ESC European Society of Cardiology

Europace (2024) **26**, euae107
https://doi.org/10.1093/europace/euae107

CLINICAL RESEARCH

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Incidence and predictors of thermal oesophageal and vagus nerve injuries in Ablation Index-guided high-power-short-duration ablation of atrial fibrillation: a prospective study

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Received 23 March 2024; accepted after revision 2 April 2024; online publish-ahead-of-print 22 April 2024

Aims

High-power-short-duration (HPSD) ablation is an effective treatment for atrial fibrillation but poses risks of thermal injuries to the oesophagus and vagus nerve. This study aims to investigate incidence and predictors of thermal injuries, employing machine learning.

Methods and results

A prospective observational study was conducted at Leipzig Heart Centre, Germany, excluding patients with multiple prior ablations. All patients received Ablation Index-guided HPSD ablation and subsequent oesophagogastroduodenoscopy. A machine learning algorithm categorized ablation points by atrial location and analysed ablation data, including Ablation Index, focusing on the posterior wall. The study is registered in clinicaltrials.gov (NCT05709756). Between February 2021 and August 2023, 238 patients were enrolled, of whom 18 (7.6%; nine oesophagus, eight vagus nerve, one both) developed thermal injuries, including eight oesophageal erythemata, two ulcers, and no fistula. Higher mean force (15.8 ± 3.9 g vs. 13.6 ± 3.9 g, $P = 0.022$), ablation point quantity (61.50 ± 20.45 vs. 48.16 ± 19.60, $P = 0.007$), and total and maximum Ablation Index (24 114 ± 8765 vs. 18 894 ± 7863, $P = 0.008$; 499 ± 95 vs. 473 ± 44, $P = 0.04$, respectively) at the posterior wall, but not oesophagus location, correlated significantly with thermal injury occurrence. Patients with thermal injuries had significantly lower distances between left atrium and oesophagus (3.0 ± 1.5 mm vs. 4.4 ± 2.1 mm, $P = 0.012$) and smaller atrial surface areas (24.9 ± 6.5 cm^2 vs. 29.5 ± 7.5 cm^2, $P = 0.032$).

Conclusion

The low thermal lesion's rate (7.6%) during Ablation Index-guided HPSD ablation for atrial fibrillation is noteworthy. Machine learning based ablation data analysis identified several potential predictors of thermal injuries. The correlation between machine learning output and injury development suggests the potential for a clinical tool to enhance procedural safety.

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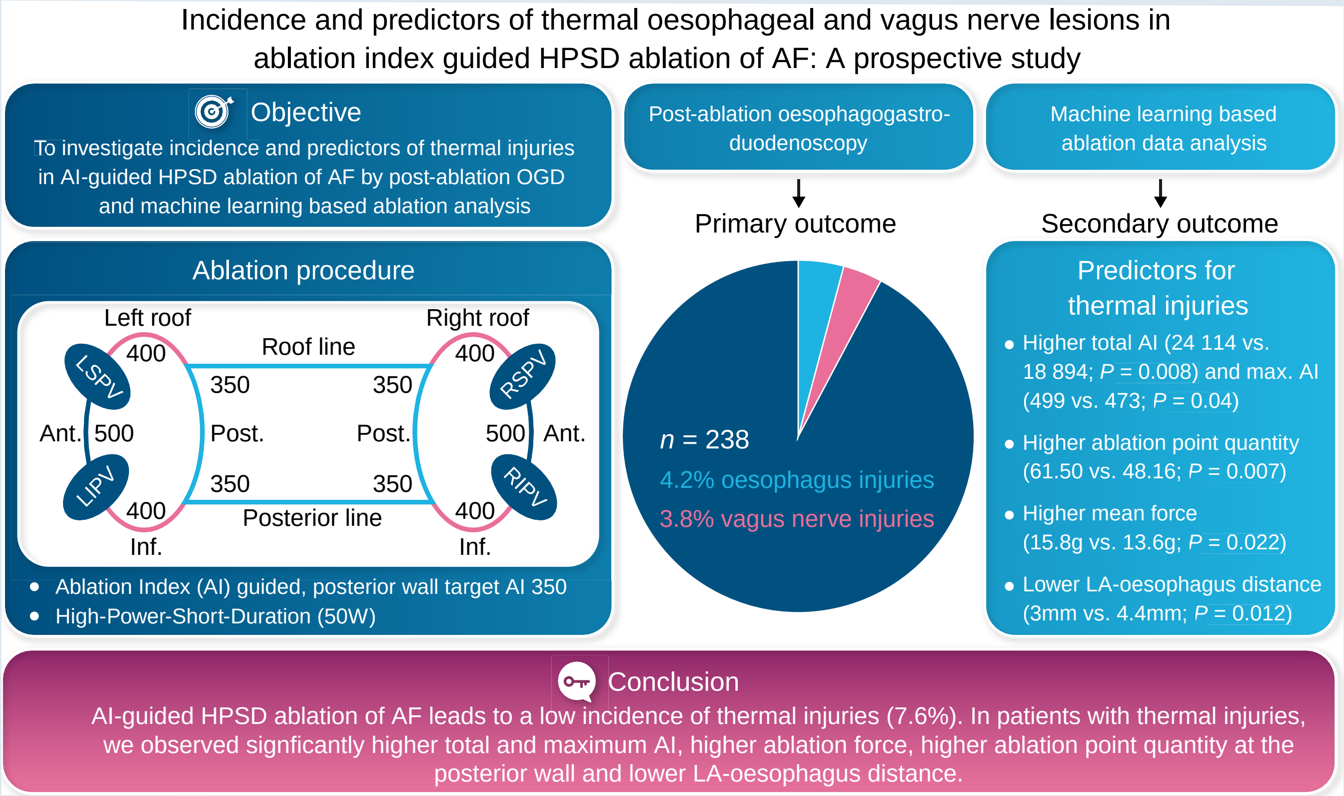
Graphical Abstract



Keywords Atrial fibrillation • Catheter ablation • HPSD • Thermal injuries • Machine learning

What's new?

- We observed a particularly low incidence of thermal injuries of the oesophagus (4.2%) and vagus nerve (3.8%) using an Ablation Index (AI)-guided HPSD approach for pulmonary vein isolation.
- Patients with thermal injuries had significantly lower distances between the oesophagus and left atrium as well as a smaller left atrial surface.
- Our machine learning algorithm refers each ablation point to an anatomical area of the left atrium and gives out the ablation variables for each area. It therefore facilitates the detailed analysis immensely.
- By analysing ablation data exclusively for the points placed at the posterior wall, we found a significant correlation between force, quantity of ablation points, number of points per surface, total and maximum AI at the posterior wall, and the occurrence of thermal injuries.
- Ablation data is currently mainly used for intraprocedural decision-making. We could suggest potential benefits of post-procedural evaluation for prediction of thermal injury.

Introduction

Atrial fibrillation (AF) is the most frequent heart rhythm disorder in adults, with a rising prevalence due to an aging population and increasing risk factors such as hypertension, structural heart disease, high BMI, and diabetes.[1] Radiofrequency (RF) catheter ablation is one of the main approaches for treatment of AF.[2] High-power-short-duration (HPSD) ablation uses more power (50 W) for a shorter time. Heat-induced lesions in the left atrium (LA) have been shown to be wider but less deep in HPSD, which may indicate less heat conduction to surrounding structures and therefore less thermal oesophageal lesions compared to Low-power-low-duration (LPLD) ablation.[3,4] The Ablation Index (AI) gives the operator real-time feedback of ablation force, power, and time in a single parameter, which correlates with lesion depth. Ablation Index-guided RF ablation has proved to be a safe and effective approach for pulmonary vein isolation (PVI).[5,6] Since the AI-guided HPSD approach leads to shorter procedure time and increased first-pass PVI, it is now widely used as the standard procedure for RF catheter ablation of AF.[4,7]

Machine learning (ML) is a rapidly evolving field with an increasing influence on data analysis in medicine. Machine learning algorithms are trained on large datasets to learn patterns and make predictions. This makes them valuable for a variety of medical tasks, such as developing predictors for patient outcome or adverse events.[8]

Thermal oesophageal lesions occur in ∼4.5–7% of patients who underwent catheter ablation using the HPSD approach.[5,9,10] These lesions reach from a circumscribed erythema without therapeutic consequences to atrial–oesophageal fistula with an incidence of 0.2% and a mortality of ∼55%.[11,12] An incidence of gastric hypomotility due to vagus nerve injury up to 33% was reported in previous studies performing HPSD ablations.[10] However, to the best of our knowledge, there are no reliable indicators on when to perform a post-procedural screening for thermal oesophageal lesions. In this prospective study, we aim to measure the incidence and find reliable predictors of thermal injuries to the oesophagus and the vagus nerve using ML.

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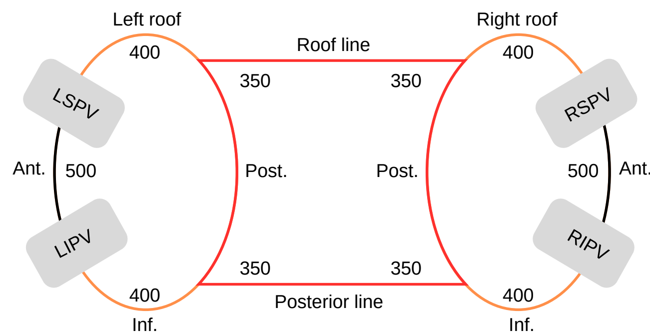

Figure 1 Ablation protocol. Posterior view of the left atrium with ablation lines and targeted Ablation Index indicated for each area. 'Posterior 1' segment includes left and right posterior ablation, roof line and posterior line; 'Posterior 2' segment additionally includes left and right roof and left and right inferior lines. LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein.

Methods

Study design

This prospective observational study at Leipzig Heart Centre, Germany, was designed to investigate the incidence of thermal injuries in patients who underwent AI-guided HPSD catheter ablation for AF. We investigated potential predictors for thermal injuries by analysing both catheter ablation data using ML and clinical, patient-related data. Between 15 February 2021 and 10 August 2023, we included patients between 18 and 80 years who had an indication for catheter ablation of AF. Patients with contraindications for either catheter ablation or oesophageal endoscopy were excluded as well as pregnant patients and patients who already had two or more prior ablations of AF. The study was registered in clinicaltrials.gov (NCT05709756). It was approved by the local ethics committee and performed in accordance with the Declaration of Helsinki. All patients gave their written informed consent prior to enrolment in this study. The data underlying this article will be shared on reasonable request to the corresponding author.

Ablation procedure

Prior to the ablation procedure, most patients received a cardiac MRI or CT enabling measurement of the LA surface, diameters of the cardiac chambers, ejection fraction, atrial–oesophageal distance, oesophageal diameter, and oesophageal position. The oesophageal position was classified into one of three categories: near the left pulmonary veins (PVs), behind the central posterior wall and near the right PVs. Exemplary MRIs for each category are pictured in Supplementary material online, *Figure S1*. Patients undergoing catheter ablation were deeply sedated with propofol infusion. After transseptal puncture, the CARTO 3® (Biosense Webster, Baldwin Park, CA, USA) 3D Mapping system was used to create a precise map of the LA. The PVs were isolated by placing circumferential lesions around ipsilateral vein pairs with point-by-point ablation. We used an irrigated-tip catheter with RF as the energy source (Thermocool-STSF, Biosense Webster, Inc.). Additional ablation lines were placed at the operator's discretion to specifically target the underlying substrate. These included mitral isthmus ablation, box lesions, roof lines, and septal lines. Neither oesophageal temperature probe nor intracardiac ultrasound guidance was used. The use of CARTO 3® allowed the operator to track the applied energy on each point in real time using the AI. The AI incorporates power, contact force, and ablation time, and therefore gives an indication for width and depth of the resulting tissue lesion at each point. As shown in *Figure 1*, we used an AI-guided approach, where the operators were asked to limit the applied energy at the posterior wall of the LA to a maximum AI of 350 per ablation point. Left and right roof lines as well as the inferior lines on both sides were limited to an AI of 400. In the remaining atrium, AIs up to 500 could be applied. Operators could however deviate from these targets at their discretion.

Ablation analysis with machine learning

In our study, we collected ablation data from the enrolled patients for further analysation after the procedure. The CARTO System generates a map with exact coordinates and ablation parameters of each ablation point. These parameters include power, contact force, ablation time, impedance drop, and AI. To analyse each point, we developed and trained a ML algorithm, which can refer each ablation point to an anatomical part of the LA. We divided the atrium into ten sections as shown in *Figure 2* and had the ML algorithm give an output for each section including quantity of ablation points, maximum, total and mean AI, mean impedance drop, mean force, and mean duration. Since the oesophagus and vagus nerve are in close anatomical relation with the posterior wall of the LA, we aimed to specifically analyse the ablation data from this area. To filter out the ablation points at the posterior wall, we clustered the sections into two posterior groups as shown in *Figure 1*. 'Posterior 1' (red lines) includes all lines that are directly at the posterior wall. 'Posterior 2' (red and orange lines) adds the upper and lower parts of the circumferential lesions around the PVs. Therefore 'Posterior 2' also includes the more peripheral ablation points at the posterior wall of the atrium. The ML algorithm allowed us to directly extract the ablation data for the posterior wall of the LA and thereby specifically analyse the relevant ablation areas for possible thermal injuries. In all first-time PVI cases, the algorithm additionally measured the minimum and mean distance between the left and right posterior ablation points to estimate the proximity of left and right circular ablation lines around the PVs at the posterior wall.

Endoscopy and thermal injuries

Each enrolled patient underwent oesophagogastroduodenoscopy (OGD) 1 day after catheter ablation, performed by gastroenterologists experienced in detecting and assessing thermal injuries after RF ablation. Endoscopically detected oesophageal lesions were photo documented and precisely described, including width and severity. Lesions were classified into three categories: erythema, ulcer, and atrial–oesophageal fistula. Vagus nerve lesions were detected by gastric food retention despite fasting for more than 6 h prior to gastroscopy due to presumed gastroparesis. The endoscopist was blinded to ablation data and specific patient data analysis. Each patient received a two-week follow-up call asking for symptoms of oesophageal injuries including dysphagia, retrosternal pain, and fever.

Statistics

The sample size for this study was calculated based on the reported incidence of thermal oesophageal lesions of 10% (7.2% erythema, 2.8% ulcer, no fistula) in the OPERA trial performed at Heart Centre Leipzig that used LPLD ablation on a total of 180 patients.[13] For the HPSD ablation approach used in our study, we estimated an incidence of thermal oesophageal lesions of ∼5%. The sample size was calculated to allow us to detect a significant difference in the incidence of thermal oesophageal lesions

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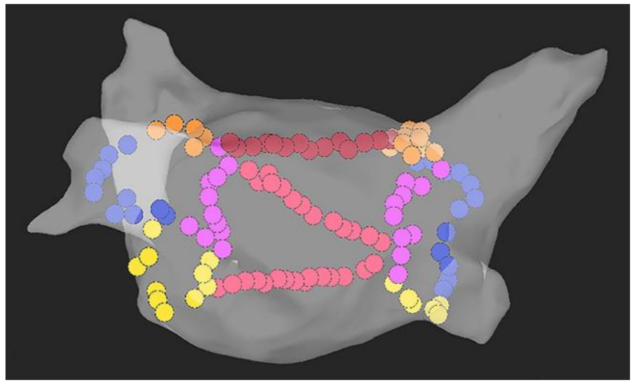

Figure 2 Machine learning output: left atrium posterior view, ablation points colour-coded. Light red: inferior line/posterior substrate; dark red: roof line; pink: left/right posterior; orange: left/right roof; yellow: left/right inferior; blue: left/right anterior.

Table 1 Patient characteristics

	Total	Thermal injury	No thermal injury	*P*
n	238	18	220	
Age	64.95 (9.98)	64.67 (9.09)	64.97 (10.07)	0.902
Sex female	95 (39.9)	11 (61.1)	84 (38.2)	0.097
BMI	29.27 (4.98)	28.55 (5.28)	29.33 (4.96)	0.523
Structural heart disease (%)	107 (45.0)	8 (44.4)	99 (45.0)	0.934
Hypertension (%)	199 (83.6)	11 (61.1)	188 (85.5)	0.019
Diabetes (%)	37 (15.5)	3 (16.7)	34 (15.5)	1.000
PPI (%)	47 (19.7)	4 (22.2)	43 (19.5)	1.000
Persistent AF (%)	154 (64.7)	11 (61.1)	143 (65.0)	0.940
CHA2DS2VASc	2.39 (1.33)	2.50 (1.10)	2.39 (1.35)	0.729
PVI-redo (%)	54 (22.7)	4 (22.2)	50 (22.7)	1.000
LA surface (cm^2)	29.18 (7.48)	24.92 (6.49)	29.53 (7.47)	0.032
LVEF %	56.82 (8.65)	57.33 (7.65)	56.78 (8.75)	0.794
LVEDD ml	51.80 (5.51)	51.29 (5.92)	51.85 (5.49)	0.715
LA-oesophagus distance (mm)	4.33 (2.13)	2.96 (1.45)	4.44 (2.14)	0.012
Oesophagus diameter (mm)	19.02 (5.90)	18.95 (5.82)	19.85 (5.91)	0.579
Additional findings OGD (%)	85 (35,7)	4 (22.2)	81 (36.8)	0.324
Oesophageal lesion (%)	10 (4.2)	10 (55.6)	0 (0.0)	
Vagus nerve lesion (%)	9 (3.8)	9 (50.0)	0 (0.0)	

Values are presented as mean (standard deviation) or *n* (%).

between patients who underwent LPLD ablation and those with HPSD ablation, with a margin of error of 5% and a power of 80%. We tested the significance of differences in continuous variables with one-way Welsh's tests and in categorical variables with χ^2 tests.[14,15] Statistical analyses were performed using R software, version 4.3.2.

Results

Patient characteristics

Two hundred sixty-two patients with the indication for catheter ablation of AF were enrolled in the study. The dropout rate of 9% was mostly due to withdrawal of consent for the OGD or study and cancellation of the catheter ablation due to findings in pre-procedural diagnostics. A total of 238 patients (39.9% female, mean age 65.0 ± 10.0 years, 64.7% persistent AF, 22.7% Redo-PVI) underwent both catheter ablation of AF and OGD, were analysed in this study and stratified by the occurrence of thermal injuries. *Table 1* shows the baseline patient characteristics. We observed a significantly lower rate of hypertension in patients who developed thermal injuries [11/18 (61.1%) vs. 188/220 (85.5%), $P = 0.019$]. The surface area of the LA, as measured by cardiac MRI, CT, or echocardiography, was significantly smaller in patients with thermal injuries than in those without (24.92 ± 6.49 cm^2 vs. 29.53 ± 7.47 cm^2, $P = 0.032$). The proportion of patients with first PVI and Redo-PVI was comparable between the groups with and without thermal injuries [4/18 (22.2%) vs. 50/220 (22.7%), $P = 1.00$]. One hundred seventy-five (73.5%) patients received an MRI prior to the procedure that allowed us to measure the minimal distance between the oesophageal mucosa and the inner wall of the LA. This distance was significantly lower in patients in whom thermal lesions were diagnosed (2.96 ± 1.45 mm vs. 4.44 ± 2.14 mm, $P = 0.012$). The transversal oesophageal diameter showed no significant difference in patients with and without thermal injuries. Among 175 analysed MRIs, in 70 patients, the oesophagus passed near their left PVs, in 81 patients, central behind the posterior wall, and in 24 patients, close to their right PVs. We did not observe a significant influence of the oesophagus' position on the occurrence of thermal injury. However, there was a tendency for patients with an oesophagus near their left PVs to be less at risk for thermal injuries as presented in *Figure 3* (2.86% left vs. 9.88% central, $P = 0.161$; 2.86% left vs. 16.67% right, $P = 0.057$). A detailed analysis of oesophageal and vagus nerve injury for each category is presented in the Supplementary material online, *Table S1*.

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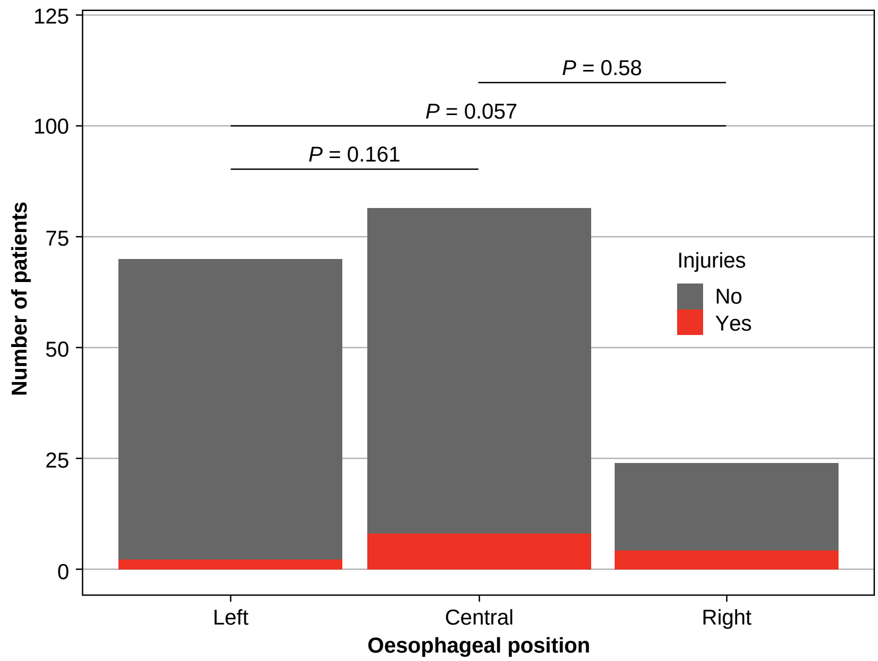

Figure 3 Total number of patients and thermal injury occurrence for each oesophageal position category. *P*-values of the χ^2 tests between each group are indicated in the diagram.

Thermal injuries

Overall, 18 out of 238 patients who received catheter ablation of AF developed thermal injuries. Nine patients had vagus nerve injury (3.8%). Ten patients showed thermal oesophageal lesions (4.2%) of whom eight lesions were categorized as 'erythema' and two lesions as 'ulcer'. No patient developed atrio-oesophageal fistula. The lesion size reached from 5 to 10 mm with a mean of 6.67 mm. Five patients with oesophageal lesions had follow-up OGDs in which all showed signs of healing and did not require intervention. One patient had both vagus nerve injury and an oesophageal lesion. In a two-week follow-up by phone call, none of the 18 patients reported signs of permanent injuries. In 85 patients (35.7%), the OGD revealed additional findings, mainly reflux oesophagitis, gastritis, and diaphragmatic hernia.

Ablation data

The ML-based analysis of each anatomical segment of the LA allowed us to analyse ablation data specifically from the posterior wall. As shown in *Figure 1*, we separately assessed the 'Posterior 1' (red lines) and 'Posterior 2' (red and orange lines) segments. *Table 2* shows the ablation data segregated by occurrence of thermal injuries. Patients with thermal injuries had a significantly higher total AI in 'Posterior 2' segment that was calculated by summarizing the AIs of every ablation point in the segment (24 113.86 ± 8764.61 vs. 18 894.13 ± 7863.28, $P = 0.008$). These results are presented in *Figure 4*. Mean AI did not differ significantly in any of the analysed groups. The maximum AI of a point in the segments 'Posterior 1 and 2' has been significantly higher in patients with thermal injuries (Posterior 2: 499.10 ± 95.15 vs. 473.09 ± 44.49, $P = 0.04$). We observed a significantly higher quantity of ablation points in the 'Posterior 2' segment in patients with thermal injuries (61.50 ± 20.45 vs. 48.16 ± 19.60, $P = 0.007$). To compare the density of ablation points, we divided the quantity of points in each segment by total atrial surface area. This index of both, 'Posterior 1 and 2', was significantly higher in patients with thermal injuries (Posterior 1: 1.28 ± 0.68 vs. 0.90 ± 0.62, $P = 0.036$; Posterior 2: 2.64 ± 1.01 vs. 1.76 ± 0.89, $P = 0.001$). The mean distance between left and right PVI circles in first-time PVI cases, measured by the machine learning algorithm, was significantly lower in patients with thermal injuries (39.76 ± 8.39 mm vs. 44.04 ± 7.15 mm, $P = 0.044$). The mean impedance drop did not differ between the two groups, whereas mean contact force was significantly higher in patients with thermal injury in all analysed segments, 'Posterior 2' being the most significant (Posterior 2: 15.76 ± 3.87 g vs. 13.55 ± 3.88 g, $P = 0.022$). Among all assessed segments, 'Posterior 2' seems to have the best predictive value for the occurrence of thermal injury with the most significant discriminators 'AI total', 'number of points', and 'number of points per surface'. The additional ablation of arrhythmogenic substrate such as box lesions, mitral isthmus, roof line, or septal line did not show significant differences between patients with and without thermal injuries. However, there is a tendency for box lesions to be more frequent in patients who developed thermal injuries [5/18 (27.8%) vs. 22/220 (10%), $P = 0.057$].

Since we observed significantly more thermal lesions in patients with smaller atria, we additionally compared ablation data between patients with below and above mean atrial surface areas. The baseline ablation data were comparable in both groups. However, the quantity of ablation points at the posterior wall in relation to the atrial surface area was significantly higher in patients with below mean atrial size (Posterior 1: 1.13 ± 0.70 vs. 0.68 ± 0.43, $P \leq 0.001$; Posterior 2: 2.24 ± 0.95 vs. 1.33 ± 0.60, $P \leq 0.001$). A detailed comparison is presented in Supplementary material online, *Table S2*.

Comparing first-time PVIs and redo cases, we did not observe significant differences in the ablation parameters. However, among the redo cases, significantly more substrate ablation was performed (mitral isthmus: 4.3% vs. 18.5%, $P = 0.002$; roof line 4.3% vs. 14.8%, $P = 0.017$). A detailed analysis of the redo cases compared to first-time PVIs is presented in the Supplementary material online, *Table S3*.

Discussion

In our prospective study, we observed a considerably lower incidence of thermal oesophageal lesions (4.2%) compared to previous studies

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Table 2 Ablation data

	Thermal injury	No thermal injury	*P*
n	18	220	
Mitral isthmus (%)	2 (11.1)	16 (7.3)	0.898
Box lesion (%)	5 (27.8)	22 (10.0)	0.057
Roof line (%)	3 (16.7)	13 (5.9)	0.207
Septal line (%)	5 (27.8)	34 (15.5)	0.304
Number of points Posterior 1	30.06 (15.56)	23.90 (14.24)	0.085
Number of points Posterior 2	61.50 (20.45)	48.16 (19.60)	0.007
Number of points total	83.83 (24.77)	71.71 (28.58)	0.084
Number per surface Posterior 1 (1/cm^2)	1.28 (0.68)	0.90 (0.62)	0.036
Number per surface Posterior 2 (1/cm^2)	2.64 (1.01)	1.76 (0.89)	0.001
Number per surface total (1/cm^2)	3.54 (1.34)	2.69 (1.52)	0.054
Total AI Posterior 1	11 379.46 (5988.15)	9074.18 (5689.16)	0.104
Total AI Posterior 2	24 113.86 (8764.61)	18 894.13 (7863.28)	0.008
Total AI total	33 552.81 (10 561.29)	28 821.08 (11 458.65)	0.094
Mean AI Posterior 1	380.51 (32.69)	382.62 (25.90)	0.749
Mean AI Posterior 2	392.45 (36.93)	390.56 (31.41)	0.811
Mean AI total	400.96 (37.56)	402.81 (28.80)	0.800
Maximum AI Posterior 1	468.03 (103.11)	432.83 (61.24)	0.032
Maximum AI Posterior 2	499.10 (95.15)	473.09 (44.49)	0.040
Maximum AI total	513.60 (90.33)	491.98 (39.39)	0.059
Impedance drop Posterior 1	6.55 (1.67)	6.75 (2.43)	0.735
Impedance drop Posterior 2	7.23 (1.75)	7.72 (2.39)	0.399
Impedance drop total	7.65 (1.86)	8.03 (2.16)	0.481
Force Posterior 1 (g)	15.47 (3.55)	13.14 (4.52)	0.035
Force Posterior 2 (g)	15.76 (3.87)	13.55 (3.88)	0.022
Force total (g)	16.09 (3.93)	13.86 (3.94)	0.023
Minimal posterior PVI circle distance (mm)	31.34 (8.70)	36.29 (8.81)	0.055
Mean posterior PVI circle distance (mm)	39.76 (8.39)	44.04 (7.15)	0.044

Values are presented as mean (standard deviation) or *n* (%).

using HPSD ablation ranging between 4.5% and 7%.[5,9,10] We identified significant correlations between higher maximum and total AI, higher mean force, higher quantity of ablation points at the posterior wall, closer proximity of the atrial wall to the oesophagus and smaller surface of the LA, and the occurrence of thermal injuries to the oesophagus and vagus nerve.

The overall frequency of thermal oesophageal injuries in our study was substantially lower than in the OPERA trial performed at Leipzig Heart Centre using non-AI-guided LPLD ablation (25 W) with an overall incidence of 10%. In the OPERA trial, the occurrence of oesophageal lesions did not differ between the two groups with and without intraoesophageal temperature probe (11% with probe vs. 9% without probe, $P = 0.62$).[13] Similar results were presented by Grosse Meininghaus *et al.* in a study with a comparable design (25 W LPLD) including 86 patients. The use of a temperature probe did not have a positive effect on lesion development (13.6% with probe vs. 4.8% without probe, $P = 0.27$).[16] However, there are studies suggesting advantages of temperature probes in terms of acute oesophageal safety. Halm *et al.*[17] observed higher oesophageal temperatures to be predictive of thermal injuries and occurrence of these injuries only if temperatures above 42°C were reached. The study highlights the potential predictive value of temperature measurement in terms of thermal lesion development. Others showed a higher incidence of thermal lesions when temperature probes were being used. A study with 80 patients conducted by Müller *et al.*[18] reported significantly more thermal oesophageal lesions after LPLD ablation (25 W) using a temperature probe (30% vs. 2.5%, $P \leq 0.01$). This might be due the probes metal acting as a RF antenna and therefore leading to tissue heating. Whilst this antenna effect of metallic probes has led to higher temperatures observed in a bovine model, other studies could not find clinically significant electrical interference due to temperature probes.[19,20] Although most studies listed above did use slightly different ablation protocols, the majority of these studies could not observe improved safety through the use of temperature probes. We therefore decided not to use a probe in our HPSD approach. To this day, there is a lack of evidence concerning the use of temperature probes in HPSD ablation. Further randomized controlled studies are needed to evaluate this issue.

The low incidence of thermal lesions observed in our study might be explained by our AI-guided approach, which has shown to be particularly effective and safe in previous studies.[21,22] Animal studies have described HPSD ablation lesions to be wider and less deep due to higher resistive heating rather than convective heating as in LPLD.[23] These

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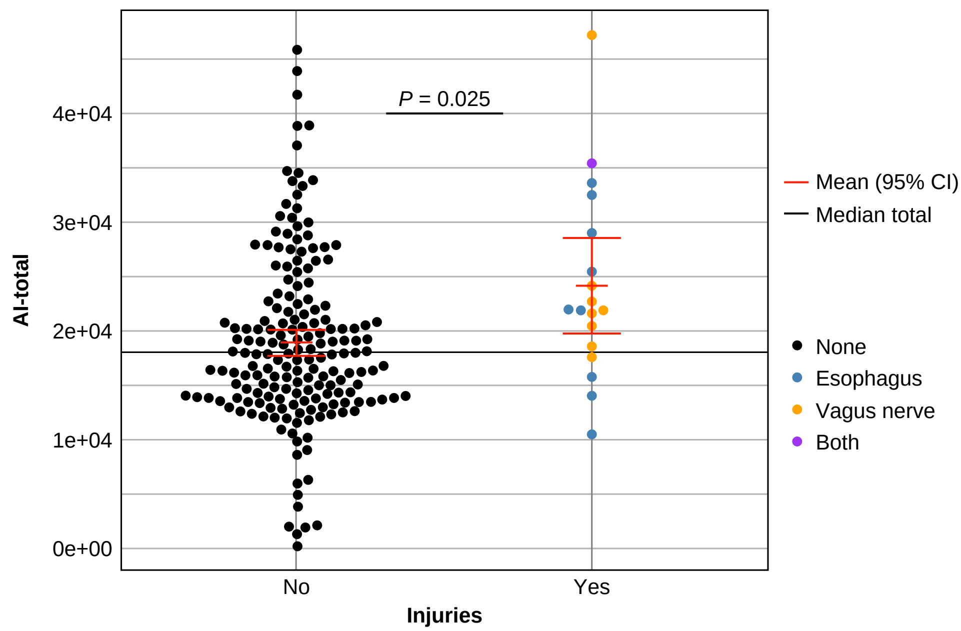

Figure 4 Total AI in 'Posterior 2' segment in patients with and without thermal injuries.

findings suggest less heat being transmitted towards surrounding structures such as the oesophagus and vagus nerve. A recent study compared AI-guided HPSD and LPLD ablation in terms of oesophageal safety and long-term success, targeting an AI of 400 at the posterior wall. Whilst procedure duration and arrhythmia recurrence were reduced in the HPSD group, the measured oesophageal temperature and incidence of thermal oesophageal lesions (4.5%) did not differ significantly.[9] Another recently conducted large-scale study including 820 patients who underwent OGD after catheter ablation proofed AI-guided HPSD ablation to be safe.[24] De Smet *et al.* used maximal protective measures to prevent oesophageal lesions incorporating the CLOSE protocol.[22] Among others, these included the use of 35–45 W, an AI limit of 400 at the posterior wall, and further AI reduction in case of temperature rise above 38.5°C measured by oesophageal temperature probe. In case of such temperature rise, endoscopy was conducted within 2–3 weeks, which revealed ulcers in 0.9% of these patients. However, the low rate of thermal lesions might be explicable by the late endoscopy. At the time of endoscopy, less significant lesions might not have been detectable anymore.

The primary objective of our study is the incidence of thermal injuries of the oesophagus and vagus nerve. Since we aimed to detect all thermal lesions, including those with minimal mucosal damage that might not have been evident in OGDs conducted later, we strategically chose to perform OGDs within 24 h after ablation. It is noted that atrial–oesophageal fistulas typically take two to four weeks to become clinically apparent, necessitating an OGD within this timeframe for accurate diagnosis.[12] Given their rare occurrence rate of ∼0.2%, our study, which included 238 participants, was not designed and powered to assess fistula formation but rather focused on detecting any oesophageal lesions.[11,12] To enhance patient safety regarding fistula development, follow-up OGDs were performed within a week after the primary OGD for patients with significant lesions at the discretion of the gastroenterologists. Further larger-scale studies are required to investigate the incidence of atrial–oesophageal fistulas following AI-guided HPSD ablation and the role of endoscopy timing for lesion detection.

There are very few studies investigating the correlation between ablation data and the occurrence of thermal injuries. Ishidoya *et al.*[25] analysed ablation data of 30 patients including AI, RF duration and contact force but could not find a significant difference in patients with and without thermal oesophageal injury. Chelu *et al.*[26] conducted a study with 36 participants, finding a significantly higher contact force used in patients who developed an oesophageal lesion. In a recent prospective study, List *et al.*[11] observed more thermal injuries of the oesophagus and vagus nerve in patients with higher AI targets at the posterior wall during ablation (380) than with lower AI targets (320–350) but did not evaluate the implementation of these targets after the procedure. A larger-scaled study with a comparable design was conducted by Müller *et al.* who analysed HPSD ablation in 795 patients with an AI target of 300 vs. an AI target of 350 at the posterior wall. A significantly lower oesophageal injury rate was observed following ablations with a lower AI target (3% vs. 7%, $P = 0.019$), suggesting the targeted AI to be predictive of thermal injuries.[27] These studies suggest a causal association between certain ablation parameters and the occurrence of thermal injuries. However, there are no larger prospective studies with detailed post-procedural analysis of ablation data. The specific analysis of ablation performed at the LA's posterior wall has not yet been explored in terms of prediction of thermal injuries. We approached the need of a structural evaluation of ablation data including AI, quantity of ablation points, contact force, and impedance by specifically analysing them subdivided into anatomical regions of the LA. This is the first study that used ML to precisely analyse data from catheter ablation of AF regarding predictive value for thermal complications. Our ML model enabled us to assort each ablation point to an anatomic area of the LA. Due to its proximity to the oesophagus and vagus nerve, we had particular interest in the ablation performed at the posterior wall.

For the first time, we discovered a significant correlation between ablation data at the posterior wall and the occurrence of thermal injuries in a large prospective study. The total and maximum AI at the posterior wall, defined as 'Posterior 2' as pictured in *Figure 1*, was substantially higher in patients who developed thermal injuries. These findings suggest a high predictive value of the AI in post-procedural

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analysis. To demonstrate its predictive value, we generated a ROC curve for 'AI total Posterior 2' shown in Supplementary material online, *Figure S2*. Due to the low incidence of thermal lesions in our cohort, the curve does not yet enable us to establish definitive cut-off values for performing an OGD. Further, larger-scaled studies are needed to validate our suggested variables as predictors of thermal injuries. The significance of total AI might be partly explicable by the higher quantity of ablation points in the 'Posterior 2' segment. A higher number of points might increase the risk of overshoots and therefore increase the maximum AI, which is also significantly higher in patients with thermal injuries. To identify the ablation area with the highest predictive value for thermal injuries, we evaluated the correlation between ablation data and thermal injuries for two differently defined posterior segments. 'Posterior 2' includes right and left roof lines as well as inferior lines in addition to the right and left posterior lines, roof line, and posterior line. It therefore covers the whole atrium's posterior wall including the more peripheral regions. Ablation in the 'Posterior 2' segment has shown a stronger effect on the occurrence of thermal injuries in both AI, ablation point quantity, and force analysis. This might be due to higher AI targets in the more peripheral areas that lead to an overall higher total and maximum AI in 'Posterior 2' compared to 'Posterior 1'. Despite our targeted AI of 350 at the posterior wall, we observed a mean maximum AI of 468 in the 'Posterior 1' segment. Although our ablation regimen has shown to be safe considering the low incidence of thermal injuries, an automated AI-guided ablation generator could further increase the procedural safety. Further research is needed to evaluate this approach.

Regarding clinical parameters, we observed significantly shorter distances between the LA and the oesophagus in pre-procedural MRI or CT in patients with thermal injuries. This distance has previously been identified as a possible predictor for thermal oesophageal injuries in a smaller study conducted by Ishidoya *et al.*[25] As many patients receive a cardiac MRI before catheter ablation, measuring the distance between oesophagus and LA should be considered when estimating the risk for thermal injury. The large number of MRIs performed on our participants allowed us to conduct a detailed analysis of the influence of anatomical relations between oesophagus and left atrium on the development of thermal injuries. We did not observe any significant differences in thermal lesion occurrence between the three categories for oesophageal position. However, a non-significant trend towards more injuries in patients with a right-sided and central compared to a left-sided oesophagus was observed as shown in *Figure 3*. Due to the low incidence of thermal injuries in our study, future research is needed to further evaluate the influence of oesophageal position on thermal injury development.

We also identified the absence of hypertension and small LA surface as possible predictors for thermal injuries. Hypertension leads to remodelling and thereby fibrosis and thickening of the LA wall.[28] This effect potentially leads to a further distance between myocardial endothelium and the oesophagus that correlates with a decreased risk for thermal injuries. A small LA surface area implies an overall smaller LA with lower diameter. The circumferential lesions around the PVs must be placed within a smaller area and with less space at the posterior wall. We confirmed this hypothesis by measuring the ablation circles' distance in all first-time PVI cases, using the machine learning tool. The observed lower distance between ablation circles at the posterior wall in patients with thermal injuries possibly leads to more energy being applied near the oesophagus and therefore more heat development. These findings align with our observation that a higher density of ablation points at the posterior wall correlates with thermal injury occurrence. Analysing the number of ablation points at the posterior wall per atrial surface revealed a higher relative density of points leading to more thermal injuries. The relative density of ablation points at the posterior wall has been significantly higher in patients with below mean atrial surface areas. This suggests the greater risk of thermal injury in patients with smaller atria to be conducted by increased density of ablation points. However, the index we calculated does not represent the actual absolute density of points at the posterior wall, but rather sets the number of posterior ablation points in relation to the overall atrial size. These findings suggest the combination of ablation and clinical data to be particularly valuable for thermal injury prediction.

Among the 238 participants in this study, 77.3% were first-time PVIs. However, we included 53 patients undergoing their second ablation for AF. Our focus was on a detailed analysis of the actual ablation on the posterior wall, rather than ensuring that a complete PVI was performed. Thermal injuries occurred in both first-time PVIs and redo cases at the same rate. Thus, redo cases do not seem to be superior in terms of acute oesophageal safety. We therefore suggest redo cases to be included in future research investigating this issue.

In conclusion

Ablation Index-guided HPSD ablation of AF has a low incidence of thermal lesions compared to previous studies on HSPD or LPLD. Automatically derived ablation parameters using ML, such as total and maximum AI, higher mean force, quantity of ablation points on the posterior wall, atrial–oesophageal distance, and LA surface area correlate with the occurrence of thermal injuries. Considering all the findings stated above, it is well conceivable to develop a ML-based tool that calculates the individual risk for thermal injuries at the end of a catheter ablation procedure. Further, larger-scaled studies are warranted to clarify this issue.

Limitations

We had a 9% dropout in our study. However, the baseline characteristics of these patients were comparable with the remaining patients. Therefore, we do not expect a bias attributable to the dropout rate. Due to the COVID-19 pandemic, the inclusion phase of the study was longer than expected. The impact of the timing of endoscopy on the detection of thermal lesions remains unclear. Additional research is needed to explore this relationship. In our study on HPSD ablation, we did not employ an oesophageal temperature probe. However, future research will determine whether its use affects acute oesophageal safety in HPSD ablations.

Supplementary material

Supplementary material is available at *Europace* online.

Funding

Supported by the Open Access Publishing Fund of Leipzig University.

Conflict of interest: none declared.

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