ECHOCARDIOGRAPHY IN PATIENTS WITH ATRIAL FIBRILLATION - WHAT SHOULD THE INTERNIST DOCTOR KNOW?

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Abstract
Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an increasing prevalence and an enormous clinical impact due to the high stroke rate, left ventricular dysfunction and excess mortality. The occurrence and maintenance of AF is favored by both the degree of left atrial (LA) dilation and the association of fibrotic lesions of the myocardium. The LA is a marker of adverse cardiovascular events in patients with AF. Atrial remodeling can be electrical (shortening atrial refractory), structural (altering geometry and altering collagen content) and contractile (loss of contractility). Cardiac imaging plays a central role in the clinical management of this arrhythmia. Echocardiography represents the routine imaging technique used in patients with AF, with a role in detecting LA dysfunction and cardiac structural changes that predispose to this arrhythmia, also having the ability to predict the maintenance of sinus rhythm after cardioversion and after ablation.

Keywords: atrial fibrillation, left atrium, echocardiography, transthoracic echocardiography.

Rezumat
Fibrilaţia atrială (AF) este cea mai comună aritmie cardiacă, cu o prevalenţă în creştere şi cu un impact clinic enorm prin rata înaltă de stroke, a disfuncţiei ventriculare stângi şi a excesului de mortalitate. Apariţia şi menţinerea fibrilaţiei atriale este favorizată atât de gradul de dilatare atrială stângă cât şi de asocierea leziunilor fibrotice ale miocardului. Atriu stâng (LA) este un marker al evenimentelor adverse cardiovascularare la pacientii cu fibrilaţie atrială. Remodelarea atrială poate fi electrică (scurtarea refractarităţii atriale), structurală (alterarea geometriei şi modificarea conţinutului de colagen) şi contractilă (pierderea contractilităţii). Imagistica cardiacă deţine un rol central în managementul clinic al acestei aritmii. Ecografia cardiacă reprezintă tehnica imagistică de rutină utilizată la pacienţii cu fibrilaţie atrială, cu rol în detectarea disfuncţiei atriale stângi, a modificărilor structurale cardiace ce predispun la această aritmie, având, de asemenea, abilitatea de a prezice menţinerea ritmului sinusal post cardioversie şi post ablaţie.

Cuvinte cheie: fibrilaţie atrială, atriu stâng, ecocardiografie, ecocardiografie transtoracică.
**Introduction**

AF is the most common arrhythmia found in clinical practice, characterized by electrocardiography with fast and chaotic atrial activity and atrio-ventricular transmission with variable, irregular frequency. Pulmonary veins are considered to be the main triggers of this arrhythmia, but other anatomical regions have been described to play a role in the initiation of arrhythmia such as Marshall's ligament, superior vena cava, crista terminalis, coronary sinus and left atrial appendage (LAA). AF may be associated with increased thromboembolic risk, hemodynamic impairment and decreased quality of life. Among the many cardiac imaging techniques, echocardiography plays a key role in risk stratification, thrombus exclusion before cardioversion, as well as in the selection of candidates who will undergo the ablation procedure.

**Evaluation of left atrial size and function in atrial fibrillation**

By installation of the AF, the pressure in the LA will increase to compensate for the decrease in heart stroke volume. AF itself is associated with atrial volume overload by loss of atrial contraction and the loss of normal fiber arrangement will create optimal ground for persistent AF installation. Current guidelines recommend the use of transthoracic echocardiography (TTE) for the analysis of LA size and function. Normally, the LA has a spherical shape. Usually, the atrial dilation occurs mainly in the mid-lateral and upper-inferior direction, the thorax limiting the extension in the antero-posterior plane.

Using M-Mode, we can measure the antero-posterior diameter of the LA in the parasternal long-axis window, but this parameter can underestimate the atrial dimensions due to an asymmetrical dilation that cannot be reflected in a single plane. The LA diameter measurement technique with the help of two-dimensional (2D) ultrasound, although it has the same limitations, has become widely used in clinical practice. According to European guidelines, the optimal analysis of LA dimensions should include the measurement of the area and volume of the atrium with indexation on the body surface. The LA dimensions will be measured at end-ventricular systole, at maximal LA size in the apical four- and two- chamber views. Each section must be optimized in order to avoid underestimation of the dimensions by foreshortening, the loss of lateral resolution of the walls, as well as the poor visualization...
Figure 1. Left atrial volume measurement by modified biplane Simpson’s method in apical 4-Chamber and apical 2-Chamber views of 2D transthoracic echocardiography.

Figure 2. Tissue Doppler Imaging study (at the level of basal segment of lateral wall) in apical 4 chamber view during sinus rhythm. $E'$ represents early diastolic filling myocardial velocity of left ventricle; $A'$ represents late diastolic filling myocardial velocity of left ventricle.

Figure 3. Measurement of $TE-e'$ using a dual Doppler system. From simultaneous recording transmitral inflow and mitral annular velocity, the time interval was measured between the onset of $E$ and of $e'(25)$. 
of the interatrial septum or the anterior wall\(^5\). It is known that the long axis of the left ventricle (LV) and LA is often in different planes, so that the length of the LA should be maximized to ensure alignment along the true long axis of the LA. Atrioventricular interface should be represented by the plane of the mitral annulus and not by the mitral valve. The LAA and pulmonary veins should not be included in the measurement of LA cavity\(^7\). The area reflects more accurately the actual size of the LA compared to the antero-posterior diameter\(^7\). For the LA 2D volumetric analysis there are various methods: cubical method, area length method, biplane method of disks\(^7\) (Figure 1). It has also been shown that volumetric measurements made using three-dimensional (3D) ultrasound technology are feasible, having the advantage of not relying on geometrical assumptions\(^5\). Compared to the 3D technique, the 2D technique has a low spatial and temporal resolution, underestimating the atrial volumes; the results of the 3D analysis correlating with those measured by nuclear magnetic resonance\(^9\).

LA dimensions represent a marker of atrial structural remodeling with prognostic importance\(^10\). Atrial diameter greater than 50 mm in patients with sinus rhythm is associated with a 4-fold increased risk of arrhythmia during the follow-up period\(^11\). Also, the LA antero-posterior diameter measured by the M-Mode method can predict the success of the pulmonary vein ablation procedure\(^12\).

LA dilation is associated with a low probability of sustaining cardioversion success in patients with persistent or permanent AF. The LA antero-posterior diameter may be a good predictor of AF recurrence but the maximum indexed atrial volume has a higher predictive value for AF recurrence after cardioversion\(^13\). Van Gelder has shown that after cardioversion, once the sinus rhythm is maintained for a long time, the LA dimensions will be reduced\(^14\). Left atrial volume indexed to the body surface (LAVI) can also be a good predictor of arrhythmia recurrence after mitral valve surgery and successful external cardioversion\(^13\). LAVI analysis combined with various biomarkers (D-Dimers, Prothrombin, thrombin-antithrombin complex, fibrin monomers) could identify patients with still undetected AF and cryptogenic stroke\(^13\).

It was also observed that in patients with ischemic stroke and without a history of arrhythmias, the cut off value of LAVI less than 40 ml/m\(^2\) may have a negative predictive value for excluding asymptomatic AF with a sensitivity (Se) and a specificity (Sp) of 50% and 86% respectively\(^15\). LAVI as well as the left atrial ejection fraction (LAEF: \(\frac{\text{LA}_{\text{volumemax}} - \text{LA}_{\text{volumemia}}}{\text{LAVI}}\))
Figure 4. (above) The normal appearance of pulmonary venous flow. Parameters evaluated by PW Doppler examination. $S_1$, $S_2$-peak systolic velocity, $D$-peak diastolic velocity. AR- atrial reverse flow.

Figure 5. Pulmonary venous flow pattern demonstrated by TTE in atrial fibrillation. $S$-peak systolic velocity, $D$-peak diastolic velocity ($S/D$ ratio $<1$). Atrial reverse flow is absent (11).

Figure 6. Image of thrombus (arrow) within the LAA discovered on a transesophageal echocardiography.
LA \text{ volume max} \times 100) is associated with high mortality independent of traditional risk factors and left ventricular parameters (LV). Decreased LAEF compared with increased atrial volume is associated with a high risk of developing AF. It was observed that after adjusting the parameters of the type structure and function LV, the correlation of the maximum volume with the mortality is significantly diminished; this finding is less obvious in the case of LAEF\textsuperscript{[16]}. The volume expansion capacity of LA is an important parameter that corresponds to atrial reservoir function, being considered a predictor of repeat pulmonary vein ablation, especially in patients with persistent AF\textsuperscript{[17]}. Volumetric analysis may be similarly useful in predicting AF recurrence after cardioversion, especially in those who associate diastolic dysfunction. It has been shown that in patients with AF, the volumetric expressed conduit function may become dominant, reflecting both atrial anomalies and ventricular filling pressures. The conduit function calculated by the formula: 

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[V_{\text{volume maxim LV}} - V_{\text{volume minim LV}}] - [V_{\text{volume maxim LA}} - V_{\text{volume minim LA}}]
\]

was most strongly associated with arrhythmia recurrence in a group of 96 patients with persistent nonvalvular AF who underwent cardioversion. Thus, a conduit value of 79% of the total ventricular volume predicted AF recurrence with a Se of 90% and a Sp of 85% (ROC area =0.93, P <0.001). By demonstrating the relationship between the conduit phase and the arrhythmia recurrence, it was emphasized that LV diastolic dysfunction is a promoter of AF recurrence. Increased conduit function relative to LV stroke volume, with reciprocal modification of the reservoir phase, reflects increased atrioventricular rigidity, a condition that is a strong predictor of immediate after cardioversion AF recurrence\textsuperscript{[18]}. 

**Analysis of diastolic dysfunction in patients with atrial fibrillation**

Diastolic dysfunction increases the risk of appearance of the first episode of AF. Ultrasound assessment of diastolic function is a challenge in these patients due to loss of atrial mechanical function, variability in cardiac cycle length, and LA dilation\textsuperscript{[19]}. The parameters analyzed by pulsed wave (PW) Doppler or tissue Doppler imaging (TDI) method should be measured for 10 consecutive cycles. At the same time, in the current practice, the average of velocities or time intervals are made for 3 non-consecutive cardiac cycles whose length does not vary by more than 10-20% compared to the average heart rate\textsuperscript{[20]}. There are authors who argue that the cycle length should be equivalent to a heart rate of 60-80
bpm and a time interval of more than 70 msec between the end of the transmitral inflow and the onset of the QRS complex. It has been observed that longer RR intervals are associated with improved LV filling and increased LV end-diastolic volume, resulting in improved subsequent LV relaxation. Using the transmitral PW Doppler one can calculate the velocity of the E wave, a parameter dependent on both LV relaxation and pressure in LA. It has been shown that patients with AF who associate the absence of the E wave velocity variation have increased LV filling pressures. Unlike the E wave, the e' wave (measured by the TDI method) is less dependent on pressure in LA (Figure 2). A study that included patients with AF and left ventricular ejection fraction (LVEF) >50% showed that in the presence of diastolic dysfunction the E/e' ratio tends to be higher compared to patients without diastolic dysfunction (14,65 2,21 vs. 7,66 1,18). There are authors who have pointed out that the E/e' value >11 has the ability to predict diastolic dysfunction with increased filling pressures with a Se of 90%. The analysis of the ratio E/e' at the lateral wall level in a single cardiac cycle in the presence of a preserved systolic LV function correlates with the blood level of the BNP and with pulmonary capillary wedge pressure (PCWP). This report has the ability to detect the improvement of diastolic function in patients with AF, being even higher than the BNP. In patients with heart failure, without the history of AF, the cut off value of 2.2 of the ratio E/(E’x S’) in the presence of sinus rhythm predicts the installation of arrhythmia with an Se of 88% and a Sp of 77%. E/(E’x S’) was calculated using the average of septal and lateral mitral annular velocities (E'- early mitral annular diastolic velocity, S'- systolic mitral annular velocity). This parameter was the best predictor of LV end-diastolic pressure and it was superior to E/e', regardless of LVEF (is useful for both patients with LV systolic dysfunction and those with normal LVEF). There are authors who evaluated the ability of diastolic ultrasound parameters in predicting AF recurrence after transcatheter ablation. Using the dual Doppler echocardiography technique, the time interval from the beginning of the transmitral flow (wave E) to the onset of wave e' in the same cardiac cycle was measured (Figure 3). It was found that this parameter is an independent predictor of arrhythmia recurrence at 1 year after catheter ablation. The isovolumic relaxation time (IVRT), another parameter measured with the PW Doppler sample in the apical three-chamber view (from the closure of the aortic valves to the onset of the transmitral flow) correlates strongly with the mean PCWP in patients with AF, being a marker of LV relaxation. High values of IVRT are recorded in patients with impaired LV relaxation, while low values reflect increased LV stiffness. PW Doppler and TDI examination of the late diastolic A wave, respectively a', may be useful for assessing the mechanical function of LA, but this parameter can not be measured in patients with AF. Atrial stunning is characterized by a reduced atrial mechanical function after cardioversion which depends on the duration of arrhythmia and which is associated with an increased risk of thromboembolism. This phenomenon can be easily identified as a result of the decrease of the velocities of the waves A and a' . Atrial stunning is maximal post-procedure and progressively improves, suggesting a dissociation between
mechanical and electrical recovery. Atrial stunning was also reported after radiofrequency ablation\(^5\). It was found that after electrical cardioversion the velocity of the wave A gradually improves, normalizing within about 6 months\(^8\).

Early transmitral flow deceleration time (TDE) can provide accurate information about diastolic function in AF conditions. There are authors who have shown that the cut off value less than 100 msec of TDE has the ability to predict a PCWP greater than 18 mmHG with an 80% Se and an 85% Sp. The restrictive pattern of diastolic dysfunction is associated with a poor prognosis. It was observed that the TDE value less than 130 msec reflects the restrictive pattern both in patients examined in AF rhythm and in those examined in sinus rhythm\(^19\).

The L wave is defined as a distinct forward flow velocity after the E wave with a peak velocity >20 cm/sec. This parameter is correlated with the prolongation and the late onset of LV relaxation time and with high pressure values in LA. After comparing 99 patients with persistent nonvalvular AF with patients examined in sinus rhythm with LVEF >50%, it was found that the prevalence of L wave was higher in the first category of patients, being associated with increased E/e' values. These patients were older, had a lower heart rate and a lower IVRT. It was concluded that the occurrence of the L-wave in patients with AF is a relatively frequent phenomenon, and the presence of it indicates advanced diastolic dysfunction with increased filling pressures and a noncompliant LA\(^26\).

Echocardiography also plays an important role in defining pulmonary flow characteristics in patients with AF. It normally has a pulsatile character, secondary to LA pressure and function as well as LV compliance (Figure 4). In the presence of AF the atrial reverse flow disappears, the systolic flow decreases and it has a late onset and the diastolic flow increases (Figure 5). The disappearance of the atrial reverse flow can be explained by the loss of the active LA contraction and the decrease of the systolic flow could be secondary to the dysfunction of the left atrial appendage and the spontaneous contrast in the atrium.

It has been hypothesized that changes in pulmonary flow in patients with AF appear to reflect impaired LA function, mainly the compliance of atrial cavity and the reservoir function. Diastolic pulmonary venous flow is useful for assessing LV diastolic pressures. The time of pulmonary diastolic venous deceleration (DT) correlates better with PCWP compared with the transmural TDE evaluated using PW Doppler. Some authors argue that pulmonary venous flow can be used as a monitoring tool for the recovery of LA mechanical function after cardioversion.
or after ablation. The decrease of the velocity of the systolic flow during the rhythm of AF as well as immediately after the success of the cardioversion is associated with the recurrence of AF at 6 and 12 months, respectively. In contrast, after the pulmonary vein isolation procedures, the high velocities of early systolic flow >57 cm/sec predict a good mechanical recovery secondary to the preservation of the LA reservoir function (11).

As mentioned above, the parameters resulting from the echocardiographic analysis can improve the early detection of AF episodes, being highly predictive compared to the clinical parameters, and can thus be used to reduce the complications of this arrhythmia. Comparing the characteristics of patients with episodes of paroxysmal AF with a group of patients without a history of AF, it was observed that the ultrasound indexes such as the velocity during atrial contraction (a'- evaluated by TDI method), the antero-posterior diameter of the LA and the diameter of the aorta root had the ability to identify the presence of this arrhythmias (27). The ultrasound parameters also have the ability to predict the transition from the paroxysmal form of AF to the chronic form of arrhythmia. Following the analysis of 336 patients over 65 years of age, patients with a pseudonormalization pattern of transmitral inflow, a lower peak atrial reverse flow and a dominant diastolic pattern of pulmonary flow were found to have a higher risk of progression to permanent AF. Thus, these patients had a significantly lower peak A velocity and a lower peak atrial reversal wave velocity, as opposed to parameters such as the velocity of the E wave and the E/e' ratio that did not differ between patients with or without the transition to chronic AF. In this context, it has been appreciated that the decrease of the reservoir (predominant diastolic pulmonary flow) and pump functions (lower peak A velocity) can predict the evolution to permanent AF. Thus, the pseudonormalization pattern could be secondary to the LA dysfunction and not the differences in the type of diastolic dysfunction (28).

**Atrial strain in atrial fibrillation patients**

The strain and strain rate parameters of LA can be measured by TDI imaging, speckle tracking and vector velocities imaging. The strain is defined as being the deformation of a comparable object with its initial form and the strain rate represents the speed with which the deformation happens. Myocardial deformation unfold on 3 levels, but in the case of the LA the longitudinal deformation will be analyzed because it contains fibers with a predominantly longitudinal disposition. LA has 3 functions: reservoir, conduit and pump. The reservoir corresponds to the isovolumic contraction and the ejection period of the LV. The conduit represents the passage of blood to the LV in the early diastole, and the pump represents the contractile function of the late diastole. LA strain can predict the risk of recurrence of AF following cardioversion and ablation procedures, as well as the risk of evolution from paroxysmal AF to persistent AF (29). It has been shown that the strain parameters are superior to the standard echocardiographic parameters in order to predict the maintenance of the sinus rhythm after cardioversion (30). At the same time, there are authors who have shown that the value of the deformation parameters increases after cardioversion and ablation, with the improvement especially of the reservoir strain in the patients maintaining their sinus rhythm, secondary improvement of the atrial
remodeling. The regional atrial strain rate could be used to analyze diastolic function in AF patients. In AF, there could be regional differences in diastolic filling depending on the LV response to the atrial fibrillating waves. The degree of deformation of the atria shortly after AF installation is reduced. The improvement of the pump function reflects the gain of the contractile function. Left atrial stasis occurs secondary to atrial mechanical dysfunction. It has been found that reservoir strain has low values especially in patients who associate spontaneous contrast in LA and thrombi in left atrial appendage. The peak systolic strain (reservoir function) is correlated with emptying flow velocities from the left atrial appendage (measured with PW Doppler) at 7 days from an ischemic stroke in both patients with sinus rhythm and those with paroxysmal AF. The peak systolic strain of the LA is a noninvasive marker of the extension of atrial fibrosis being a parameter dependent on both LA relaxation and stiffness and LV systolic function.

**Role of transesophageal echocardiography in atrial fibrillation**

Transesophageal echocardiography (TOE) is less used for measurements because of underestimation of LA size, but this technique is very important for identifying LAA thrombus (Figure 6) and severe spontaneous contrast in patients with AF. To appreciate the mechanical function of the LAA, the PW Doppler is used to measure the emptying and filling flow velocities of this structure. Low emptying flow velocities (less than 20 cm/sec) correlate with the presence of spontaneous contrast or thrombi, whereas LAA emptying flow velocities >40 cm/sec predict the chance to remain in sinus rhythm 1 year after the successful of cardioversion.

The echocardiographic predictors of thromboembolism in patients with AF are: LA dilatation, LV systolic dysfunction, valvular disorders, atheroma plaques at the level of the aorta, thrombi from the LAA and low velocities at its level. The last 3 elements can be identified mainly through TOE. The 3D TOE technique would have the ability to discriminate very well the muscles combated by the thrombi in the LAA.

The cardioversion of patients with AF at sinus rhythm has a high success rate, but at a small percentage of patients complications of thromboembolic events may occur, especially if the procedure was not preceded by the administration of anticoagulants at the therapeutic dose. Thus, TOE would play an important role in the early cardioversion guided by this ultrasound technique in patients who have an absence of thrombi, reducing the required 3-weeks...
anticoagulation duration before the procedure. At the same time, TOE guided early cardioversion can prevent left atrial remodeling along with a high conversion rate and maintaining sinus rhythm. Thromboembolic events usually occur in patients without optimal anticoagulant dosage, in the context of undetectable extremely small thrombi or thrombi resulting from atrial stunning\(^{(11)}\).

The presence of thrombi in the LAA or the LA is an absolute contraindication for the ablation procedure\(^{(5)}\).

**Conclusions**

TTE is a noninvasive routine imaging technique that allows a rapid analysis of cardiac anatomy and function, identifying structural and functional alterations that favor AF installation. TOE is a semi-invasive procedure that can create discomfort for patients, but useful in assessing thromboembolic risk and in guiding AF cardioversion. These techniques are also very useful in monitoring and detecting early and late post-ablation complications.

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