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Capabilities of transesophageal echocardiography in patients with atrial fibrillation

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Abstract
Transesophageal echocardiography is widely used in clinical practice in patients with atrial fibrillation and it is mainly applied to determine the morphology of the heart, the presence of intracardiac thrombi, quantify the structures of the heart, as well as to determine the tactics for surgical interventions. Transesophageal echocardiography has an advantage over transthoracic echocardiography in visualizing the left atrium and left atrial appendage, common sites of thrombus formation in patients with atrial fibrillation. Due to the anatomical proximity of the esophagus to the heart, the transesophageal access avoids signal fading and incorrect interpretation of the study results. The possibilities of transesophageal echocardiography in patients with atrial fibrillation have expanded with the development of medical technology, and three-dimensional transesophageal echocardiography has become widespread. In recent years, the studies on the use of the transesophageal echocardiography in patients with atrial fibrillation during the coronavirus pandemic have been published. The review presents the results of studies, meta-analyzes of pooled samples, as well as clinical cases, demonstrating capabilities of transesophageal echocardiography in patients with atrial fibrillation. A brief history of the development of the method, work on the study of the technology features and capabilities of transesophageal echocardiography for pulmonary vein ablation, cardioversion, occlusion of the left atrial appendage in patients with atrial fibrillation, as well as studies on disadvantages of the transesophageal echocardiography and possible options for their elimination are presented. Comparison of the transesophageal echocardiography with transthoracic and intracardial echocardiography is also highlighted. In preparing the review, the literature search method in PubMed databases for the period 2012–2021 was used, as well as data from an earlier period to indicate the history of the method development.
Keywords: transesophageal echocardiography, atrial fibrillation, left atrial appendage thrombosis, review.

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Transesophageal echocardiography (TEE) is an important imaging modality for the cardiovascular system. Transesophageal access improves the "ultrasound window" by visualizing the cardiac structures that are detected by transthoracic echocardiography (echoCG) and, due to the proximity of the esophagus to the heart, allows the avoidance of attenuation of the ultrasound signal due to anatomical structures, such as the subcutaneous fat layer, large mammary glands in women, pathological changes in the lungs, and chest deformity.

TEE is widely used in clinical practice. It is important in patients with arrhythmias, specifically atrial fibrillation (AF), when there is diastolic dysfunction of the left ventricle, followed by dilatation of the left atrium (LA), blood congestion, and thrombogenesis. TEE can visualize the left atrial appendage (LAA), which is a common site of thrombogenesis in patients with AF, which, given its anatomical location, cannot be assessed using transthoracic echoCG. LAA accounts for >90% of thrombosis in patients with AF [1].

The TEE method was first recorded in 1971 for measuring blood flow velocity in the aortic arch [2]. With the advent of flexible probes with transducers and steerable tips, the modern era of transesophageal ultrasound of the heart has begun [3, 4]. In 1980, Matsumoto et al., for the first time, used it in operating conditions to control the function of the left ventricle [5]. The technical advances in the XXI century have led to the improvement of the technique and the emergence of a more modern modification, i.e., three-dimensional (3D) TEE.

In 1999, the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists published guidelines for performing

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a comprehensive intraoperative multi-view TEE, which defined and announced a set of 20 TEE images to ensure consistency in technique training, reporting, image archiving, and establishing a single quality standard of research [6].

The latest recommendations of the American Society of Echocardiography for TEE were published in 2013 [7]. They provide general recommendations on the technique, anesthesia, visualization of individual heart structures, assessment of their functions (heart valves, aorta, ventricles, LA and pulmonary veins, and right atrium), protocol for 3D-TEE, and imaging algorithm for chronic heart failure. The 2013 recommendations are primarily focused on adult patients with structurally normal hearts. They were followed in 2019 by recommendations on standardized presentations and methods of TEE that can be used in the evaluation of children or adults with congenital heart diseases [8]. In Russia, no clinical guidelines have been established for TEE; the Perrino practical guidelines translated into Russian, which described this technique, were also published [9].

In patients with AF, TEE is used during pulmonary vein ablation, before cardioversion, to visualize the LA and LAA thrombi. TEE is an important part of the LAA occlusion procedure.

According to modern concepts, the so-called "arrhythmogenic" pulmonary veins are the most significant in AF development. Thus, one of the treatment methods is ablation (isolation) of the pulmonary veins, which can be performed using radio waves (radiofrequency ablation) or exposure to low temperatures (cryoablation) [10].

Both ablation methods are usually used under X-ray control. However, the general aim of medical imaging is to keep exposure to harmful ionizing radiation "as low as reasonably achievable" [11]. Thus, several studies have reported performing AF ablation with minimal or no fluoroscopy. Generally, these studies were either focused on radiofrequency ablation (which is easier to perform without fluoroscopy, compared with cryoablation) through electroanatomical mapping or they have used resource-intensive imaging methods such as intracardiac echoCG [12, 13].

Erden et al. reported that TEE-guided transseptal puncture for AF ablation was associated with shorter fluoroscopy time and overall cryoablation and procedure time and facilitated lower pulmonary vein cryoablation [14].

In a study by Sun et al., pulmonary vein ablation with and without TEE showed no difference in the procedure time. The fluoroscopy time and amount of contrast agent in the TEE group were lower than that in the non-TEE group. At follow-up, the success rates of the procedures were similar for both groups. Thus, in this study, cryoablation using TEE for pulmonary vein occlusion was safe and effective. TEE can help the operator achieve complete occlusion by real-time monitoring of the balloon position at the orifice of each pulmonary vein [15].

The first case of successful AF cryoablation without fluoroscopy under TEE control alone was published in 2018 by Balmforth et al. A 65-year-old man underwent cryoablation of paroxysmal AF only under TEE control without fluoroscopy. TEE was used at all stages of the procedure, including guidance on the transseptal puncture, control of the balloon position in the pulmonary veins, and test of pericardial effusion after the procedure. After 5 months of follow-up, sinus rhythm was still registered, and he stopped taking all antiarrhythmic and anticoagulant drugs [16].

Leftheriotis et al. described a case of pulmonary vein isolation under continuous TEE monitoring in a patient with dextrocardia. The procedure was safe and effective. The authors revealed that the use of TEE ensures safety during transseptal puncture and real-time visualization of the venous entry anatomy and 3D images improves the process. This case highlights the growing role of echoCG in interventional cardiology, especially in electrophysiology [17].

TEE can also be used to predict the risk of AF recurrence after radiofrequency catheter ablation. Istratoaie et al. showed significantly increased diameter and volume of the LA, whereas the rate of LAA emptying was much lower in recurrent AF than in non-recurrent cases after radiofrequency ablation. A low LAA emptying rate was the only independent predictor of AF recurrence within 1 year after radiofrequency ablation [18].

TEE for pulmonary vein occlusion during ablation shortens the overall procedure and fluoroscopy time and reduces the contrast agent load, ensuring the efficiency and safety of the procedure.

In acute hemodynamic disorders, to eliminate the clinical manifestations of AF with poor subjective arrhythmia tolerance, in situations where adequate control of the ventricular contraction rate is impossible and the "rate control" strategy does not improve the condition, sinus rhythm restoration (electrical or pharmacological cardioversion) is used [10].

According to current recommendations for the management of patients with AF, the relief of prolonged paroxysms of AF (lasting > 48 h) and the restoration of sinus rhythm in persistent disease should be performed along with the use of adequate anticoagulant therapy (the previous intake of at least 3 weeks; or the presence of blood clots in the cavities and appendages according to TEE data should be ruled out) [10].

The predisposition to thrombogenesis in AF can be described in relation to Virchow's triad (i.e., abnormal blood flow, abnormal vascular structure, and abnormal blood composition), which can be applied to AF with reduced LAA velocity, spontaneous echo contrast, endothelial damage, coagulation abnormalities, decreased fibrinolysis, and platelet levels in patients with AF [19]. TEE is the "gold standard" for detecting thrombi in the LA and LAA in AF [20].

A 1991 study compared the sensitivity and specificity of transthoracic echoCG, left atrial angiography, coronary angiography, and TEE in detecting left atrial thrombi in patients with mitral stenosis. The specificity was high for all research methods. The sensitivity was the highest during TEE at 83%, whereas the sensitivities of transthoracic echoCG, left atrial angiography, and coronary angiography were 28%, 28%, and 14%, respectively [21].

TEE provides excellent visualization of the LAA and LA in the presence of a thrombus, with high sensitivity (92%–100%), specificity (98%–100%), and negative predictive value (98%–100%) [22].

Morphologically, there are four LAA types, namely, chicken wing (most common type), broccoli, windsock, and cactus. The risk of thrombus formation in windsock and broccoli morphology is 4–6 times higher than in chicken wing LAA [23]. TEE best fulfills a binary description of LAA morphology (if the shape is a chicken wing type or not). There is no standard definition of the cactus LAA using TEE [24].

TEE before cardioversion improves the selection of patients who require anticoagulant therapy and thus reduces the incidence of ischemic stroke in these patients. In addition, TEE is useful in clinical scenarios where early cardioversion is preferable because of debilitating clinical symptoms and acute arrhythmia, or the adequacy of prior anticoagulation is uncertain [25].

At present, the TEE technique is widely used, which allows for early cardioversion in patients without waiting for 3 weeks of drug preparation to expire. However, even in the XX and XXI centuries, the approach to TEE was more cautious.

A large randomized trial in 1994 showed that a negative TEE result eliminated the need for long-term anticoagulation before cardioversion, but this did not rule out the presence of intracardiac thrombi that could be completely embolized before the study [26].

The first multicenter, randomized, prospective clinical trial conducted by Klein et al. included 1222 patients with AF lasting more than 2 days. These patients received treatment based on the TEE results or conventional treatment. According to the study results, no significant difference was found between the two treatment groups regarding the incidence of embolic events; however, the incidence of hemorrhagic events was significantly lower in the TEE group. The TEE group also had a shorter time to cardioversion and a higher rate of successful sinus rhythm recovery. After 8 weeks, no significant differences were noted between the two groups in terms of mortality, maintenance of sinus rhythm, or functional status. The authors concluded that TEE can be considered a clinically effective strategy and alternative to conventional therapy for patients undergoing elective cardioversion [27].

Currently, owing to the use of TEE, early cardioversion in patients with paroxysmal AF is possible by ruling out an LAA thrombus [10].

If sinus rhythm cannot be restored to prevent ischemic stroke in patients with absolute contraindications to anticoagulants and patients with a high risk of hemorrhagic complications, injuries, falls, and severe renal dysfunction, and if adequate control over the intake of anticoagulants is impossible, LAA occlusion may be performed [10].

TEE plays an important role in percutaneous LAA occlusion. Before occlusion, TEE is used to rule out any thrombus in the LA or LAA, as this is a contraindication for device deployment. This method also allows determining the LAA morphology and size before the procedure. TEE is used to measure the LAA dimensions (orifice, neck width, and depth), and based on these measurements, the size of the occlusive device is selected. Direct positioning of the device in the LAA cavity is also made possible with TEE. TEE is also used to avoid any complications after the procedure and during a long follow-up period [28, 29].

For a long time, transthoracic echoCG was used to detect left atrial formations (including thrombi) [30]. However, this approach had limitations. Even large formations, including thrombi located in the LA, could be invisible or its size underestimated by ultrasound methods available at an earlier period [31]. LAA thrombi were also often not detected using traditional two-dimensional (2D) echoCG, which was of great clinical importance, since the LAA is the most common site of thrombogenesis [1].

TEE and transthoracic echoCG were first compared by Aschenberg et al., who examined the sensitivity and specificity of the two methods for detecting LAA thrombi in patients with mitral stenosis. In 6 of 21 patients with mitral valve stenosis, LAA thrombi were diagnosed by TEE when transthoracic echoCG was ineffective. The TEE results in all cases were confirmed intraoperatively [32].

Initially, LAA occlusion was performed under general anesthesia due to the need for a long-term TEE. One of the reasons for the use of general anesthesia for LAA occlusion is that patients experience significant discomfort because of severe irritation of the esophagus during intraoral TEE [33].

General anesthesia has disadvantages, including the inhibitory effect of general anesthetics on the heart. Recently, the advancing experience of operators has led to the use of local anesthesia and various technological solutions. According to clinicians, deep sedation with noninvasive ventilation using a Janus mask (Biomedical Srl; Florence, Italy) may be a reasonable and safe alternative to general endotracheal anesthesia in patients who require long-term TEE for noninvasive cardiac procedures, including LAA occlusion [34].

Another solution is transnasal TEE, which is an advanced and safe technology that has emerged in recent years. It provides excellent images and is well tolerated by patients without general anesthesia for long periods [33].

A 2021 study published data on the use of pediatric probes in adults for LAA occlusion with TEE to increase the efficacy and safety in some patients [35]. Britez et al. presented their initial experience with the latest generation TEE microprobe, which provides multi-view 2D imaging with a probe with very small distal tip, with a diameter of 5.6 mm × 7.7 mm. The occluder implantation procedure in the described clinical cases was successful, did not cause complications, and lasted <1 h [36].

However, studies of microprobe and nasal probe technology are limited, and further investigations are required to confirm the applicability and diagnostic accuracy of the microprobe instrument. Thus, to assist in making a comprehensive and accurate diagnosis, Wang et al. preoperatively conducted a complex traditional study using conventional TEE, and directly during the surgery, they guided with a microprobe and completed successfully the percutaneous closure of the LAA under the control of transnasal TEE with local anesthesia. Wang et al. evaluated the safety and clinical efficacy of percutaneous LAA occlusion under TEE control with local anesthesia. The study included 159 patients. The device was successfully implanted in 152 (95.6%) patients and allowed instant monitoring of patient discomfort, which may be a sign of some complications [37].

Another alternative is intracardiac echoCG. Intracardiac echoCG is advantageous in patients with contraindications for general anesthesia for LAA occlusion [38]. One of the latest works is a meta-analysis of eight studies published in 2021. This meta-analysis demonstrated that although TEE is the “gold standard” for perioperative imaging in LAA occlusion, intracardiac echoCG is a feasible and safe alternative that diminishes the effects of general anesthesia and associated potential risks [39]. Computed tomography (CT) angiography is another alternative to TEE in patients in whom the risks associated with the study outweigh the benefits [40].

Nielsen-Kudsk et al. revealed in the largest multicenter study that intracardiac echoCG-guided procedures were safe and had similar success rates and adverse event rates after 1 year to TEE-guided interventions, with no increased risk of procedural or vascular complications. Assistance with intracardiac echoCG has been associated with longer procedure time and use of more contrast agents [41].

The 2D-TEE technique has several limitations associated with the complex structure of the LAA (four different types of structure, presence of several lobules, a spiral main axis, etc.); therefore, the prospects for TEE development are associated with 3D visualization of the heart, which will provide more accurately an assessment of the LAA morphofunctional aspects.

Data on the sensitivity and specificity of 3D-TEE for detecting LAA thrombi are still limited; however, 3D-TEE is known to be superior to 2D-TEE in assessing left atrial thrombus mobility, thrombus, and myocardial differentiation, and detecting changes in thrombus structure (calcification, degeneration, or thrombus lysis), solves the problem of inadequacy of image planes [42–44].

3D-TEE provides an excellent overview of the left atrial anatomy before AF ablation procedures, and these procedures are associated with favorable long-term outcomes [45]. 3D-TEE allows better assessment of LAA morphology and a more accurate determination of the area of the LAA ostium than 2D-TEE, which is important in the size selection of the occlusive device. Moreover, the measurement results are associated with less variability depending on the specialist conducting the study and higher reliability of the study [46–54].

The calculation of the LAA volume and ejection fraction obtained from the volume can only be estimated using 3D-TEE [55]. Compared with conventional 2D-TEE, 3D-TEE cannot only assess the size of the pulmonary veins but also establish additionally the corresponding diameters and areas, as well as their spatial relationship to surrounding structures [56].

Authors have also proposed supplementing the TEE technique with the results of laboratory tests to expand the possibilities of TEE in patients with AF and improve the accuracy of information about left atrial thrombi. In a study of 59 patients undergoing TEE for suspected intracardiac thrombi, a negative D-dimer level (<200 ng/mL) ruled out the presence of intracardiac thrombi. When comparing D-dimer-positive patients with and without thrombus, patients with thrombus had decreased LAA velocity and left ventricular ejection fraction, increased proportion (%) of neutrophils, decreased proportion (%) of lymphocytes, and increased monocyte count. The area under the receiver operating characteristics curve for thrombus diagnostics was greater for combinations of clinical and biochemical data than for each parameter alone. Thus, in this study, the addition of the "gold standard" (TEE) with analysis of LAA velocity, left ventricular ejection fraction, D-dimer levels, and hemostatic markers provided additional useful diagnostic information [57].

Kosmalska et al. assessed the usefulness of TEE before cardioversion by evaluating factors that influence the risk of thrombosis and/or dense spontaneous echo contrast, with the intention of extending the indication for TEE in the group with high risk for thrombosis or omitting TEE in the group with low risk for thrombosis. Low LAA velocities, presence of spontaneous echo contrast, prolonged arrhythmia, consecutive (not first) episodes of arrhythmia, and evidence of dementia from the mini-survey of mental status increased the risk of having an LAA thrombus. There might be a need to expand the indications for TEE in patients with atrial arrhythmias, most often due to the unpredictable occurrence of a thrombus and potentially hazardous thromboembolism. The only exception could be the group of patients with CHA_2DS_2–VASc score of ≤1. None of the patients with CHA_2DS_2–VASc score ≤ 1 had an LAA thrombus or sludge. Among patients with CHA_2DS_2–VASc score >1, the prevalence of LAA thrombi or sludge was independent of the CHA_2DS_2–VASc score [58].

Recent studies have demonstrated that the use of ultrasound contrast agent during TEE in patients with AF also increases the procedure reliability, level of interpretive confidence of the doctor, speed of the theoretical transition to electrical cardioversion, and cost-effectiveness of cardioversion in AF [59–61]. However, in a 2021 study, the use of an ultrasound contrast agent had no significant effect on the determination of LAA size [62].

One of the limitations of TEE is false-positive results in relation to thrombogenesis. The clot usually appears on echoCG as an echocardiographic opacification. However, does such an opacification in the LAA on echoCG always imply a clot or thrombus? Cases have been described when a pectoral muscle [42] or a dense fatty pad of the epicardium could be mistaken for a thrombus [63].

False-positive LAA thrombus may be indicated on TEE, when the thrombus is described as "soft" rather than "hard." In a study of 21 patients, LAA thrombus was detected during TEE before electrocardioversion or AF ablation. These patients underwent intracardial echoCG of the pulmonary arteries. In TEE of 7 (33%) patients, the LAA thrombus was described as "hard," and in the remaining 14 (67%) cases, it was described as "soft." A discrepancy between TEE and intracardiac echoCG data (thrombus in TEE and no thrombus in intracardiac echoCG) was noted in 9 (43%) patients. In the group with "hard" thrombi, intracardial echoCG confirmed the presence of thrombi in six patients and ruled out blood clots in one patient, whereas in the group with "soft" thrombi, it confirmed the presence of thrombi in six patients and excluded blood clots in the remaining eight patients. This study suggested that intracardiac echoCG can be a valuable option to test the presence of a thrombus diagnosed based on TEE [64].

Artifacts are one of the reasons for false-positive TEE results. The LAA foramen is separated from the left pulmonary veins by Marshall's ligament, which is also called the left lateral ridge or coumadin ridge. It is a prominent muscular ridge lying in the LA between the left superior pulmonary vein and the LAA. It often appears to be attached to the LAA roof, with the rounded end entering the LA. It may not always look round. When viewed along the parasternal long axis, it may appear as a linear band in the LA, which is mistaken for a thrombus [65].

Improper interpretation of imaging results can lead to erroneous patient management and unnecessary procedures. The evaluation of multi-plane and multi-angle TEE is of paramount importance for making a correct diagnosis, and additional information from other imaging techniques, such as CT of the heart, can sometimes be of additional value, especially if the diagnosis remains unclear.

Another area is the use of the TEE method in the context of the coronavirus disease 2019 (COVID-19) pandemic, as a source of an increased risk of virus spread through an aerosol created in the air. The American Society of Echocardiography issued a statement protecting patients and echoCG providers during the 2019 novel coronavirus outbreak. In their statement, experts note that TEE bears an increased risk of spreading severe acute respiratory syndrome coronavirus 2 because it can provoke aerosolization of large amounts of the virus due to coughing or vomiting during the examination. Thus, TEE requires particular attention when deciding the time, the need for this examination, and its precautions. Careful consideration of the benefits of TEE should be weighed against the risk of exposure of medical staff to aerosolization in a patient with suspected or confirmed COVID-19. TEE should be delayed or canceled if an alternative imaging method is available [e.g., transthoracic echoCG, including ultrasound-enhancing agent, CT, or contrast-enhanced magnetic resonance imaging (MRI)]. The use of these methods to avoid aerosolization must be balanced against the risk of transporting the patient through the hospital to a CT or MRI scanner, need to disinfect the CT or MRI room, use of iodinated contrast and radiation for CT, and long scan times for MRI. Some US institutions have special CT scanners designed for patients with COVID-19 [66].

The evaluation of left atrial deformity with transthoracic echoCG instead of an invasive study of LAA functions using TEE in patients with AF for ≥48 h or of unknown duration, who are scheduled for electrical cardioversion, may also help reduce the spread of coronavirus infection [67].

In patients with AF who have undergone LAA closure, TEE is usually performed after 45 days to assess the blood flow through the device and the absence of a device-associated thrombus before the cessation of oral anticoagulant therapy. Tan et al. also sought to reveal whether 45-day TEE is necessary for patients with a history of LAA occlusion during the COVID-19 pandemic.

A total of 200 patients after the WATCHMAN procedure were retrospectively studied. At the time of the WATCHMAN procedure, 189 (94.5%) of the 200 patients had no blood flow through the device, and blood flow through the device was 1–5 mm in 11 (5.5%) patients. The 45-day TEE revealed no device-related thrombi in any of the patients. The authors point out that this calls into question the current practice of evaluating device-related thrombus during the intake of oral anticoagulants for 45 days. It may be rational to evaluate a device-related thrombus after the cessation of the anticoagulant therapy. This issue requires further study [68].

Conclusion

TEE takes an important place in cardiology and complements the results of the classical transthoracic study. It is also performed to clarify several anatomical and hemodynamic parameters. TEE is the gold standard in patients with arrhythmias, particularly AF, for detecting blood clots in the heart cavities (especially the LAA), studying structural and functional changes in the atria, and evaluating the efficiency of anticoagulant therapy in these patients. Intraoperative TEE is an effective control method for various manipulations on the heart. High-quality TEE and correct interpretation of data depend on the qualifications of the doctor, and the technology and methods of conducting are constantly being improved.

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