is more likely to be observed in patients with high BMI. Finally, despite changes in esophageal position, a personalization of ablation lines to avoid the AAR based on preoperative imaging significantly reduced the AAR covered by ablation lines (by 75 ± 36% for WACA, and 53 ± 34% for WACA + L).

4.1 | Determinants of the AAR and esophageal position change

The larger AAR in women may be due to the gender difference in chest morphology. Indeed, the distance between the LA and the vertebral body may differ between genders and has been associated with the space around the esophagus.¹⁴ The present study also suggests that LA dilatation may increase the risk of esophageal injury. This is likely due to a greater excursion of the LA posterior wall in the vicinity of the esophagus. Our finding that low BMI was associated with the AAR is consistent with a prior study reporting higher rates of esophageal injury in patients with low BMI.¹⁵ The mechanism of this relationship is still unclear, but it may be partly explained by the fact that the epicardial fat volume is positively correlated with BMI.¹⁶ However, even among patients with high BMI, epicardial fat interposition between the LA and the esophagus is rather rare.¹⁵ Obesity may make a space between the LA and the esophagus by changing the positional relationship of organs. Conversely, high BMI was the determinant of the AAR mismatch between two CTs. This result is in accordance with a previous study reporting an association between the large esophageal position change and high BMI.¹⁴ The increase in the LA-esophagus distance may provide space for the esophagus to move in patients with high BMI. Fortunately, the clinical consequences of large esophageal position change in obese patients may be limited because these are precisely the ones with less contact between the LA and the esophagus, as attested by the smaller AAR in the present study.

4.2 | Existing measures to prevent esophageal injury

Esophageal injuries are not rare, as these have been observed in up to 40% of patients after AF ablation on acute imaging or endoscopic studies.^{2,15,17,18} The majority of esophageal injuries are asymptomatic; however, the outcome can be serious as it can evolve towards atrial-esophageal or pericardial-esophageal fistulas.¹ Moreover, peri-esophageal nerve injury can cause acute pyloric spasms and gastric hypomotility.¹⁹ Esophageal temperature monitoring has been proposed to prevent esophageal injury.^{3,4} However, heat conduction to the esophagus can be underestimated because the temperature monitoring device cannot cover the entire width of the esophagus, and the luminal temperature rather than intramural tissue temperature is monitored.²⁰ Another preventive measure consists of

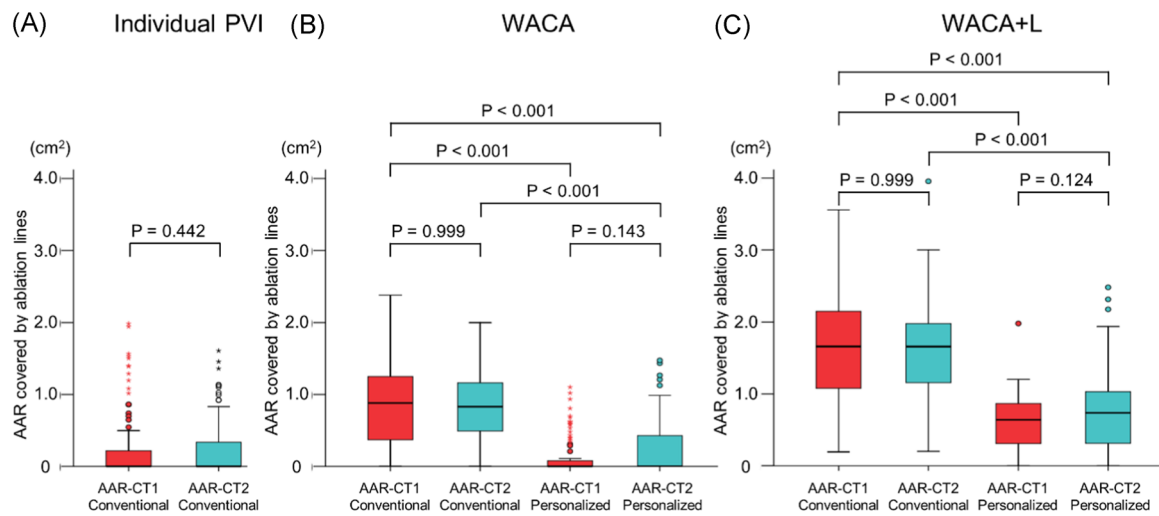


FIGURE 4 The area at risk of esophageal injury (AAR) covered by ablation lines according to each strategy. The AARs covered by ablation lines on each computed tomography study are shown for individual pulmonary vein isolation (PVI, panel A), wide antral circumferential ablation (WACA, panel B), and WACA and linear ablation (WACA + L, panel C). CT1, the first computed tomography; CT2, the second computed tomography

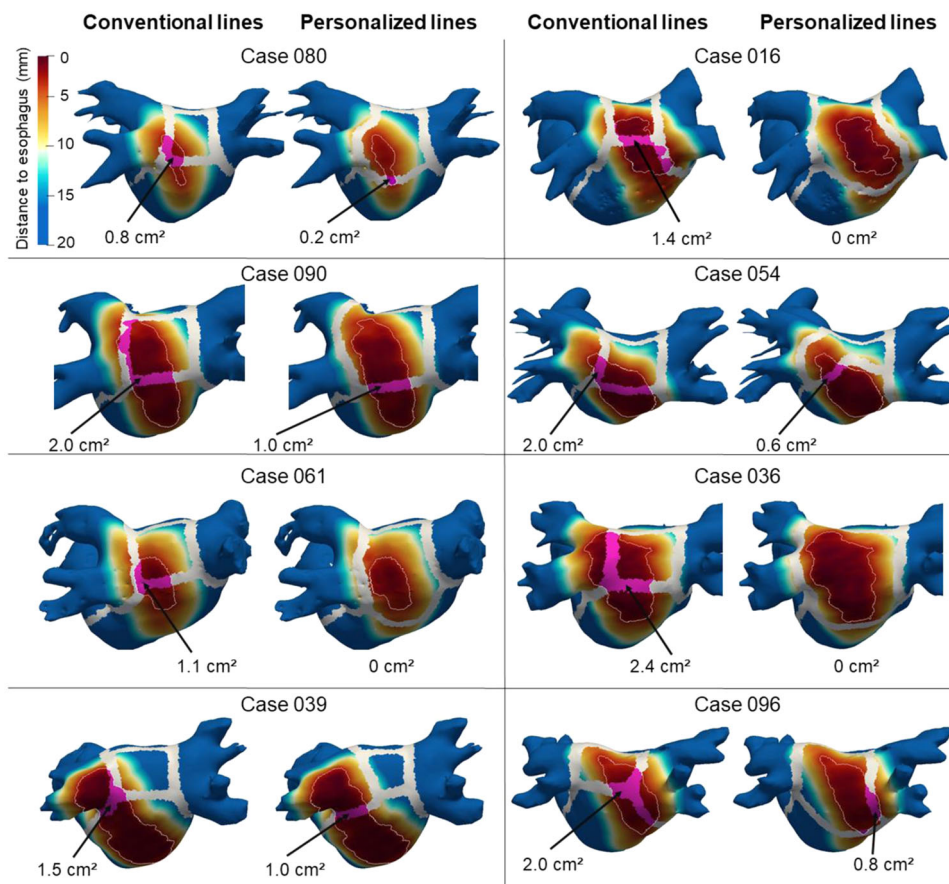


FIGURE 5 Examples of the area at risk of esophageal injury (AAR) covered by conventional versus personalized ablation lines. For each case, conventional (left) and personalized (right) ablation lines based on CT1 are displayed over the LA-esophagus distance map from CT2. Colors on the LA surfaces indicate the distance to the esophagus on CT2. The AAR, defined as the LA surface ≤ 3 mm from the esophagus, is enclosed by a white contour. The AAR covered by ablation is highlighted in pink. CT1, the first computed tomography; CT2, the second computed tomography; LA, left atrium

decreasing the radiofrequency energy when delivering lesions to the LA posterior wall.⁵ However, this reduction of radiofrequency energy may increase conductive heating via the long radiofrequency application time needed for creating a transmural lesion and consequently increase the risk of esophageal injury.⁶ On the other hand, high-power, short-duration radiofrequency application has been used to shift from conductive heating to resistive heating and potentially avoid esophageal injury.^{3,6} However, using this technique, the esophageal temperature can rise after the end of the radiofrequency application. Furthermore, attempts have been made to deliver active cooling or mechanical displacement maneuvers on the esophagus.^{7,8} However, the effectiveness of these procedures is still controversial, and they can be traumatic.

4.3 | Use of preoperative imaging to prevent esophageal injury

An accurate assessment of the esophagus location would be useful to avoid ablation to the AAR. Unfortunately, since the esophagus is a mobile organ, the preoperative esophageal location may not accurately reflect its location at the time of ablation. Although short-term esophageal motion during the cardiac cycle does not seem to be critical,²¹ a series of studies have reported conflicting results on the magnitude of esophageal position change across serial imaging studies, with some suggesting minimal motion,^{22,23} and others reporting large position changes and concluding to the inefficacy of a personalization strategy based on prior imaging.^{10,24,25} None of these prior studies have assessed the actual LA-esophagus distance, but rather the projection of the entire course of the esophagus on the LA. In addition, the impact of changes in esophageal position on the ablation strategy has never been thoroughly assessed in previous studies. Consequently, it is still unclear whether the magnitude of esophageal motion is sufficient to discard personalization strategies based on preoperative imaging. In the present study, we introduced an automated method to compute color-coded maps of the actual LA-esophagus distance, allowing for an accurate definition of the AAR. We also analyzed the ability of ablation strategies personalized at a given time point to decrease the risk of esophageal injury at a distant time point. Our results indicate that despite the substantial changes in esophageal position, personalization still dramatically reduces the risk of esophageal injury. Therefore, the proposed personalized ablation approach may help prevent esophageal injury. Nonetheless, since a large esophageal displacement was observed in some cases, we would still recommend repeating a CT scan before repeating ablation procedures and not relying on the findings of a CT scan acquired months or years prior.

4.4 | Study limitations

This study has several limitations. First, maximum changes in the AAR may have been underestimated as only two-time points of CTs were used for the assessment of the AAR. Second, changes in the LA

morphology may have affected the results as there was more than 1 year of delay between two CTs. Third, the effectiveness of the personalized ablation approach was not confirmed in clinical practice. Further prospective studies are needed to assess the impact of this approach on the rate of acute esophageal injury and patient outcomes.

5 | CONCLUSIONS

In AF patients undergoing catheter ablation, female gender, low BMI, and high LA volume are independently associated with a larger AAR. Changes in esophageal position between two distant time points are moderate, with 77% of the AAR correctly predicted by prior imaging. A large esophageal position change is more likely to be observed in patients with high BMI, and these are also the ones with smaller AAR. Despite esophageal motion, a personalization of ablation lines to avoid the esophagus based on prior imaging can significantly reduce ablation on the AAR. These results support the use of LA-esophagus distance maps derived from preoperative CT to decrease the risk of esophageal injury.

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DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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