Intracardiac Echocardiography for Detection of Thrombus in the Left Atrial Appendage: Comparison With Transesophageal Echocardiography in Patients Undergoing Ablation for Atrial Fibrillation: The Action-Ice I Study

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Background—Transesophageal echocardiography (TEE) is the gold standard for the exclusion of thrombi in the left atrial appendage (LAA) before ablation for atrial fibrillation (AF). However, the sensitivity of TEE in excluding LAA thrombi is not perfect, especially when adequate LAA imaging cannot be achieved. In addition, in some situations, TEE is contraindicated (esophageal injury or diverticulum) or not feasible under conscious sedation (dysphagia or inability to swallow TEE probe). Thus, alternative tools are needed for LAA imaging.

Methods and Results—Seventy-six consecutive patients (56 men; mean age, 55±9.6 years) scheduled for atrial fibrillation ablation underwent TEE before the procedure and LAA assessment by ICE. An 8F AcuNav probe was introduced into right atrium, pulmonary artery, and coronary sinus. LAA structure was analyzed by the echocardiographer and electrophysiologist who were blinded to the results of TEE. ICE probe was positioned in the right atrium in all patients, in the pulmonary artery in 64 of 74 (86%) patients, and in the coronary sinus in 49 of 74 (66%) patients. The LAA was properly visualized in 56 of 64 (87.5%) patients from the pulmonary artery versus 13 of 49 (26%) patients from the coronary sinus (P<0.001). From the right atrium, the whole LAA cavity could not be seen in any patient. In those patients in whom LAA was visualized properly by ICE, a perfect agreement between ICE and TEE was obtained (both techniques detected LAA thrombus in 2 patients and excluded LAA thrombus in the remaining patients).

Conclusions—ICE can be used safely and effectively for the evaluation of LAA in patients undergoing atrial fibrillation ablation. ICE imaging from pulmonary artery is accurate for LAA visualization.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01371279.
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Key Words: atrial fibrillation • echocardiography, transeophageal • intracardiac imaging techniques • thrombosis

Transesophageal echocardiography (TEE) is the gold standard for the exclusion of thrombi in the left atrial appendage (LAA) before ablation for atrial fibrillation (AF). However, the sensitivity of TEE in excluding LAA thrombi is not perfect, especially when adequate LAA imaging cannot be achieved. In addition, in some situations, TEE is contraindicated (esophageal injury or diverticulum) or not feasible under conscious sedation (dysphagia or inability to swallow TEE probe). Thus, alternative tools are needed for LAA imaging.

Clinical Perspective on p 1081

In many hospitals, intracardiac echocardiography (ICE) has been used during AF ablation for guiding the transseptal puncture and further imaging during the procedure. The ICE probe is usually positioned in the right atrium (RA). It is not known whether ICE can be used effectively for LAA imaging and which ICE views are the most accurate for this purpose. The standard RA views do not provide adequate consistent visualization of the complete LAA cavity because of the relatively long distance from the LAA to the ICE probe. Placing the ICE catheter in locations that are more proximate to the LAA, such as the pulmonary artery (PA) or the coronary sinus (CS), might improve sensitivity and specificity in detecting the LAA thrombus. The results of a retrospective study have already supported the use of ICE in patients with equivocal TEE findings obtained before electrophysiological procedures. However, the issue of ICE probe placement and whether this technique is not only additive to TEE but may also replace TEE in some patients have not yet been addressed. The present study aimed at answering these questions.
Methods

Patients

The study group included consecutive patients who were scheduled for AF ablation at our institution between September 2011 and August 2012. In total, 76 patients (56 men; age, 55±9.6 years) who gave informed written consent for participation in the study were enrolled. The study protocol was approved by the Ethics Committee of the Postgraduate Medical School, Warsaw, Poland. Most patients had paroxysmal AF (84%), whereas the remaining participants had persistent AF (10%) or long-standing persistent AF (6%). Baseline demographic and clinical characteristics are described in Table 1.

Study Design

All patients underwent computed tomography (CT) of the heart 24 to 48 hours before the procedure. TEE was then performed, and patients underwent ablation within 24 hours from TEE. The ICE probe was inserted at the beginning of the ablation procedure and placed consecutively in the RA, PA, and CS for left atrium (LA) and LAA imaging. The electrophysiological procedure was then started with the ICE probe that was kept inserted in the RA to assist the transseptal puncture and for the entire ablation procedure to visualize the cardiac structures and catheters, as well as to monitor potential complications.

Computed Tomography

Cardiac CT images were obtained using Somatom Definition or Somatom Definition Flash equipment (Siemens AG Medical Solution, Munich, Germany). The LA cavity shape, volume, and dimensions were assessed. The number and diameter of the pulmonary veins were analyzed. The LA and LAA cavities were examined for the presence of thrombus. The LAA morphology was analyzed according to Wang et al.8 The chicken wing LAA is an anatomy characterized by an obvious bend in the proximal or middle part of the dominant lobe or folding back of the LAA anatomy on itself at some distance from the perceived LAA ostium. The wind sock LAA is an anatomy in which 1 dominant lobe of sufficient length is the primary structure. Variations of this LAA type depend on the location and number of secondary or even tertiary lobes arising from the dominant lobe in the inferior direction. The cauliflower LAA is an anatomy that has limited overall length with more complex internal characteristics, several significant lobes, lack of 1 dominant lobe, and close proximity of internal separations or prominent pectinate ridges to the perceived LAA ostium. The cactus LAA is an anatomy where there is a dominant central lobe with secondary lobes extending from the central lobe in both superior and inferior directions. Variations in anatomy are because of the variable number, location, and orientation of the secondary lobes.

Transesophageal Echocardiography

TEE was performed according to the standard practice guidelines9,10 using a multiplane TEE probe 6T (Vivid 9, GE Vingmed Ultrasound, Horten, Norway).

Intracardiac Echocardiography

The AcuNav electronic phased-array diagnostic ultrasound catheter (Siemens AG Medical Solution, Munich, Germany; 5.5–10 MHz; 8F) was introduced through a 10F or 11F hemostatic sheath positioned in the left femoral vein and moved under fluoroscopic guidance to the RA. Next, a 7F multipolar diagnostic catheter (CS; Biotronik, Vicath 10, Berlin, Germany; 2-6-2 spacing—40 mm long from distal...
to proximal pole) was introduced via the left femoral vein and positioned in the CS. The ICE probe was then advanced into the CS, and LAA imaging was performed. In the next stage, the CS catheter and ICE probe were introduced into the PA and positioned parallel in close proximity to each other. The CS catheter was used not only as a guiding wire for the ICE while introducing it into the right ventricular outflow tract (RVOT) and PA but also to ensure the position of the ICE in the PA, above the pulmonary valve, by examining intracardiac signals recorded from the CS catheter. We also felt that it was safer to introduce a more flexible diagnostic catheter first, followed by a stiffer ICE probe. The distance between the tip of the ICE probe with proper visualization of the LAA and level of pulmonary valve was calculated based on the distance between the tip of diagnostic catheter and the most distal pole where intracardiac signals were recorded. To summarize, the diagnostic catheter was used as a marker for the CS and PA to guide the insertion of ICE probe and to measure certain distances (the ICE probe does not record intracardiac potentials). Both fluoroscopic imaging (right anterior oblique and left anterior oblique views) and intracardiac signals were used to ensure the correct position of the ICE probe.

Images obtained by the ICE probe were analyzed online using an echocardiographic system (Cypress, Siemens AG Medical Solution, Munich, Germany). Fluoroscopy was performed with a single-plane digital angiographic system (Integris CV, Philips Healthcare, DA Best, The Netherlands).

The electrophysiologist performing the ICE examinations and an experienced echocardiographer who attended the electrophysiology laboratory and assessed the LAA images were blinded to the preprocedural TEE results, which were performed by another echocardiographer. The thrombus was a well-defined mass, which could be immobile or show varying degrees of mobility. The quality of visualization of the LAA from the PA and CS was measured on a 6-grade scale: grade 5, excellent view (entire LAA was imaged); grade 4, good (entire LAA was imaged but quality was <5); grade 3, average (only the ostium of the LAA to LA and proximal part of the LAA trunk was imaged); grade 2, low (only the ostium of the LAA to LA was imaged); grade 1, poor (only a part of LAA was visualized as part of the trunk without clear image); grade 0, no diagnostic view. The presence of a thrombus in the LAA was assessed using a binary scale (yes or no). When it was not possible to image the entire LAA, the result was graded as 3. The presence of a spontaneous echo contrast was also assessed but was not subjected to statistical analysis in the present study because it did not influence the decision to perform the AF ablation procedure as much as the thrombus did.

After completing the ICE examination, a transseptal puncture, an ablation, and, if necessary, an intraprocedural electric cardioversion were performed on the condition that the preprocedural TEE had excluded the LAA thrombus.

The time spent from the RA to the PA and CS to achieve a proper view of the LAA was measured. The time spent advancing the ICE from the RA to the CS and PA to achieve a satisfactory view was limited to 15 minutes each, after which the attempt was regarded as a failure and the view was graded 0. Additional radiation exposure during ICE probe positioning in the PA and CS was also measured.

Statistical Analysis

The results are presented as means±SD or as numbers and percentages. Qualitative variables were compared using the χ² or Fisher test. The McNemar test for paired binary data was used to compare the percentages of view grades 4 and 5 from PA and CS. A value of P<0.05 was considered significant. A learning curve was constructed as a classical Kaplan–Meier plot to present and compare the learning progress of the operator. In addition, the number of procedures after which the success rate was constant was identified. The event of interest was getting an excellent and good quality image instead of a typical survival event usually considered in context of the Kaplan–Meier formalism.

Results

Overall Results

Of the 76 patients enrolled in the study, 74 underwent TEE and were enrolled in the study. TEE was not performed in 2 patients because of the presence of esophageal varices in 1 patient and inability to swallow the TEE probe in the other patient. CT and ICE excluded thrombus in the LAA, and both patients underwent uneventful AF ablation. In another 2 patients, a thrombus in the LAA was detected both by TEE and by ICE. The anticoagulation regimen was modified and ablation deferred. The patients’ flowchart is presented in Figure 1.

Intracardiac Echocardiography

Positioning of the ICE probe in the RA was possible in all patients, in the PA in 64 (86%) patients, and in the CS in 49 (66%) patients. In those patients in whom the ICE probe was positioned in a prespecified location, the LAA was properly visualized with a grade 4 or 5 image quality in 56 of 64 (87.5%) patients from the PA, in 13 of 49 (26.5%) patients from the CS, and in none of the patients from the RA (usually the distal part of the LAA was not clearly seen). Visualization of the LAA was possible in 58 of 74 patients (78%), regardless of the ICE probe position. The LAA was significantly better visualized when the ICE was located in the PA than in the CS (P<0.001). Representative ICE images of the LAA from the PA and CS are presented in Figures 2 to 4 (see additional
images: supplemental video files). Fluoroscopic views of the catheters positioned in the CS and PA are shown in Figure 5.

In those patients in whom the LAA was clearly visualized by ICE from the PA, an excellent agreement between TEE and ICE was obtained. Of these 56 patients, 43 subjects had grade 5 on ICE and the remaining 13 had grade 4. In 13 patients, visualization of the LAA from the CS had perfect agreement with TEE: 5 patients had grade 5 on ICE and the remaining 8 had grade 4. The mean time for achieving a satisfactory image of the LAA from the PA was 4±4.5 minutes and from the CS was 4.2±3 minutes (non-significant [NS]). Examination of the LAA by ICE from the PA and CS increased the fluoroscopy time by a mean of 6.8±3.8 minutes.

The possibility of obtaining high-quality images of the LAA (grades 4 or 5) from the PA and CS was independent of factors such as sex, age, hypertension, coronary artery disease, history of myocardial infarction, diabetes mellitus, heart failure, morphology of the LAA based on CT images, or type of AF (all NS; Table 2).

Based on the success rate and time required for visualization of the LAA, a learning curve for the electrophysiology laboratory was drawn (Figure 6), which shows that after 28 procedures an operator gained enough experience in LAA evaluation by ICE. Analysis performed after 28 examinations showed no significant differences between ICE and TEE in the assessment of thrombi. ICE grade 4 or 5 was significantly more often obtained after performing 28 ICE examinations from the PA than during the first 28 procedures (12 [44%] versus 44 [92%]; \( P=0.0001 \)). The likelihood of obtaining good LAA images from the PA (grade 4 or 5) steadily increased throughout the study: procedures 1 to 10, 20%; procedures 11 to 20, 50%; procedures 21 to 30, 70%; procedures 31 to 40, 90%; procedures 41 to 50, 100%; procedures 51 to 60, 100%; procedures 61 to 74, 93%. The time needed to achieve grade 4 or 5 LAA images

Figure 3. The intracardiac echocardiography images of the left atrial appendage (LAA) from the pulmonary artery in various phases of left atrial (LA) systolic function are presented. A and B, The ostium of the LAA and middle part of the trunk are visualized, and the LA cavity is displayed. C and D, Middle and distal parts of the LAA with pectinated muscles are visualized. The morphology of the LAA is a non-bended wind sock type. The left main coronary artery (LMA) is displayed. The image quality is graded 5.
from the PA was significantly shorter after completing 28 ICE examinations (8.2±3 versus 2.9±4.3 minutes; \( P<0.0001 \)).

**Procedural Complications**

In 1 adverse event, a woman aged 57 years with paroxysmal AF and normal ejection fraction (60%) reported chest pain when the ICE probe was advanced from the RV to the RVOT. The ICE probe was withdrawn from the RA to the home view position, and pericardial effusion was detected with 6 to 8 mm of fluid in the pericardial space in front of the RV. Standard transthoracic echocardiography confirmed these findings. The procedure was discontinued, and the patient recovered fully without hemodynamic consequences or other sequelae.

**Discussion**

The present study showed that (1) ICE is a useful tool for evaluating the LAA to detect a thrombus, (2) the PA seems to be the optimal location for the ICE probe for this purpose, and (3) ICE can be used effectively when TEE is unequivocal or not possible to perform.

The optimal location of the echocardiographic probe for LAA imaging has not yet been established. In clinical practice, TEE is usually used for this purpose, and the TEE probe obviously can be positioned only in the esophagus, whereas the ICE probe can be placed in various sites inside the cardiac chambers. Hence, identification of the best site for LAA imaging with ICE is possible. In an animal study, RVOT and PA have been suggested as good locations to visualize the whole LAA. However, no data on this issue in humans have been published.

The anatomic proximity of the LAA to the site location of the ICE probe is of paramount importance. The PA and LAA are located close to each other. CT scans and pathology specimen analysis revealed only a few millimeters of pericardial space present between these 2 structures. Such a localization of the PA enables a satisfactory view of the every part of the LAA from the proximal ostium to the middle trunk and distal LAA appendix. To visualize the entire LAA cavity, an operator has to rotate the ICE probe clockwise at different levels. When the ICE is located at the pulmonary valve level, usually only the LAA entrance is visualized. However, advancing the ICE further into the PA and repeating rotating maneuvers give additional views of the LAA and enable scanning of the entire LAA. When the ICE probe is located \( \approx 1 \) cm above the PA, the LAA in a long axis can be seen and an operator may notice trabeculation inside the LAA. The view obtained by locating the ICE probe >3 cm above the pulmonary valve in the main trunk of the PA or in the left PA can be named the...
short axis. In this position, additional lobes of the LAA, the apex, and even the space between the apex of the LAA and pericardium can be imaged.

Our study showed that LAA imaging from the PA is more accurate than from the CS. This may be explained by the fact that the course of the CS is posterior, whereas the LAA is located more anteriorly, with the left superior pulmonary vein left behind the LAA. In addition, advancing the ICE probe into the CS was more complicated than into the RVOT and PA.

In our study, we placed the ICE probe only in the right heart cavities and CS. Placing the probe in the LA could have provided better LAA visualization (especially the ostium). However, it would require crossing the interatrial septum with the ICE probe, which is contraindicated when a thrombus in the LAA is present or suspected. Because we were blinded to the TEE results, the protocol did not allow the transseptal use of the ICE probe.

Our study shows that an electrophysiologist can quickly gain experience in the visualization of LAA from the PA. Satisfactory LAA views were obtained after 28 procedures. The safety profile of this examination is acceptable because only 1 complication occurred with no further consequences. It seems that using additional diagnostic electrodes, such as a guidewire, facilitates the advancement of ICE probe and decreases the risk of side effects. However, we think that ICE probe can be safely advanced to the RVOT and above PA without any guiding catheter when performed by experienced electrophysiologists.

The findings of the study are applicable only for the 8F ICE catheter because we did not use a 10F ICE catheter in our laboratory. The 10F catheter may be more supportive and stable in some intracardiac locations (such as the CS) compared with 8F catheter and is probably more widely used because it is commercially available in some ultrasound-based electrophysiological systems. The ICE examination from the PA is a valuable option for patients in whom TEE cannot be performed or when TEE results are unequivocal. In our study, TEE could not be performed in 2 patients; ICE images of the LAA were of excellent quality, and based on this examination we felt that we could proceed safely with ablation. An unequivocal result of TEE in the assessment of LAA is not uncommon. For example, data from our center showed that of the 200 consecutive TEE examinations, the experienced echocardiographer had uncertainties when analyzing the LAA.

### Table 2. Possibility of Obtaining Quality Images of the LAA From PA and CS

<table>
<thead>
<tr>
<th>Characteristic of Patient</th>
<th>Quality of View From PA</th>
<th>Quality of View From CS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grades 0 to 3</td>
<td>Grades 4 to 5</td>
</tr>
<tr>
<td>Age (≤60, &gt;60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10 (14%)</td>
<td>45 (61%)</td>
</tr>
<tr>
<td>No</td>
<td>4 (5%)</td>
<td>15 (20%)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (15%)</td>
<td>45 (60%)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (7%)</td>
<td>13 (18%)</td>
</tr>
<tr>
<td>Concomitant disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>6 (8%)</td>
<td>22 (30%)</td>
</tr>
<tr>
<td>Yes</td>
<td>10 (14%)</td>
<td>36 (49%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10 (14%)</td>
<td>42 (57%)</td>
</tr>
<tr>
<td>Yes</td>
<td>5 (7%)</td>
<td>17 (23%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>15 (20%)</td>
<td>52 (70%)</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (1%)</td>
<td>6 (8%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>14 (19%)</td>
<td>43 (58%)</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (3%)</td>
<td>15 (20%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>14 (19%)</td>
<td>48 (65%)</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (3%)</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (18%)</td>
<td>51 (69%)</td>
</tr>
<tr>
<td>No</td>
<td>3 (4%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>Morphology of the LAA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Banded LAA (chicken wings)</td>
<td>7 (10%)</td>
<td>22 (32%)</td>
</tr>
<tr>
<td>Nonbanded LAA (wind socks, cauliflower, cactus)</td>
<td>9 (13%)</td>
<td>30 (45%)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; CS, coronary sinus; LAA, left atrial appendage; and PA, pulmonary artery.
In addition, data from the literature show that TEE may not be feasible in 1% to 2% of patients scheduled for this procedure, and unequivocal results on LAA imaging may be as frequent as 17.8%. Using ICE instead of TEE would only be clinically feasible if the likelihood of obtaining good ICE images was ≈100%. We showed in our study that such a high success rate is achievable after performing first 28 ICE procedures. Thus, TEE can be possibly replaced by ICE in some clinical situations; however, this needs to be assessed prospectively.

Imaging with ICE is invasive and increases costs. It also increases the duration of the procedure and x-ray exposure, although to a limited extent. It requires 1 standard additional puncture in the groin; however, in our study, it was well tolerated by patients, and no significant local complications in the left groin (where the ICE was introduced) were observed. Furthermore, in many laboratories, ICE is routinely used to assist transseptal puncture; therefore, no additional costs are present in such a situation.

An observational retrospective study has shown that some LAA morphologies, assessed by CT, may be associated with an increased risk of stroke in low-risk patients. However, the association of specific LAA morphologies with an increase in the risk of thrombus development in the LAA has not been investigated. We showed that the PA–ICE approach is effective in obtaining a grade 4 or 5 image of the LAA; thus, it may become a useful alternative to TEE or CT in the assessment of stroke risk in patients with AF. However, this has to be demonstrated in larger prospective studies. In conclusion, our study showed that adequate LAA imaging can be achieved by placing the ICE probe in the PA. We think that ICE may become a useful clinical tool for LAA assessment in patients undergoing catheter ablation of AF.

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Disclosures
Drs Baran, Stec, Kryński, and Kułakowski have received travel grants from J&J. The other authors report no conflicts.

References


**CLINICAL PERSPECTIVE**

Stroke is the most severe complication of atrial fibrillation (AF). The main source of thromboembolic material in patients with AF is the left atrial appendage (LAA). Therefore, every effort is made to exclude the presence of LAA thrombi in patients with AF, especially in those undergoing cardioversion or ablation for AF. Transesophageal echocardiography (TEE) is a gold standard to exclude thrombi in LAA; however, sensitivity of TEE in excluding LAA thrombus is not perfect, and in some patients TEE is contraindicated. The present study was set up to examine whether intracardiac echocardiography (ICE) can be used in this setting and what are the most accurate views using this novel technique. The study showed that of the 74 patients undergoing AF ablation, ICE adequately imaged the LAA in 58 (78%) patients, achieving ≈100% success rate after the learning curve was completed. The pulmonary artery occurred to be the best site for ICE probe placement. Thus, the present study documented the usefulness of ICE for evaluation of LAA in patients undergoing AF ablation. Because ICE is routinely used in many centers during AF ablation for other purposes such as transseptal puncture guidance, the study suggests that this technique may replace TEE, especially in patients with equivocal TEE images or in those who cannot undergo TEE.

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SUPPLEMENTAL MATERIAL

Video number 1 - LAA PA1 – LAA imaging by ICE from pulmonary artery, ICE was rotated clockwise. The LAA with additional lobes is displayed.

Video number 2 - LAAPA2 - LAA imaging by ICE from pulmonary artery, ICE was rotated clockwise. Pectinate muscles are displayed.

Video number 3 - LAAPA3 - short movie of LAA imaging by ICE from pulmonary artery. Pectinate muscles are displayed.

Video number 4 - LAAPA4 – from the same patient as in LAAPA3, longer movie of LAA imaging by ICE from pulmonary artery is presented in order to show various phases of left atrial systole function. ICE was rotated clockwise.

Video number 5 - ICE_PA_THROMBI1 - thrombi located in the LAA visualized by ICE from the PA

Video number 6 - TEE LAA THROMBI - thrombi located in the LAA by TEE examination – the same patient as in ICE_PA_THROMBI movie

Video number 7 - ICE_PA_THROMBI2 - LAA imaging by ICE from pulmonary artery, organized thrombus filling out LAA is presented