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Intracardiac Versus Transesophageal Echocardiographic Guidance for Left Atrial Appendage Occlusion

The LAAO Italian Multicenter Registry

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ABSTRACT

OBJECTIVES This study sought to evaluate the feasibility, safety, and efficacy of intracardiac echocardiography (ICE)-guided versus transesophageal echocardiography (TEE)-guided left atrial appendage occlusion (LAAO) by the use of Amplatzer Cardiac Plug or Amulet devices included in a large Italian registry.

BACKGROUND TEE is widely used for LAAO procedure guidance. ICE may be a potential alternative imaging modality in LAAO.

METHODS Data from 604 LAAO procedures performed in 16 Italian centers were reviewed. ICE-guided LAAO was performed in 187 patients, whereas TEE was used in 417 patients. Procedural success was defined as LAAO without occurrence of pericardial tamponade, stroke, systemic embolism with end organ damage, major bleeding, and device embolization. Stroke, transient ischemic attack, major bleeding, overall and cardiovascular death were analyzed.

RESULTS CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, sex category) and HAS-BLED (hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly, drugs or alcohol) scores were similar between the ICE and TEE groups. TEE implied lower procedural (delta 12 min) and fluoroscopy time (delta 5 min) when compared with ICE. Procedural success was similarly high (≥94%) between the TEE and ICE groups with a complication rate of 6.5% for TEE versus 4.2% for ICE (odds ratio: 1.468; 95% confidence interval: 0.681 to 3.166; $p = 0.327$). At median follow-up of 451 days (interquartile range: 162 to 899 days), the rate of cerebral ischemic events was similar between TEE-guided and ICE-guided procedures.

CONCLUSIONS ICE-guided LAAO by means of Amplatzer devices may represent a second alternative imaging modality after an appropriate learning curve and bearing in mind that pre-procedural computed tomography imaging is mandatory. When comparing ICE with TEE, TEE remains the gold standard. (J Am Coll Cardiol Intv 2018;11:1086–92)

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Percutaneous left atrial appendage (LAA) occlusion has been proven to be a safe and effective procedure, and it has been included in the guidelines as potential treatment of patients with absolute or relative contraindications to oral anticoagulant agents (OACs), as compared with historical data (1–9). Briefly, the procedure consists of positioning a dedicated device in the left atrial appendage (LAA), to seal it, through atrial transseptal puncture (10). As angiography has several limits for detailed guidance of such a procedure, transesophageal echocardiography (TEE) has been the first and actually the most widely used imaging modality for LAA occlusion (LAAO) guidance. It has the advantage of being familiar to most cardiologists with a high definition of the right and left atrium, atrial septum, and LAA anatomy, and it also provides good 3-dimensional imaging. Nevertheless, it has some important limitations, such as the need for general anesthesia and for a dedicated operator as well as interference with fluoroscopy. Intracardiac echocardiography (ICE) has been proposed as an alternative to TEE for LAAO procedure guidance (11,12). Accordingly, we aimed to evaluate feasibility and safety of ICE guidance for LAAO, in comparison with TEE, in a large Italian registry (13).

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METHODS

STUDY POPULATION. We retrospectively collected procedural and follow-up data from 604 LAAO procedures performed in 16 Italian centers between December 2008 and April 2015. Patients had paroxysmal, persistent or permanent nonvalvular atrial fibrillation (NVAF), a CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, sex category) score ≥2 and contraindication for OAC or previous stroke during treatment with OAC. The CHA_2DS_2-VASc (14) and HAS-BLED (hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly, drugs or alcohol) (15) scores were calculated.

DEVICE AND IMPLANTATION PROCEDURE. All patients were implanted with the Amplatzer Cardiac Plug (ACP) device or Amplatzer Cardiac Plug II (Amulet) device (St. Jude Medical, Plymouth, Minnesota). Device characteristics have been described elsewhere (10). Briefly, they both consist of a distal lobe and a proximal disk connected by an articulating waist, being self-expanding devices made of a nitinol mesh and 2 patches of polyester sewn into both the lobe and the disk. The lobe is implanted within the LAA and has stabilizing wires (6 for ACP, 16 for Amulet) to retain its position. The disc seals the orifice of the LAA (10). Before the device implantation TEE or cardiac computed tomography (CT) were performed to exclude left atrial and LAA thrombus, explore the relevant anatomy, and determine the appropriate device size.

TEE or ICE were used during the procedure to characterize LAA and correctly size the device; guidance of transseptal puncture; verification of the delivery sheath position; confirmation of location and stability of the device before and after release and continuous monitoring to detect procedural complications (11,12). TEE procedures were performed under general anesthesia, whereas ICE procedures were all performed under local anesthesia, and the ICE probe was advanced through a contralateral femoral vein access. The choice of using ICE was left to the operator, according to his or her and the center's experience, as well as to ICE availability.

ICE imaging was performed using an AcuNav (Siemens Healthcare, Erlangen, Germany) electronic phased-array 8-F, sterile single-use, diagnostic ultrasound catheter, providing ultrasound images down to 15 cm in the heart. The catheter was attached to a VIVID*i* system (GE Healthcare, Fairfield, Connecticut). The 4-way steerable AcuNav catheter (anterior, posterior, left, and right) comes with 2-dimensional and M-mode imaging, color, continuous and pulsed wave Doppler capabilities. The choice of the best ICE position (right atrium, left atrium, upper left pulmonary vein, pulmonary artery) was left to the operator, according to experience. Left atrium placement of ICE probe was obtained through the first transseptal puncture.

Technical success was defined as the successful deployment and implantation of the device, whereas procedural success was defined as technical success without major procedure-related complications (pericardial tamponade requiring drainage, stroke, systemic embolism, major bleeding, and device embolization requiring surgical removal). Major bleedings were defined according to the International Society on Thrombosis and Haemostasis criteria (16). Minor bleedings were defined as clinically overt bleedings that did not satisfy the criteria for major bleeding and lead to hospital admission, or physician-guided medical or surgical treatment. Events were labeled as periprocedural if they occurred within 7 days of the procedure or pre-discharge.

ABBREVIATIONS AND ACRONYMS

ACP = Amplatzer Cardiac Plug
CT = computed tomography
ICE = intracardiac echocardiography
LAA = left atrial appendage
LAAO = left atrial appendage occlusion
NVAF = nonvalvular atrial fibrillation
OAC = oral anticoagulant agent
TIA = transient ischemic attack
TEE = transesophageal echocardiography

TABLE 1 Baseline Characteristics of Patients Who Underwent Left Atrial Appendage Occlusion Procedure Under TEE or ICE Guidance

	TEE (n = 417)	ICE (n = 187)	p Value
Age, yrs	74 ± 7	76 ± 8	0.045
Women	35	34	0.890
LVEF, %	52 ± 11	53 ± 9	0.654
Permanent AF	64	68	0.438
Creatinine, mg/dl	1.3 ± 1.1	1.1 ± 0.5	0.013
eGFR, ml/min/1.73 m^2	63 ± 11	68 ± 12	0.163
CHA_2DS_2-VASc	4.25 ± 1.40	4.27 ± 1.40	0.498
HAS-BLED	3.15 ± 1.10	3.25 ± 1.00	0.541

Values are mean ± SD or %.

AF = atrial fibrillation; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, sex category; eGFR = estimated glomerular filtration rate; HAS-BLED = hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly, drugs, or alcohol; ICE = intracardiac echocardiography; LVEF = left ventricular ejection fraction; TEE = transesophageal echocardiography.

TABLE 2 Procedural Characteristics and Complications and In-Hospital Outcome of Patients Who Underwent Left Atrial Appendage Occlusion Procedure Under TEE or ICE Guidance

	TEE (n = 417)	ICE (n = 187)	p Value
TEE pre	91	44	0.009
CT pre	30	74	<0.001
Procedure time, min	92 ± 34	108 ± 33	<0.001
Fluoroscopy time, min	20 ± 11	25 ± 12	<0.001
Attempts, n	1.21 ± 0.70	1.10 ± 0.50	0.071
Ischemic stroke	1 (0.24)	0 (0)	0.999
TIA	1 (0.24)	1 (0.53)	0.527
Device embolization	1 (0.24)	1 (0.53)	0.527
Pericardial tamponade	8 (1.90)	3 (1.60)	0.999
Major bleeding	16 (3.80)	3 (1.60)	0.201
Procedural success	93.5	95.8	0.587

Values are %, mean ± SD, or n (%).

CT = computed tomography; TIA = transient ischemic attack; other abbreviations as in Table 1.

FOLLOW-UP. Follow-up was performed by clinical visits or telephone follow-up between 6 and 12 months and then yearly. No anticoagulation therapy was administered after the procedure. Antiplatelet therapy consisting of aspirin (80 to 325 mg/24 h) plus clopidogrel (75 mg/24 h), or aspirin or clopidogrel alone was given according to the operators' discretion for 30 to 180 days after the procedure, after which single antiplatelet therapy was given.

Stroke, transient ischemic attack (TIA), major or minor hemorrhage, and death from cardiac or any cause were analyzed.

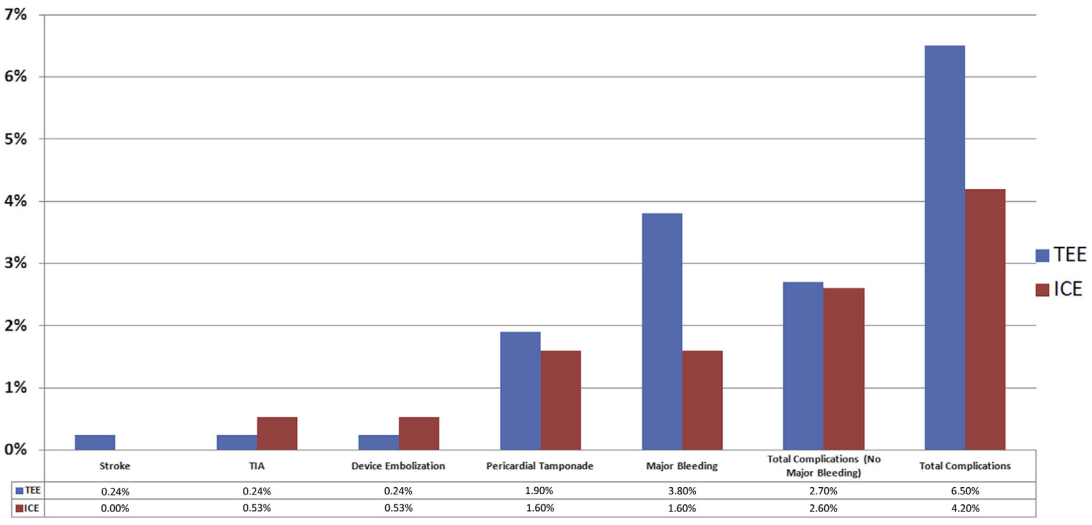
STATISTICAL ANALYSIS. Continuous data were expressed as mean ± SD. Technical and procedural success rates were calculated as percentages of the total number of patients. For proportions, numbers and percentages were used. Differences between TEE and ICE groups were evaluated with the Student's *t*-test for continuous variables. Binary logistic regression analysis was used to evaluate occurrence of complications in TEE and ICE groups. Odds ratios and 95% confidence intervals were calculated. Events curves were analyzed using the Kaplan-Meier estimate. Differences in survival curves were tested with the log-rank test. Statistical analysis was performed using SPSS version 19 (IBM Corporation, Armonk, New York). A p value <0.05 was considered significant.

RESULTS

PATIENT POPULATION. Baseline characteristics of the entire population and of TEE and ICE groups are displayed in Table 1. A total of 187 procedures were guided by ICE and 417 were guided by TEE. ICE was performed in 6 of 16 participating centers (102, 45, 15, 10, 8, and 7 cases, respectively). Clinical characteristics were comparable between groups, except that patients in the ICE group were older with lower serum creatinine values. The proportion of patients with permanent atrial fibrillation was about 70% with no difference between TEE and ICE patients. The mean CHA_2DS_2-VASc score was 4.2 ± 0.9 and the mean HAS-BLED score was 3.1 ± 1.1, with no difference between the TEE and ICE patients. Pre-procedural TEE was performed in 91% of patients in the TEE group and in 44% of ICE patients, whereas pre-procedural cardiac CT was performed in 30% of patients in the TEE group and in 74% of ICE patients (Table 2). Both pre-procedural TEE and cardiac CT were performed in 22% of patients in the TEE group and in 45% of ICE patients, respectively.

PROCEDURAL RESULTS AND IN-HOSPITAL OUTCOMES. Procedural characteristics, complications and in-hospital outcome in the entire population and in TEE and ICE groups are shown in Table 2. TEE-guided procedures had shorter procedure and fluoroscopy times than ICE procedures did. The number of attempts to finally implant the device was similar for TEE and ICE. Procedural success was similarly high (≥94%) between the TEE and ICE groups with a complication rate of 6.5% for TEE versus 4.2% for ICE (odds ratio: 1.468; 95% confidence interval: 0.681 to 3.166; p = 0.327). The most common complication was major bleeding for both groups. Excluding major bleeding events, the rate of patients experiencing at

FIGURE 1 Periprocedural Complications



Periprocedural complications (stroke, transient ischemic attack [TIA], device embolization, pericardial tamponade, major bleeding) for the transesophageal echocardiography (TEE)- and intracardiac echocardiography (ICE)-guided procedure groups.

least 1 major complication was similar between TEE and ICE groups (Figure 1).

When comparing the impact of pre-procedural CT in the ICE group (74%), we found that those patients receiving a CT scan before procedure had lower fluoroscopy time and less frequent need for a second device, with lower occurrence of pericardial tamponade (Table 3). Comparative imaging of different LAAO procedural steps by angiography and intracardiac echocardiography are visualized in Figure 2.

FOLLOW-UP. Median follow-up was 451 days (interquartile range: 162 to 899 days), 889 patient-years, available for 88.6% of the study population. The stroke or TIA rate during follow-up was similar between the ICE and TEE groups (Figure 3). Similarly, the rate of cardiac mortality and overall mortality did not differ between groups.

DISCUSSION

The main finding of this large multicenter registry on LAAO by means of Amplatzer devices analyzing the comparative value of ICE versus TEE in guiding LAAO is that the ICE-guided procedure appears to be feasible and safe at early and midterm follow-up when compared with patients undergoing TEE-guided procedures. LAAO procedure is considered a viable option in NVAF patients with absolute or relative contraindications to OAC therapy or who have experienced ischemic stroke despite OACs. Many registries have been conducted in this subset of patients (1–9). From the start, high periprocedural success has been demonstrated. In terms of efficacy, LAAO has demonstrated to reduce by about 60% the rate of cerebral embolism in comparison with historical NVAF populations without OACs, at follow-up. At the same time, LAAO warranted for a 60% reduction in the rate of hemorrhagic events in comparison with historical populations under OAC treatment. Accurate pre-, peri-, and post-procedural imaging to avoid

TABLE 3 Procedural Characteristics and Complications of Patients Who Underwent Left Atrial Appendage Occlusion Procedure Under ICE Guidance With or Without Pre-Procedural CT

	Pre-CT (n = 137)	No Pre-CT (n = 50)	p Value
Procedure time, min	108 ± 32	115 ± 40	0.259
Fluoroscopy time, min	22 ± 9	30 ± 18	<0.001
Use of a second device	4 (2.9)	4 (8)	0.049
Ischemic stroke	0 (0)	0 (0)	0.999
TIA	0 (0)	1 (2.0)	0.527
Device embolization	0 (0)	1 (2.0)	0.527
Pericardial tamponade	1 (0.7)	2 (4.0)	0.047

Values are mean ± SD or n (%).
Abbreviations as in Tables 1 and 2.

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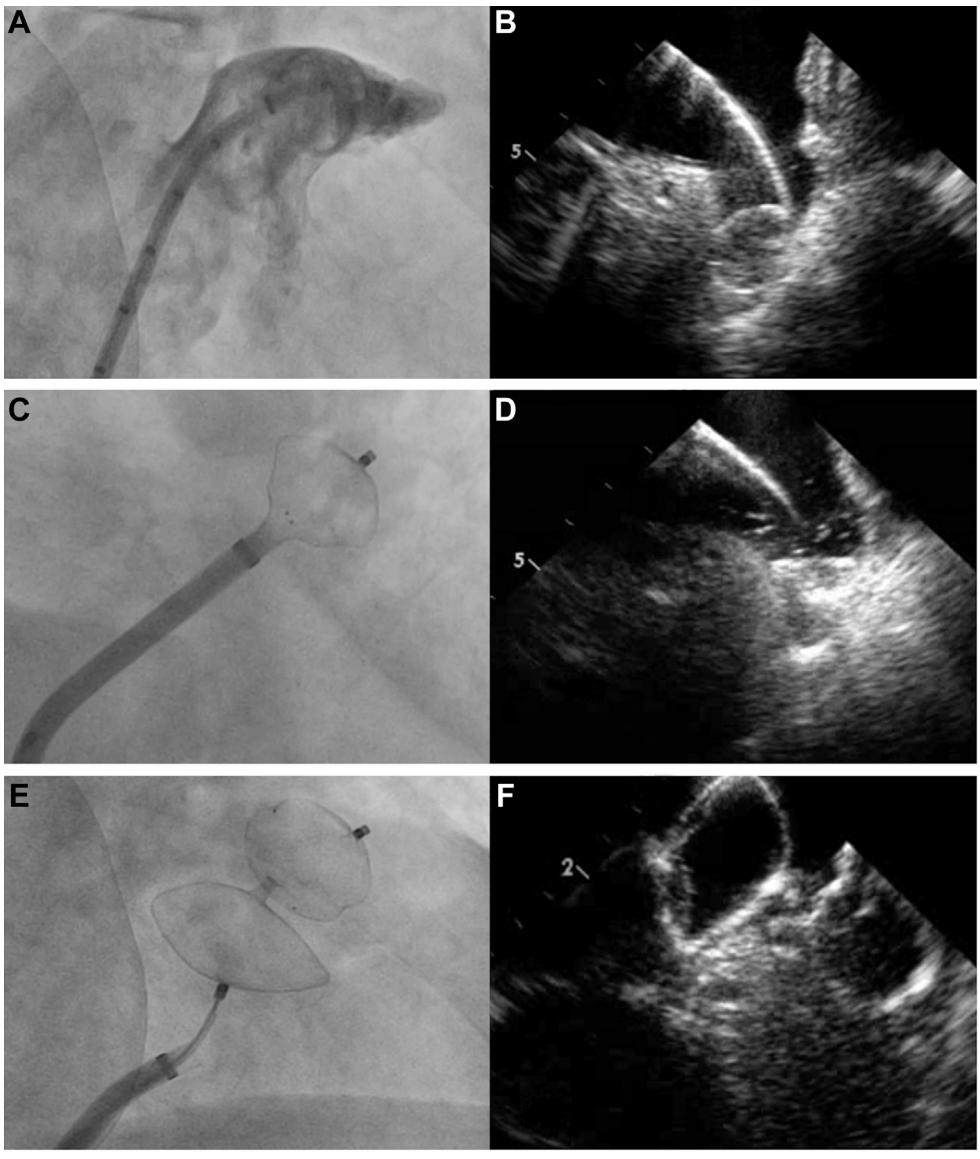
FIGURE 2 Fluoroscopic and ICE Left Atrial Appendage Occlusion Imaging



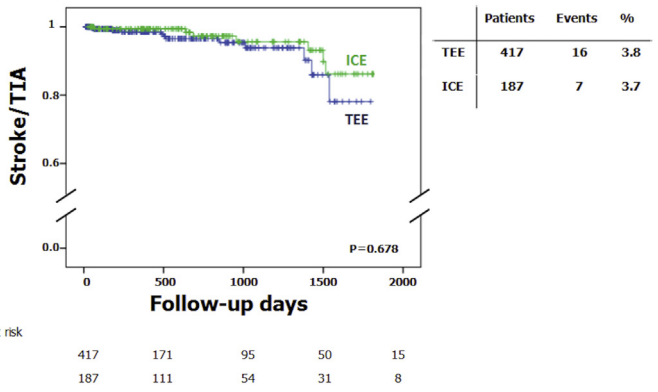
Comparative imaging of different left atrial appendage occlusion procedural steps by angiography and intracardiac echocardiography: 1) catheter positioning in the left atrial appendage as imaged by **(A)** angiography and **(B)** left atrium–placed intracardiac echocardiography (ICE); 2) lobe device positioning inside the left atrial appendage, aligned with the landing zone and with a slight deformation of its body, as imaged by **(C)** angiography and **(D)** left atrium–placed ICE; 3) view of the device traction or stability test as imaged by **(E)** angiography and **(F)** left atrium–placed ICE.

complications, optimize the procedure, and predict clinical events at follow-up is of utmost importance. As fluoroscopic guidance is insufficient, the periprocedural use of TEE has become the mainstay of the imaging modalities to guide all the different phases of the LAAO. As a matter of fact, TEE has the advantage of being familiar to most cardiologists given its high definition of right and left atrium, atrial septum, and left atrial appendage anatomy and it also provides good 3-dimensional imaging. Nevertheless, TEE use has some critical drawbacks. First, TEE needs general anesthesia, which may be harmful, especially for

older patients, and implies the logistic presence of an anesthesiologist. Moreover, TEE and endotracheal intubation may contribute to complications such as injuries and bleeding of gastroesophageal and respiratory tract, laryngospasm, and bronchospasm requiring additional intervention and prolonged hospitalization (17). Last, interference with fluoroscopy may represent a limit for TEE. ICE has been proposed as an alternative to TEE for LAAO procedure guidance. However, only a few small reports are available on the role of ICE to guide LAAO. A recent single-center study showed periprocedural safety of ICE LAAO guidance in comparison with TEE guidance (18). Our study is a multicenter study that confirms in a large series of patients that ICE may overtake the limitations of TEE without influencing procedure safety and feasibility. Even if ICE may provide inferior image quality, this does not seem to affect the technical success in our study. In all cases, LA placement of the ICE probe was attempted and obtained in 72 cases by the first transseptal puncture to improve ICE image quality and procedural guidance (19). However, considering the inherent limit to size LAA by ICE and, by our data, that patients receiving CT scan before procedure had lower fluoroscopy time, less frequent need for a second device, and fewer complications such as pericardial tamponade, we discourage the use of ICE as the only tool to characterize and size the LAA. Moreover, with this in mind, it is important to highlight the fact that although the event rates were too low for comparison between TEE (early cohort) and ICE (later cohort), we cannot exclude that the similar observed outcome between TEE- and ICE-guided LAAO may be, as least partly, due to greater LAAO experience among interventionalists when ICE rather than TEE was used.

Considering this, our work is the first demonstrating on a large population that, when performed by experienced LAA operators, the use of ICE-guided LAAO procedures had a similar rate of thromboembolic events at long term follow-up in comparison with TEE-guided LAAO procedures. As demonstrated by previous works, the immediate efficacy and results of LAAO procedure have important consequences on patient follow-up, in terms of cerebral embolism rate reduction. ICE procedure guidance appears equivalent to TEE at long-term clinical follow-up. The higher cost of ICE equipment may be balanced with the saving of expenses deriving from TEE complications, the need for additional operators, total case time by reducing anesthesia induction time, and post-anesthesia recovery.

FIGURE 3 Cerebral Ischemic Events at Follow-Up



Kaplan-Meier curves for stroke or TIA occurrence in the TEE- and ICE-guided procedure groups respectively. Abbreviations as in Figure 1.

STUDY LIMITATIONS. This was an observational, retrospective, nonrandomized study. Even if the complication rate is slightly high in this series, it is in the range of similar registries (7,9) and is probably affected by the learning curve of all centers. In this series ICE was used mainly in centers with a high volume of LAAO procedures. Investigations are required to evaluate the length of the ICE use learning curve and confirm its safety for LAAO procedure guidance in low volume centers. Moreover, given the inherent limits of ICE movement within the left atrium, we may underestimate the rate and extent of peridevice leaks. Results of this study cannot be generalized to devices different from Amulet or ACP devices.

CONCLUSIONS

TEE is actually the gold standard for LAAO procedure guidance. ICE-guided LAAO by means of Amplatzer devices may represent a second alternative imaging modality after an appropriate learning curve and bearing in mind that pre-procedural CT imaging is mandatory.

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PERSPECTIVES

WHAT IS KNOWN? TEE is actually considered the gold standard for LAAO procedure guidance. ICE may represent an alternative imaging modality.

WHAT IS NEW? In a large cohort of patients from a multicenter Italian registry ICE is not inferior to TEE for guiding of LAAO procedures in terms of procedural success and periprocedural complications, as well as for embolic events at follow-up.

WHAT IS NEXT? To confirm ICE as the gold standard for LAAO, these results need to be confirmed on a larger cohort of patients with adequate imaging follow-up.

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