

# EACVI/EHRA Expert Consensus Document on the role of multi-modality imaging for the evaluation of patients with atrial fibrillation

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Atrial fibrillation (AF) is the commonest cardiac rhythm disorder. Evaluation of patients with AF requires an electrocardiogram, but imaging techniques should be considered for defining management and driving treatment. The present document is an expert consensus from the European Association of Cardiovascular Imaging (EACVI) and the European Heart Rhythm Association. The clinical value of echocardiography, cardiac magnetic resonance (CMR), computed tomography (CT), and nuclear imaging in AF patients are challenged. Left atrial (LA) volume and strain in echocardiography as well as assessment of LA fibrosis in CMR are discussed. The value of CT, especially in planning interventions, is highlighted. Fourteen consensus statements have been reached. These may serve as a guide for both imagers and electrophysiologists for best selecting the imaging technique and for best interpreting its results in AF patients.

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Atrial fibrillation • Cardiac imaging • Cardiac magnetic resonance • Doppler echocardiography • Computed tomography • Pathophysiology

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## Introduction

Evaluation of patients with atrial fibrillation (AF) requires an assessment of cardiac structure and function. Such an assessment complements the clinical evaluation, and helps decision-making regarding rhythm strategy (rhythm control vs. rate control), stroke risk stratification, and prognosis. Increasingly sophisticated imaging techniques are now available and have been used for this purpose.

To address the role of multi-modality imaging for the evaluation of patients with AF, a Task Force was convened by the European Association of Cardiovascular Imaging (EACVI) and the European Heart Rhythm Association (EHRA), with the remit to comprehensively review the published evidence available, to publish a joint expert consensus document on the role of imaging techniques and their applications in patients with AF, and to provide recommendations for their use in clinical practice.

## A. Epidemiology, pathophysiology, and clinical background

AF is the commonest sustained cardiac arrhythmia and represents a global healthcare problem, with an increasing prevalence and incidence.<sup>1</sup> People over the age of 40 have a one in four lifetime risk of developing AF, which is more common in association with increased age, medical comorbidities [e.g. systemic arterial hypertension, heart failure (HF), prior myocardial infarction, sleep apnoea, obesity, alcohol excess, etc.].<sup>2</sup> Some of the risk factors for AF also contribute to its complications, particularly stroke and thromboembolism and HF.

Most commonly, patients have so-called non-valvular AF, which is defined as AF in the absence of prosthetic mechanical heart valves, or 'haemodynamically significant valve disease'.<sup>3,4</sup> The 2012 focused update of the ESC guidelines states that it is conventional to divide AF into cases that are described as 'valvular' or 'non-valvular'.<sup>5</sup> Valvular AF was defined as rheumatic valvular disease (predominantly mitral stenosis) or prosthetic heart valves. Similarly, the 2014 AHA/ACC/HRS Guideline for the management of patients with AF defined non-valvular AF as AF in the absence of rheumatic mitral stenosis, or a mechanical heart valve, but explicitly added bio-prosthetic heart valves or mitral valve (MV) repair.<sup>6</sup> Of note, significant valve disease was generally excluded from the recent randomized trials of stroke prevention in AF. In the RE-LY trial, patients with 'severe heart valve disorder' were excluded, whereas the ROCKET-AF trial

excluded those with 'haemodynamically significant MV stenosis' and the ARISTOTLE trial excluded those with 'moderate or severe mitral stenosis'.<sup>7–10</sup>

Cardiovascular imaging can provide insights into the aetiology, pathophysiology, risk stratification, and some therapeutic interventions in patients with AF. Management decisions on rate and/or rhythm control are determined by patient symptoms and ECG phenotypes.

Nonetheless, AF is a chronically progressive disease. In the ESC guidelines, the five clinical subtypes of AF encompass the progression from undiagnosed episodes through first diagnosis and infrequent paroxysms to long-lasting persistent and eventually permanent AF<sup>11</sup> (Box 1).

While AF increases the risk of stroke and thromboembolism five-fold, this risk is not homogeneous, and depends on the presence of various stroke risk factors.<sup>12</sup> The major guidelines (European,<sup>13</sup> American,<sup>14</sup> NICE<sup>15</sup>) all now recommend the use of a clinical risk factor-based approach, with the CHA<sub>2</sub>DS<sub>2</sub>-VASc score.<sup>16</sup>

The 'C' criterion in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score refers to:

- Recent congestive HF whether with reduced or preserved ejection fraction (EF) (thus, including patients with moderate–severe systolic impairment, cardiomyopathy, etc.).
- LV systolic dysfunction defined by LVEF  $\leq$  40%.

Left atrial (LA) dilatation is often associated with AF. It is associated comorbidities. It has not been demonstrated as an independent prognostic marker of stroke in multivariable analysis.<sup>17,18</sup>

Additional refinement of stroke risk stratification is obtained by imaging, for example, using transoesophageal echocardiography (TOE) where spontaneous echo-contrast, reduced LA appendage (LAA) velocities, or complex aortic plaque all increase the potential for stroke risk.<sup>19</sup> Given that most thrombi form within LAA, cardiac

imaging plays a role when LAA occlusion is being considered as an interventional procedure.

## B. Overview of anatomy of the atria and of the pulmonary veins

### Normal LA structure and function

The LA modulates LV filling through three components: reservoir phase of expansion during systole, a conduit phase during early diastole, and an active contractile component during late diastole.<sup>20</sup> Augmented LA booster pump function is one of the mechanisms compensating for decreased early filling in patients with reduced LV compliance, whereas a loss of atrial contraction reduces cardiac output by  $\sim$ 15–20%.<sup>21,22</sup> An increase in LA contractility is considered to be caused by the increase of LA volume (Frank–Starling's law) (Figure 1). As a result of optimal use of the Frank–Starling mechanism of the atrial muscle, atrial shortening is remarkably augmented with chamber dilation. When the extent of LA shortening and expansion is diminished, despite the geometrical advantage of a further increase in atrial diameter, extreme dilation no longer provokes the Frank–Starling response and the atrial myocardium is made to operate on a 'descending limb' of function.<sup>23</sup> The body forms the central part of LA with LAA bulging superiorly and leftward as a tube-like structure to pass round the origin of the pulmonary trunk.<sup>24</sup>

Surrounding the mitral orifice is the vestibular component. The pectinate muscles are confined within the appendages. The muscles build a complicated network of muscular ridges lining the endocardial surface.<sup>24</sup> The LA is smooth walled on its internal aspect. In general, LA walls are thicker than right atrial walls.<sup>25</sup> The thickness of LA muscle ranges from 3.5 to 6.5 mm.<sup>26</sup> The LA wall thickness ranges from 2.5 to 4.9 mm. The LA anterior wall ranges from 1.5 to 4.8 mm.<sup>24</sup> Interestingly, there is an area of the anterior wall just behind the aorta that is exceptionally thin, an area noted by McAlpine as the 'unprotected' area at risk of perforation. The posterior LA wall, closely related to the oesophagus, has a thickness of  $4.1 \pm 0.7$  mm.

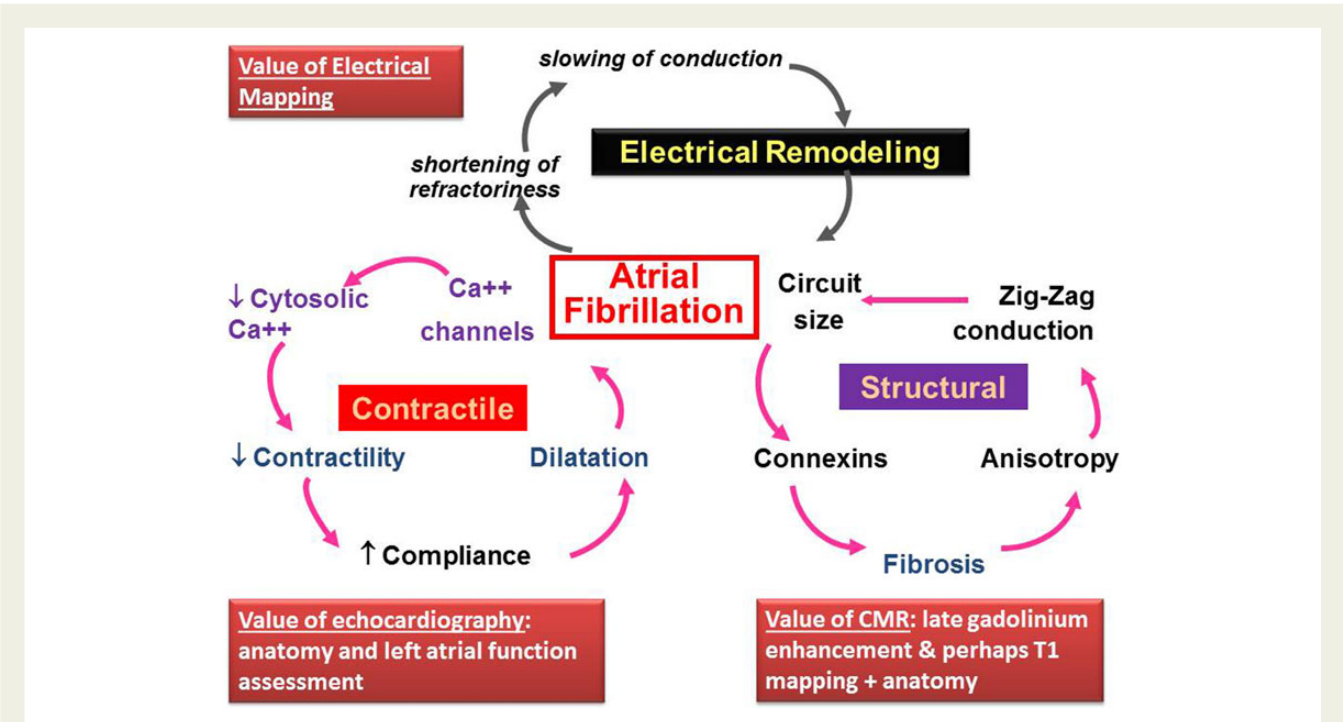
The posterior part of LA is the venous component.<sup>24</sup> During heart development, the oblique vein of LA (vein of Marshall) passes from a superior aspect onto the epicardial surface of LA in between LAA and the left superior pulmonary vein to descend along the posterolateral LA wall to join the coronary sinus. In the minority of patients, the lumen of the oblique vein remains patent.<sup>25</sup> In the majority, however, the vein is obliterated and forms the ligament of Marshall. Within LA itself, there is a much more irregular arrangement of the myocytes, the alignment often changing at different depths within LA walls. In general, myocytes are aligned parallel to the atrioventricular grooves in the vestibule, but transversely across the atrial roof.<sup>22</sup>

### Pulmonary veins

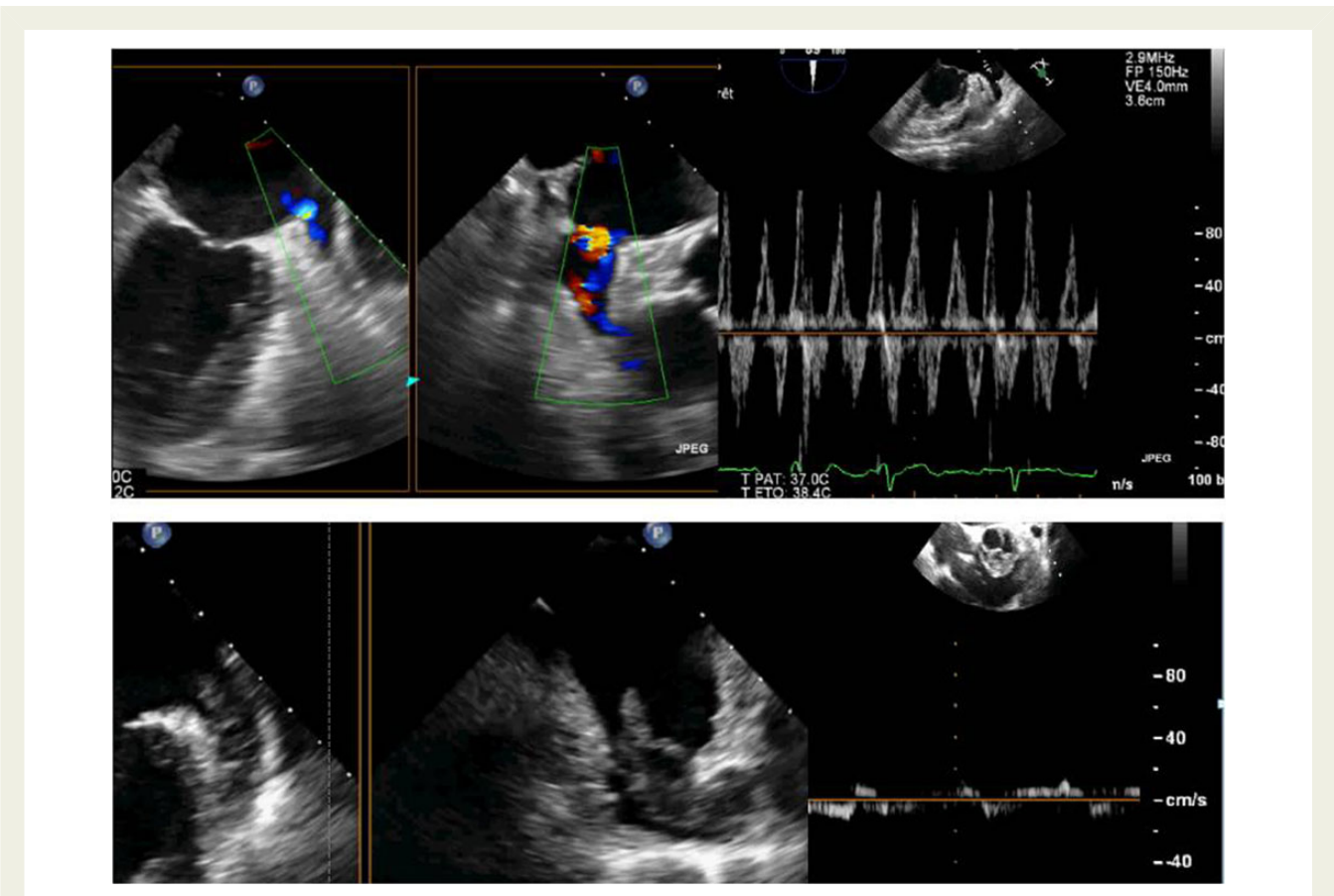
In general, four pulmonary veins enter the LA (common ostia, accessory pulmonary veins are some of the possible anatomic variants that can be found especially by cardiac CT) (Figure 2). However, the anatomy is variable with common ostia from superior and inferior veins or additional veins. The histology is complex and described elsewhere.

#### Box 1 Clinical subtypes of AF in the ESC guidelines on AF.<sup>11</sup>

1. Every patient who presents with AF for the first time is considered a patient with first diagnosed AF, irrespective of the duration of the arrhythmia, or the presence and severity of AF-related symptoms.
2. Paroxysmal AF is self-terminating, usually within 48 h. Although AF paroxysms may continue for up to 7 days, the 48 h time point is clinically important. After this period, anticoagulation must be considered and the likelihood of spontaneous conversion decreases.
3. Persistent AF is present when an AF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion (DCC).
4. Long-standing persistent AF has lasted for more than 1 year.
5. Permanent AF is said to exist when the presence of the arrhythmia is accepted by the patient and physician. Hence, rhythm control interventions are, by definition, not pursued in patients with permanent AF.



**Figure 1** Presentation of the pathophysiology of LA (AL) remodelling and the relationship between each kind of remodelling.



**Figure 2** Example of the LAA cavity and the corresponding emptying flows. (A) Normal left appendage with normal emptying flows; (B) complex morphology of the left appendage with a large thrombus coming from the bottom to the mouth of the cavity and the corresponding severely blunted flows recorded with the pulse Doppler at the level of the appendage mouth.



Of note, at the veno-atrial junctions, there are abundant autonomic nerve bundles, ganglia, and nerve plexuses situated in the epicardial fat pads.<sup>27,28</sup> The mitral isthmus extends between the orifice of the left inferior pulmonary vein and the mitral hinge line. An imaging analysis of 169 patients with cardiac CT showed a significant, direct, relationship between AF burden and the thickness of the posterior peri-atrial fat pad between the oesophagus and the left atrium.<sup>29</sup>

## LA appendage

The LAA can be considered as a remnant of the embryonic LA.<sup>30,31</sup> The anatomy and volume of LAA is highly variable with estimated surface areas of 3.0–6.0 cm<sup>2</sup>.<sup>30</sup> Dilatation of the atria appears to be induced, to some extent, by increased expression of protease (ADAM), which causes loss of cell–cell and cell–matrix interactions.<sup>32</sup> In physiology, LAA appears to contribute to the regulation of cardiovascular pressure–volume relations since it is the main source of synthesis of atrial natriuretic peptides.<sup>20,33</sup> Amputation of both appendages may induce significant alterations in fluid haemostasis and oedema formation.

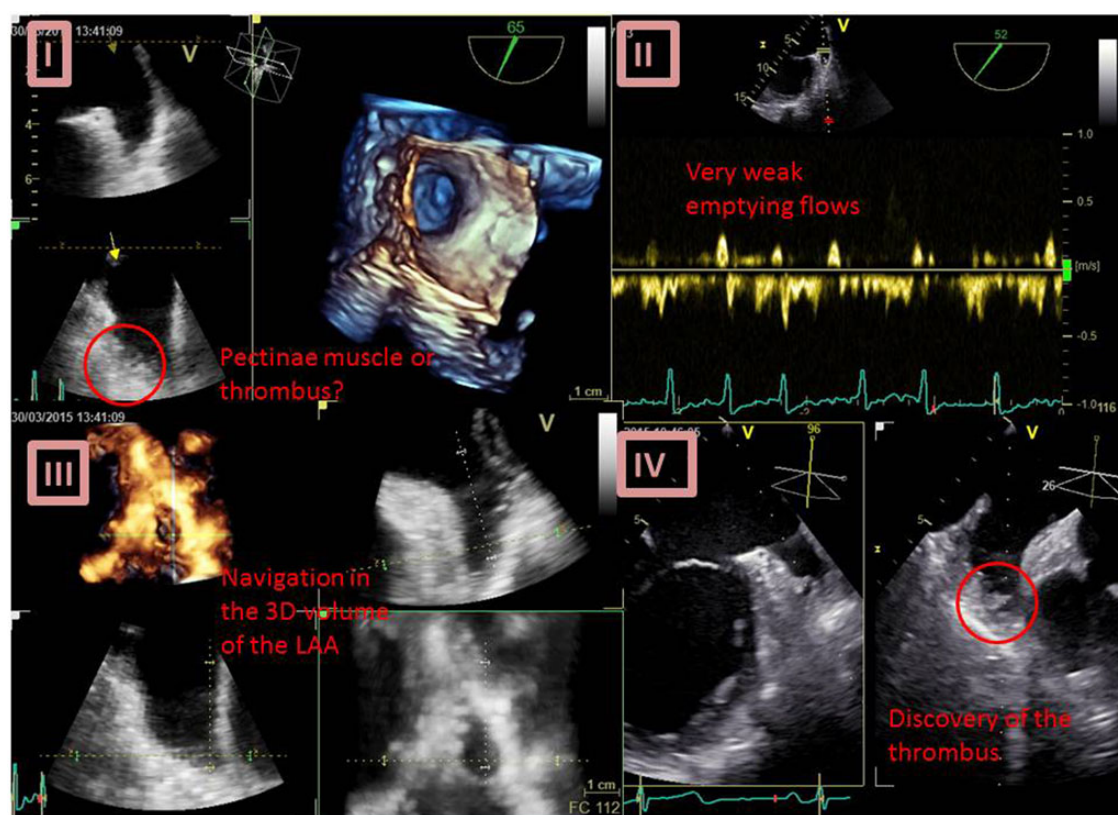
LAA is the most prominent site for LA thrombus formation, especially in patients with AF.<sup>22</sup> Loss of regular atrial contractions reduces blood flow velocities, particularly in the atrial appendages, and activates the clotting system (Figure 3).

## C. Non-valvular AF: how to assess the atria and the heart functions

### 1. Standard echocardiography

#### 1.1 LA size and function

Among patients with AF, LA enlargement has been suggested as a predictor of stroke in several studies.<sup>34</sup> Most of the investigations regarding the prognostic impact of LA size relied on the antero-posterior diameter measured by M-mode (AP diameter). However, this method is based in several geometric assumptions that often result in LA size under-estimation.<sup>35</sup> LA enlargement is often asymmetrical, as enlargement in AP axis may be limited by the thoracic cavity, and it may also occur in medial–lateral or superior–inferior axes.<sup>36</sup> In 317 patients in normal sinus rhythm, LAVi measured from biplane 2D-apical views was superior to four-chamber LA area and M-mode LA dimension in predicting the development of first AF, congestive heart failure (CHF), stroke, transient ischaemic attack, acute myocardial infarction, coronary revascularization, and cardiovascular death over 3.5 years of follow-up.<sup>37</sup> Unfortunately, the maximal LA volume that one might tolerate to predict the success of an intervention remains unknown. From AFFIRM, the need for more than two cardioversions in the first year in patients taking anti-arrhythmic medication included left atrial diameter >4.5 cm. Nevertheless, sensitivity and specificity of this was low.<sup>38</sup>



**Figure 3** Analysis of the LA appendage. (I) 3D and corresponding 2D images; (II) pulse Doppler). (III) Navigation in the LAA volume for distinguishing a pectinae muscle from a thrombus. (IV) Corresponding 'ideal' 2D image showing a small thrombus within trabeculations.

Of note, mitral annular calcification has been shown to be an independent predictor of the occurrence of AF. Also mitral annular calcifications have been shown to be an independent predictor of adverse outcomes such stroke and death,<sup>39,40</sup> and has been associated with aortic atheroma.<sup>41</sup>

Thus, LA AP diameter has been considered inaccurate, while LA areas or volumes assessed by TTE rely on fewer geometric assumptions.<sup>42</sup> However, a complete assessment of the LA size and function may not rely on maximum LA volume alone, as LA dimensions vary widely during the cardiac cycle. An electrocardiogram-guided echocardiography allows an accurate quantification of LA functions by measuring LA volumes at different times during the cardiac cycle: at end-systole, the LA maximum volume, at end-diastole, minimum LA volume, at mid-diastole, just before atrial contraction, pre-A-volume.<sup>43</sup> The combination of these LA volumetric measurements allows the calculation of the indices corresponding to the three basic functions of the LA, reservoir function, conduit function, and booster pump function.<sup>23</sup>

Functional assessment of the LA also includes the evaluation of the pulmonary vein and transmitral flow, also used to describe LV diastolic function, which was shown to greatly influence LA size and function. One previous study<sup>44</sup> demonstrated that reduced LA reservoir function increases the risk of new-onset AF independently of LA volume. More recently, Hirose et al.<sup>45</sup> showed that LA booster pump function was a much better predictor of new-onset AF than LA dimension or LA volume (Figure 4).

LA structural remodelling is often accompanied by a change in LA function with a progressive increase in interstitial fibrosis.<sup>46,47</sup> The reduction in LA booster pump function may be a manifestation of LA mechanical remodelling leading to the development of new-onset AF, up to the loss of booster function in patients with permanent AF.

### Key point 1

Measuring LA biplane volume, using either the area–length or the discs formula indexed by body surface area (BSA), is the method currently recommended for LA size quantification. A normal LA volume is defined as  $<34 \text{ mL/m}^2$ .

### 1.2 LA/LAA thrombi and their predictors

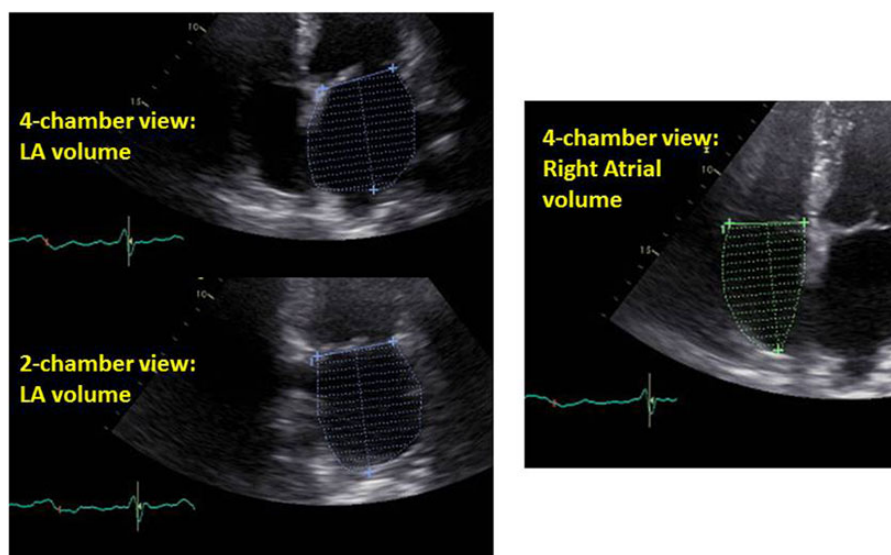
Thromboembolism is the most dangerous complication of AF. Echocardiography is a widely used technique that allows gathering a variety of information about thrombo-embolic risk in patients with AF.<sup>48</sup>

The complementary role of echocardiographic measurements to better refine the predictive value of clinical risk scores such as CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc is well recognized.<sup>49–51</sup> LA size and independently LVEF are predicting the risk of thrombo-embolic events in SPAF.  $e'$  and  $s'$  have been demonstrated as well as LA strain, LAA spontaneous echo-contrast is other study summarized recently, by Szymanski et al.<sup>51</sup>

TOE allows the following information to be obtained in a patient with AF:

- A 2D multiplane or 3D analysis of the complexity of LAA anatomy.
- A semi-quantitative classification of the degree of spontaneous echo-contrast.
- A Doppler measurement of the LAA emptying flows.

Spontaneous echocardiographic contrast (SEC), also known as 'smoke' or 'swirl', can be considered as the initial stage of thrombus formation<sup>52</sup> and is associated with low flow states<sup>53</sup> (Table 1). Moreover, increasing severity of SEC is associated with decreased LAA flow velocity and increased LA size.<sup>54,55</sup> Sludge is a dense SEC, with a viscid, but not solid echodensity. It is often difficult to



**Figure 4** Parameters for estimation of right atrial filling pressures.

**Table 1** Classification of the spontaneous echo-contrast according to corresponding emptying flow velocities<sup>54,55</sup>

	2D Echocardiographic description	Emptying flow velocities
Sludge	Dense smoke, viscid echodensity, not solid	<20 cm/s
Severe spontaneous echo-contrast	Intense echodensity and very slow swirling patterns in the left atrial appendage,	20–40 cm/s
Mild to moderate spontaneous echo contrast	Swirling pattern in the LA appendage	40–60 cm/s

differentiate from a thrombus that represents a stage beyond SEC along the continuum towards thrombus formation and appears to have greater prognostic significance than smoke<sup>56–58</sup> (Figure 3).

LAA thrombus and dense SEC are independent predictors of cardiovascular death, even if compared with other clinical risk factors, such as congestive HF, diabetes mellitus, systemic arterial hypertension, and vascular disease.<sup>59,60</sup>

Transthoracic echocardiography (TTE) parameters are useful tools for the refinement of clinical risk scores.<sup>61</sup>

TTE-derived measurements can allow the prediction of pro-thrombotic changes in the LA and LA appendage but cannot avoid TOE in most individuals.

In the Stroke Prevention in AF study, systolic dysfunction was identified as an independent predictor of ischaemic stroke and systemic embolism.<sup>17,18</sup> In the AF Investigators analysis, the presence of moderate–severe LV dysfunction on 2D echocardiography was the only independent predictor of stroke.<sup>62</sup> LA dilatation or LV hypertrophy was only predictive of stroke on univariable analysis but did not emerge as an independent predictor on multivariable analysis.

Thus, an LVEF <40% is considered to be the equivalent of the congestive HF criterion in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score.<sup>16</sup> A normal LV EF has been associated with the weak prevalence of LAA thrombus in patients with AF undergoing TOE.<sup>63</sup> Moreover, assessment of the LVEF has increased the discriminative capability of clinical classifications (CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores):<sup>64</sup> LVEF, indexed LA volume, and CHADS<sub>2</sub> score were independent predictors of LAA thrombus formation, and their combination was a useful measure for identifying patients at low risk for LAA thrombus formation.<sup>64</sup>

In a study about 295 patients with non-valvular AF and CHADS<sub>2</sub> scores of 0 or 1. All patients underwent TOE before cardioversion and authors reached to the conclusion that: an LVEF < 40% and an LA antero-posterior diameter > 50 mm are independent predictors of the presence of SEC and thrombus.<sup>65</sup> This measurement of LA diameter has been used for many years and has been demonstrated to be related to the prognosis. Nevertheless, current practice should be based on the LA-indexed volume. Epidemiological evidences of the value of LA volume are existing and will confirm that LA diameter should be replaced.<sup>37</sup>

In addition, LV diastolic function has a relationship with thrombo-embolic risk in patients with AF: the E/e' ratio was independently associated with ischaemic stroke on multivariable analysis in a cross-sectional study including 330 patients with persistent AF and preserved LVEF.<sup>66</sup> Peak annular systolic (s') and early diastolic (e') velocities, particularly when combined, have been shown to be independent predictors of a composite of cardiovascular death, recurrent HF, and ischaemic stroke in a cohort study of 148 patients with AF and HF with preserved LVEF with a median follow-up of 27 months.<sup>67</sup>

### Key point 2

*An echocardiographic examination is recommended for every patient with AF to assess cardiac structure and function. An estimate of the degree of atrial remodelling is important (value of indexed LA volume). In addition, transthoracic echocardiography can help to assess the risk of LAA thrombus and help to select patients with an indication to TOE.*

*Past studies have used the theoretically simple measurement of LA diameter using the para-sternal long-axis M-mode approach. Nowadays, LA-indexed volumes should be preferred.*

### Key point 3

*TOE is the most reliable test to rule-out the presence of an LAA thrombus before cardioversion of AF in non-anticoagulated patients and in patients with past diagnosis of LAA thrombus or stroke/TIAs.*

## 1.3 Guiding cardioversion

Pre-cardioversion: assessment of associated cardiac diseases and outcome of cardioversion.

Echocardiographic screening is part of the evaluation of every patient with AF.<sup>68,69</sup> First, before cardioversion a TTE is indicated to decide whether or not to proceed with a cardioversion strategy.<sup>5,70</sup> Clinical markers of failure of a rhythm control strategy have been identified, e.g. summarized in the HATCH score (which stands for hypertension, age > 75 years, thrombo-embolic event, pulmonary disease and HF.<sup>71</sup> Also, echocardiography is providing essential information. Atrial sizes (indexed LA volume), LV systolic and diastolic functions, severity of valvular diseases, and presence of LV hypertrophy all affect the outcome of rhythm control.

Therefore, echocardiography is needed to assess the likelihood of successful rhythm control.<sup>72</sup>

### Key point 4

*The absence of randomized study or large registry demonstrating the prognostic value of imaging techniques in AF patients is nevertheless a real weakness for echocardiography and other imaging techniques.*

Pre-cardioversion: assessment of stroke risk in not anticoagulated or inadequately anticoagulated patients.

TOE-guided cardioversion is an alternative to anticoagulation prior to cardioversion if AF lasts >48 h in patients who were not anticoagulated or were inadequately anticoagulated during the last 3 weeks prior to cardioversion.<sup>73</sup> The presence of a thrombus in the LAA is a contraindication to the performance of cardioversion because of the associated risk for stroke. Therefore, when a rhythm control strategy is chosen in not anticoagulated or inadequately coagulated patients with AF > 48 h or if the duration is unknown, TOE is recommended to exclude LAA thrombus as an alternative to 3 weeks of effective pre-cardioversion anticoagulation.

Per and post-cardioversion: echocardiography can be used for monitoring the heart recovery (LA, LAA but also LV stunning).<sup>74</sup> The difficulty is that the duration of that stunning is variable and has not been extensively studied during the 3 weeks following a cardioversion despite the recommended duration of the anticoagulation of 3 weeks after the cardioversion that one is classically considering.<sup>75</sup>

#### 1.4 Echocardiography and LV systolic function

AF is frequently associated with LV systolic dysfunction or its exacerbation by worsening haemodynamics, sympathetic activation,<sup>76</sup> and by tachycardia-induced cardiomyopathy.<sup>77</sup> Tachycardia-induced cardiomyopathy is a condition in which atrial or ventricular tachyarrhythmias or frequent ventricular ectopy result in left ventricular (LV) dysfunction, leading to systolic HF. The hallmark of this condition is partial or complete reversibility once arrhythmia control is achieved. Tachycardia-induced cardiomyopathy can be classified into two categories: one in which arrhythmia is the sole reason for ventricular dysfunction (arrhythmia induced) and another in which the arrhythmia exacerbates ventricular dysfunction and/or worsens HF in a patient with concomitant heart disease (arrhythmia mediated).<sup>78</sup>

*Tachycardia-induced cardiomyopathy* is a distinct entity that could be characterized by:

- LV systolic dysfunction that is completely or at least partially reversible after the correction of the arrhythmia or the control of the rhythm.
- LV dysfunction without any severe LV enlargement<sup>79</sup> and no specific aetiology except the rhythm disorder.
- The related to the arrhythmia LV systolic dysfunction is hardly predictable.

#### Key point 5

*In AF, the LV systolic dysfunction might be totally or at least partially related to some degree of tachycardia-induced cardiomyopathy. Usually in tachycardia-induced cardiomyopathy, the LV is weakly or not enlarged.*

In the opposite, LV systolic dysfunction is associated with an increased risk of AF.<sup>62</sup> This association is at high risk of stroke.<sup>80</sup>

While most information is available from HF patients with reduced LV function, stroke risk may also be increased in patients with newly diagnosed HF and in those suffering from HF and preserved EF.<sup>81,82</sup>

LVEF is still the most used parameter of LV-systolic function and in clinical practice. It has an important prognostic value in all cardiac disorders, including AF.<sup>83</sup>

The LVEF affects the pharmacological agents that could be chosen. No flecainide if LVEF is decreased, but instead, amiodarone or digoxin could be discussed.

However, echocardiographic assessment of LV longitudinal function may overcome many limitations of LVEF and provide additional and/or incremental prognostic information. Mitral annular plane systolic excursion using guided 2D M-mode imaging is a direct, early, and sensitive index of LV systolic dysfunction, even in the presence of preserved LVEF in several cardiac pathologies, including arterial systemic hypertension.<sup>84</sup> The measurement of  $s'$  at the junction between basal myocardium and mitral annulus by pulsed tissue Doppler is another parameter of LV longitudinal function at LV base, an early marker of subtle LV systolic dysfunction, simple to measure and with good reproducibility and feasibility. When available, global longitudinal strain (GLS) by speckle tracking echocardiography is the optimal parameter to quantify accurately LV longitudinal function, even in AF patients.<sup>85</sup> One beat 3D or tri-plan acquisition can be performed in AF patients. For the prediction of the risk of cardio-vascular events, a cut-off of  $-12.5\%$  has been proposed.<sup>86</sup>

#### *Atrial cardiomyopathy, atrial Fibrillation, and thromboembolism*

Recently, Hirsh et al.<sup>87</sup> highlighted the concept of atrial cardiomyopathy, proposed previously, and characterized by an unusual extensive fibrosis of the LA. As discussed in the present paper, advances in non-invasive cardiac imaging allow the detection, localization of atrial fibrosis as well as its consequences on the LA functions. Inflammation, genetic factors might explain why some patients do develop this cardiomyopathy and some other don't. That inter-patient variability might have to be assessed for a best individual prediction of the thrombo-embolic risk.

#### 1.5 LV diastolic function and estimate of LV filling pressures

LV diastolic dysfunction is an independent predictor of AF in the elderly.<sup>88</sup> Approximately 25–35% of patients with new onset of diastolic HF have evidence of AF<sup>89</sup> and the prevalence increases with the severity of HF, reaching up to 40% in advanced stages.<sup>90</sup> In HFrEF, up to 70% of the population has a history of AF.<sup>91</sup>

In the echocardiographic evaluation of diastolic dysfunction in AF, atrial contraction is lost; consequently, there is no transmitral A (mitral end-diastolic inflow) velocity and no pulmonary Ar (pulmonary vein reversal flow) velocity. Therefore, transmitral E/A ratio and the difference in Ar-A time duration cannot be used. Nonetheless, other diastolic parameters independent of atrial influence could be measured such as E-velocity deceleration time (DT) on transmitral E wave, isovolumetric relaxation time (IVRT), systolic velocity (S) on pulmonary venous flow,  $e'$  velocity on pulsed tissue Doppler, E/ $e'$  ratio.<sup>92</sup> The E/ $e'$  ratio has been



**Table 2** Parameters which can be used to evaluate LV filling pressure in patients with AF

Parameter	Cut-off values for increased LV filling pressure	References	Comment
Mitral flow EDT	<150 ms	Matsukida, 2001 <sup>95</sup> Nagueh, 1996 <sup>93</sup> Temporelli, 1999 <sup>96</sup> Chirillo, 1997 <sup>97</sup>	Correlation with LVFP is stronger when LVEF is reduced and it should not be used when LVEF is normal. EDT should be measured only when the E velocity ends before the onset of QRS
IVRT	<65 ms	Nagueh, 1996 <sup>93</sup>	Rather poor reproducibility
Pulmonary venous flow DDT	<150 ms	Matsukida, 2001 <sup>95</sup> Chirillo, 1997 <sup>97</sup>	A value >220 ms suggests normal LV filling pressure
E/e'	≥11	Sohn, 1999 <sup>98</sup>	Septal e' was used in this study
E/Vp	>1.4	Nagueh, 1996 <sup>93</sup>	Limited clinical value because of reproducibility

EDT, E-wave deceleration time; IVRT, isovolumic relaxation time; DDT, D-velocity deceleration time; E/e', the ratio of mitral E to TDI-derived early diastolic myocardial velocity; E/Vp, the ratio of mitral E to colour M-mode flow propagation velocity.

demonstrated to be an accurate estimate of LV filling pressures in patients with AF<sup>93</sup> (Table 2).

The Doppler estimation of LV-filling pressures in AF is limited by the variability in cycle length, the absence of organized atrial activity, and the frequent occurrence of LA enlargement. In general, when LVEF is depressed, mitral DT ( $\leq 150$  ms) has a reasonable accuracy for the prediction of increased filling pressures. Other Doppler measurements that can be applied include: the peak acceleration rate of mitral E velocity ( $\geq 1900$  cm/s<sup>2</sup>), IVRT ( $\leq 65$  ms), DT of pulmonary venous diastolic velocity [ $\leq 220$  ms, eventually the E/Vp ratio ( $\geq 1.4$ )], and the E/e' ratio ( $\geq 11$ ) that predicts LVEDP  $\geq 15$  mmHg. The variability of mitral inflow velocity with the RR cycle length should be taken into account, because patients with increased filling pressures have less beat-to-beat variation. The average of measurements from 10 cardiac cycles is most accurate, though velocities and time intervals averaged from three non-consecutive beats with cycle lengths within 10–20% of the average heart rate and measurements from one cardiac cycle with an RR interval corresponding to a heart rate of 70–80 b.p.m. are still useful.<sup>93,94</sup>

### Key point 6

*In AF, the comprehensive assessment of LV diastolic function and filling pressures required a combination of several parameters. Mitral annular early diastolic velocity by pulsed tissue Doppler is a marker of LV diastolic dysfunction, and septal e' < 8 cm/s has a reasonable accuracy to identify LV delayed relaxation.*

## 1.6 RA size and function

The right atrium (RA) assists in filling the right ventricle (RV) by acting as a reservoir for systemic venous return when the tricuspid valve is closed, acting as a passive conduit in early diastole when the tricuspid valve is open and acting as an active conduit in late diastole during atrial contraction.

Relationship between enlargement and remodelling of both atria and AF has been described.<sup>99</sup> The RA area is even a prognostic index

of maintenance of sinus rhythm after AF ablation and its reverse remodelling has been described, for instance, after radiofrequency ablation treatment of AF.<sup>100</sup>

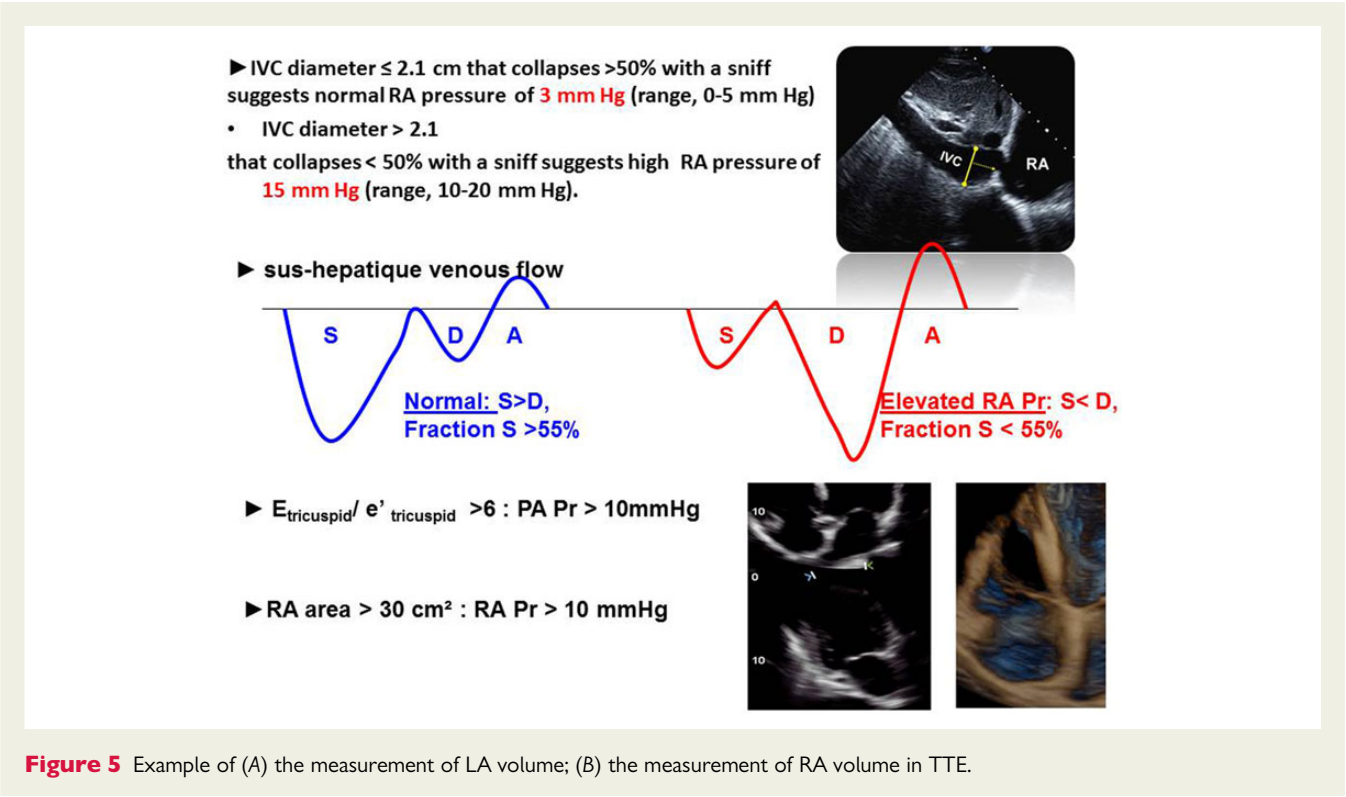
Two-dimensional echocardiographic assessment of RA diameter has been performed by measuring the following:<sup>101</sup> (i) RA area (traced at the end of ventricular systole (largest volume), normal value  $< 18$  cm<sup>2</sup>); (ii) RA length (maximal long-axis distance from the centre of the tricuspid annulus to the centre of the superior RA wall, parallel to the interatrial septum, normal value  $< 53$  mm); and (iii) RA diameter (mid-RA minor distance, defined from the mid-level of the RA free wall to the interatrial septum, perpendicular to the long axis, normal value  $< 44$  mm). RA volume has to be now the main measure that is advised by the 2015 ASE/EACVI recommendations<sup>42</sup> (Figure 5).

### Key point 7

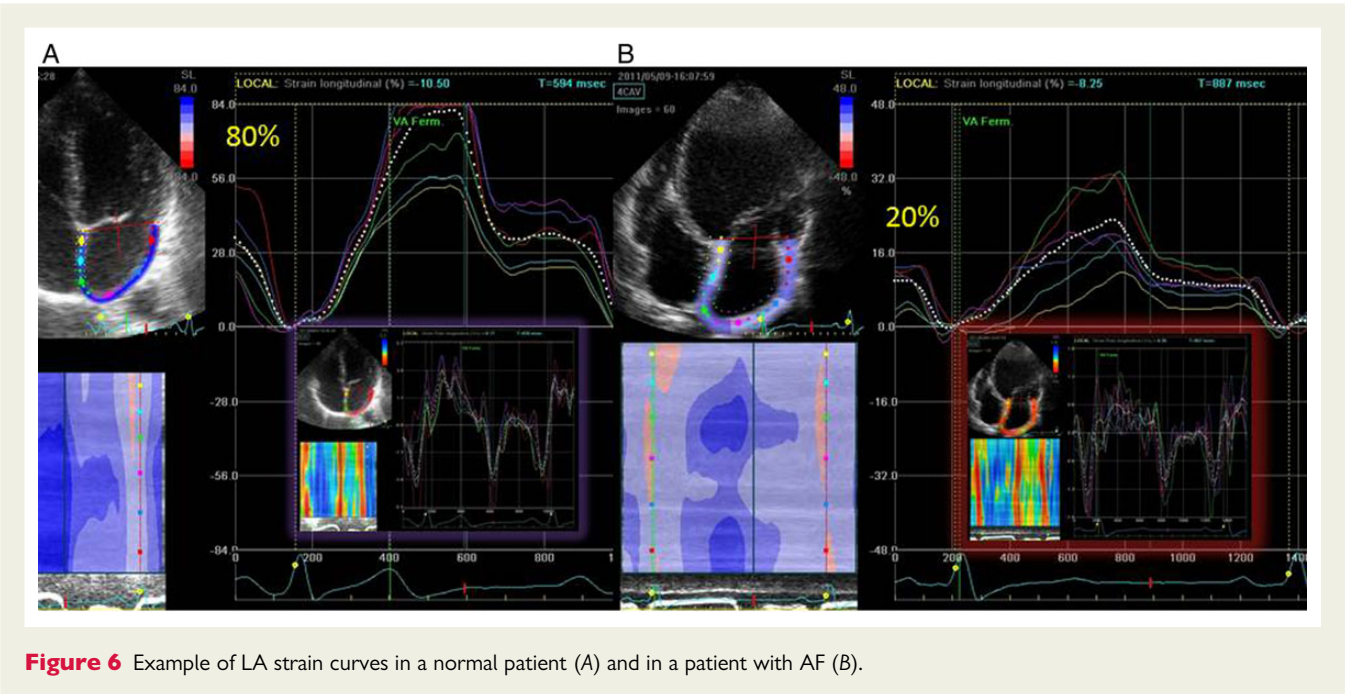
*The normal range for 2DE RA volume index is  $25 \pm 7$  mL/m<sup>2</sup> in men and  $21 \pm 6$  mL/m<sup>2</sup> in women.<sup>42</sup> RA volume  $> 30$  mL/m<sup>2</sup> represents for sure a pathological enlargement of the RA.*

RA pressure is most commonly estimated by inferior vena cava diameter and the presence of inspiratory collapse. In cases where these parameters are not discerning, complementary indices are considered such as hepatic vein flow pattern and the diastolic filling pattern of the RV measured through Doppler imaging (Figure 6). Normally, using Doppler, the hepatic vein systolic filling fraction, which is the ratio of the velocity–time integrals (VTIs) ( $VTI_{systole} / [VTI_{systole} + VTI_{diastole}]$ ), can be obtained. A value  $< 55\%$  was found to be the most sensitive (86%) and specific (90%) sign of RA pressure  $> 8$  mmHg. With higher RA pressure, there was a decrease in systolic filling fraction. The presence of atrial fibrillation causes the hepatic vein systolic flow to be diminished regardless of RA pressure.<sup>102</sup>

TEE: it has recently been discussed the relevance of analyses of the right atrial appendage and not only the LAA in patients presenting an atrial arrhythmia. Among 983 patients with complete anatomic studies of the LAA and RAA, the incidence of LAA thrombus was 9.3% (91 of 983) and 0.73% (7 of 983) in the RAA ( $P < 0.01$ ).<sup>103</sup>



**Figure 5** Example of (A) the measurement of LA volume; (B) the measurement of RA volume in TTE.



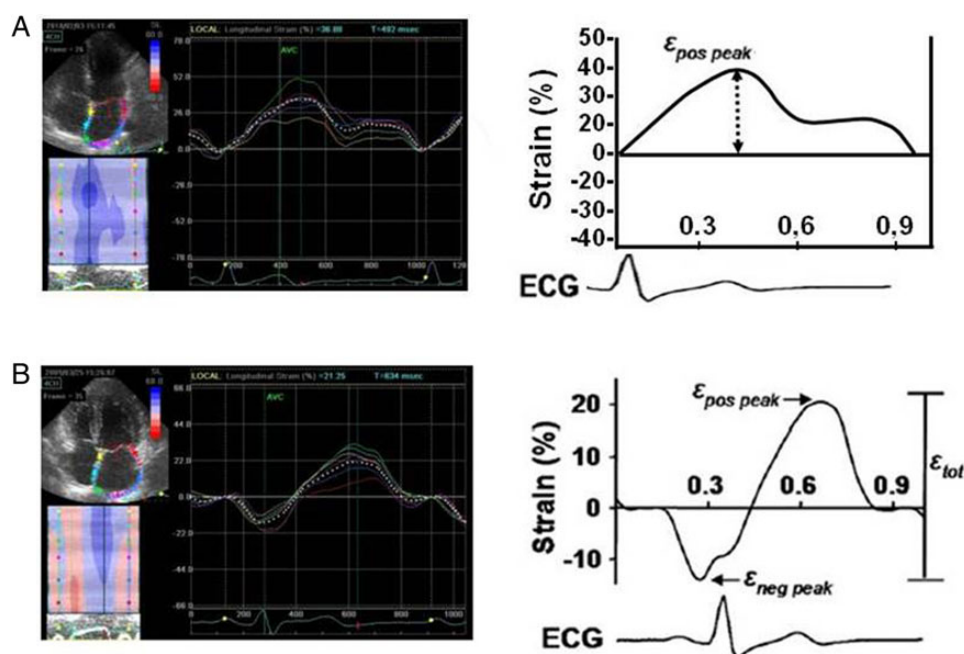
**Figure 6** Example of LA strain curves in a normal patient (A) and in a patient with AF (B).

**1.7 RV function**

While the relationship between the dimension and the function of the RA and AF is properly documented, there are poor data about the RV function in patients with AF, although the importance of heart rhythm for RV function is well known. Moreover, atrial tachyarrhythmias are most common in patients with depressed RV function and their occurrence may be one of the clinical

manifestations of RV failure. Atrial flutter or AF may also cause haemodynamic compromise and worsen prognosis in patients with RV failure.<sup>104,105</sup>

Ventricular interdependence implies the fact that dysfunction of both ventricles often co-exist, mainly dependent on the function of the intraventricular septum: LV failure can lead to RV dysfunction and, on the other hand, RV failure aggravates the prognosis of



**Figure 7** Presentation of the two techniques currently proposed for measuring LA strain. The difference is based on the definition of the start of the analysis at the R-wave (A) or the P-wave (B) of the ECG.

patients with dysfunctional LV.<sup>106</sup> Cohen *et al.*<sup>107</sup> demonstrated, in patient with AF, the relationship between echocardiographic indices of RV systolic and diastolic function [tricuspid annular plane systolic excursion (TAPSE),  $e'$ ] and LV diastolic function. Doppler measurements of RV function ( $s'$ ,  $e'$ ) also correlated with functional capacity, calculated through 6MWT. All these data underline the importance of a complete evaluation of RV function during an echocardiographic examination, particularly in AF patients.

There are several measurements that can be employed:

- End-diastolic basal and mid-cavity RV diameters that are dimensional data useful to evaluate RV dilatation in response to volume or pressure overload. It is equally important to assess whether D-shape pattern of ventricular septal curvature is present as a result of dilatation of the RV;
- Two-dimensional fractional area change (RVFAC), defined as (end-diastolic area – end-systolic area)/end-diastolic area  $\times 100$ , is an index of systolic function that has been shown to correlate with RVEF by magnetic resonance imaging (MRI);<sup>108</sup>

TAPSE is a simple, less dependent on optimal image quality, and reproducible index of RV longitudinal systolic function. It is very feasible and reliable even in patients with AF; TAPSE should be used routinely as a simple method of estimating RV function, with a lower reference value for impaired RV systolic function of 16 mm.

- Tissue Doppler imaging enables measurement of peak systolic velocity of the tricuspid annulus ( $s'$ ) which is another complementary method for evaluating RV longitudinal function at RV base.

The parameters used to assess RV diastolic function are essentially similar to those used to assess the left side. Lang *et al.*<sup>40</sup> reported extensively on that subject. Tricuspid  $E/e' > 6$  is in favour of an increase in right atrial pressure. Tricuspid  $e' < 7.8$  cm/s evokes a right heart diastolic dysfunction.

## 2. Advanced echocardiography

Not mandatory yet but very promising tools to implement in clinical practice.

### 2.1 Speckle tracking

Assessment of atrial function with conventional approaches could be challenging and imperfect. Transmitral flow velocity with pulsed Doppler imaging shows the flow velocity due to atrial contraction. This can be used to measure atrial force, an indirect measure of atrial function.<sup>23</sup> Unfortunately, the A-velocity is absent in AF, recovers gradually after successful electric cardioversion, and is highly dependent on loading conditions and LV diastolic and systolic functions. Thus, the A-velocity is a limited tool for assessing atrial mechanical function. Another way of assessing atrial function is to measure the LA emptying fraction. In sinus rhythm, atrial emptying comprises both passive (conduit) and active (atrial contraction or atrial booster pump function) phases. In AF, there is only a passive phase, hence the term 'emptying fraction' rather than 'ejection fraction'. Myocardial mechanics by strain imaging, which is widely used to assess ventricular function, has also been applied to assess atrial function in a few studies (Figure 7).<sup>109</sup>

Cameli *et al.*<sup>47</sup> measured LA longitudinal strain by speckle tracking and reported a global LA strain of 42%. But that cut-off value cannot necessarily be applied for all studies. The different vendors use

different algorithms in their speckle tracking techniques. For instance, VVI tracks the motion of mitral annular plane in addition to speckle tracking to generate strain curves. Other software are just speckle tracking originally developed for assessment of LV function and then used for assessment of the atrial function, without further validation studies. Differences in these techniques probably result in different values for strain and strain rate in normal subjects and patients. The very thin LA wall poses challenges to pure speckle-tracking techniques. An effort of standardization for assessment of LA function by speckle tracking is therefore needed from the different manufacturers.<sup>110</sup> The acquisition should also be standardized; using the zoom mode, define the optimal frame rate and agree on a standardized reference point. The ECG-derived R-wave is usually the reference point for the assessment of the LV function, but it might generate different strain than a study performed using the P-wave as 'reference zero' value (for instance, normal value of reservoir function =  $46.8 \pm 7.7\%$  for Sun et al. using the R-wave as reference and  $21.4 \pm 6.7\%$  for Saraiva et al. using the P-wave.<sup>111,112</sup> The use of the P-wave is nevertheless limited by its non-applicability to patients in atrial arrhythmia (Figure 7).

Studies on a larger population comparing the different approaches are needed to provide standard or reference values. Kupahally et al. demonstrated that LA fibrosis by cardiac magnetic resonance (CMR) has significant correlation with mid-lateral strain and strain rate, independent of other LA size measurements.<sup>113</sup> The mid-septal area is probably not the area that one has to measure when compared with mid-lateral LA strain because this region is thin and also because of the presence of fossa ovalis or septal aneurysms. The filling pressure in the RA can influence its movement. Nevertheless, most studies have used the average atrial strain without considering the regional strain curves generated by software.

Large population series will have to be conducted to define normal values and values associated with the risk of AF, stroke, or HF. Using CMR approach, and using the MESA cohort, a recent study demonstrated that LA longitudinal strain might be an independent predictor of development of HF in asymptomatic individuals. Also with a cut-off point of 25.8%, LA GLS can predict the existence of a paroxysmal AF in a stroke population with sensitivity of 70% and specificity of 75%. In an observational study, LA strain has also been demonstrated to provide incremental diagnostic information over that provided by the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, suggesting that LA strain analysis could improve the current risk stratification of embolism in patients with AF.<sup>114</sup>

LA contraction, which is seen as negative strain and strain rate, is absent in AF. LA relaxation or peak lengthening strain during ventricular systole, represented by positive strain and strain rate, are important indicators of LA compliance or reservoir function that is impaired in AF caused by fibrosis. Blunted atrial strain was demonstrated to not be directly related to elevation of LV filling pressure (as assessed by the E/e' ratio).

Also, one can keep in mind that from the LV function perspective, LV GLS has been reported to be an independent prognostic marker in patients with persistent AF referred for echocardiography. In this study, GLS was a major parameter and stronger predictor of adverse cardiovascular events than LVEF or pulsed tissue Doppler.<sup>86</sup>

### Key point 8

- (1) The LA lateral wall strain can be reliably imaged and is not constrained by other cardiac chambers and may be used as the best surrogate of LA wall fibrosis by CMR.
- (2) A LA strain (in systole) <30% indicates significant alteration of LA reservoir function, which predicts the poor outcome.

### Key point 9

LA should be measured from the R-wave of the ECG in AF. The beginning of the P-wave should be preferred in sinus rhythm.

## 2.2 Three-dimensional echocardiography

Evaluation of the LA volume is important, as it is a marker of cardiovascular disease and outcomes and correlates with LV diastolic dysfunction severity. LA volume measurements, by different imaging modalities (including 2D and 3D echocardiography (2DE and 3DE), are not interchangeable. Although 2DE underestimates LA volumes, most normative as well as predictive data have been obtained using this modality. Standardization, with established normative data and classification criteria, needs to be established for other imaging modalities, additionally incorporating assessment of LA minimum and phasic volumes. Despite the limitations of the more simplistic 2DE (relies on geometric assumptions regarding the LA shape), its measurements are well defined with a significant prognostic value and still has to be promoted instead of the LA diameter got from the parasternal long-axis view. The incremental prognostic value of the more complex imaging techniques needs to be further validated. The available data have to be considered and the improved workflow of echocardiographic platforms will facilitate its outspreading.<sup>115,116</sup>

Real-time 3DE is free of assumptions and accordingly an attractive alternative for the evaluation of LA volume. The best validation we have for the 3D approach of direct measurement of LA volume includes 92 patients with a wide range of it. Patients underwent CMR (1.5-T) and echocardiographic imaging on the same day. 2DE images were analysed by the biplane area-length technique and 3DE images by TOMTEC LA Function software.<sup>117</sup> 3DE-derived LAV measurements were more accurate than 2DE-based analysis, resulting in fewer patients with undetected atrial enlargement when compared with the CMR reference. Inter- and intra-observer variabilities of 2DE and 3DE measurements of maximal LA volume were similar (7–12%) and approximately two times higher than CMR. Another relevant study included 556 patients with high prevalence of cardiovascular disease. After excluding patients with AF, because (except for one echo-machine) 3D volumes are requiring an acquisition on 4–6 cardiac beats. Four hundred and thirty-nine subjects were followed up to record major adverse cardiovascular events. It was demonstrated that indexed LA volumes (LAVIs) by both 2DE and 3DE are powerful predictors of future cardiac events. Of notice, 3D



minimum LA volume tended to have a stronger and additive prognostic value than 3D maximum LA volume.<sup>61</sup>

#### Key point 10

*Assessment of LA volumes by 3D echocardiography will have to be implemented in clinical practice. It is still not available widely, but it has been demonstrated as really valuable. Like LV volume by 3D echocardiography, it has been proposed as superior to the 2D approach that remains the standard approach.*

### 2.3 Imaging of the LAA

3D is now the standard method of TOE in many echo laboratories. The 3D volumetric and multiplan TOE provides a new window on the complexity of the LAA architecture (Figures 2 and 3). Precise knowledge of LAA orifice size is crucial for correct sizing of LAA closure devices; it will be developed in an upcoming chapter. The implantation of these devices required 3D TOE. Also, patients with a history of stroke had larger LAA mean volumes than control subjects (28.8–13.5 vs. 21.7–8.27 cm<sup>3</sup>,  $P = 0.002$ ). Stroke risk is highest in patients with an LAA volume of >34 cm<sup>3</sup> (multivariable OR 7.11,  $P = 0.003$ ). In conclusion, larger LAA volume is associated with stroke in patients with AF, and this measure can potentially improve risk stratification for stroke risk management in AF patients. As mentioned later, specific 3D guiding is needed for correct positioning of the guide catheter inside the LAA and following the expansion of the occluder.<sup>118</sup>

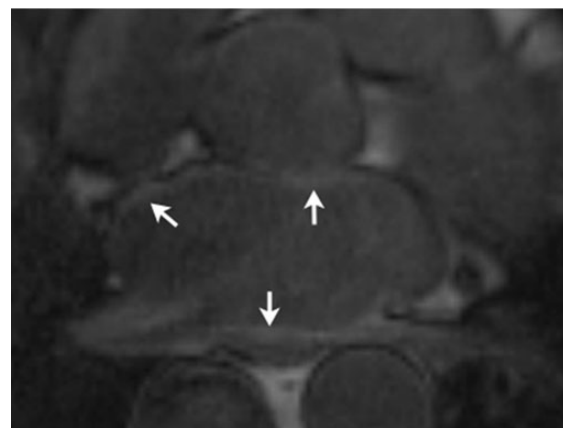
## 3. Cardiac magnetic resonance

Histological studies have demonstrated proliferation of myofibroblasts and variable levels of collagen deposition in the LA myocardium of patients with AF.<sup>119</sup> LA tissue fibrosis is associated with anisotropy, with changes in electrical activation (reduction in myocardial voltage and decrease in the effective refractory period) and is thus considered a substrate perpetuating AF.<sup>120</sup>

The term fibrotic atrial cardiomyopathy is describing a specific, primary form of biatrial pathology, characterized by extensive fibrosis as the substrate underlying atrial arrhythmias and thromboembolism.<sup>87</sup>

#### Technical aspects of CMR in atrial fibrotic tissue characterization

Late-gadolinium enhancement (LGE) CMR is the established method for visualizing, *in vivo*, myocardial tissue fibrosis within cardiac ventricles<sup>121</sup> (Figure 8). However, standard LGE CMR is challenged by the thin-walled atrium. An important step towards assessing atrial fibrosis using CMR has been achieved with the advent of a 3D respiratory-navigated sequence allowing improved spatial resolution.<sup>122</sup> Unlike standard LGE CMR, this free-breathing sequence is not limited by breath-hold duration and thus allows coverage of the whole atrium using a 1.25 × 1.25 × 2.5 mm voxel size. LA fibrotic changes are visible as thin areas of delayed enhancement along the LA wall. Subsequent image post-processing allows quantification of LGE areas. It generally includes two steps: (i) segmentation of LA wall voxels using slice-by-slice manual contouring of epicardial and endocardial borders and (ii) segmentation of enhanced LA



**Figure 8** Example of a CMR with the LGE within the LA walls (arrows).

myocardium (i.e. LA tissue fibrosis) from the histogram of LA wall voxels using a threshold-based algorithm. The resulting segmented volume is then displayed, either qualitatively through a rendered 3D model of LA showing the spatial extent of LGE or quantitatively as a percentage of LA volume.

However, high-resolution LGE CMR of atrial fibrosis remains technically challenging and the post-processing is fairly time-consuming (up to 1 h per patient).

In the multicentre prospective DECAAF study,<sup>123</sup> 17% of LGE datasets were excluded due to poor quality images related to CMR technologist error or patients arrhythmia during acquisition. An alternative approach based on the quantification of LA extracellular volume fraction by T1 mapping technique was recently proposed.<sup>124</sup> T1 relaxation times measured in LA posterior wall were shorter in patients with AF than in controls, thereby suggesting that T1 value might be a surrogate for diffuse interstitial LA fibrosis burden. However, these preliminary results need further confirmation, especially given the limitations of the T1 mapping technique in terms of accuracy and reproducibility.<sup>125</sup>

#### Impact of pre-ablation LGE CMR on AF recurrence

Oakes *et al.* have shown that LA fibrotic remodelling identified by LGE MRI is positively correlated with the likelihood of recurrent arrhythmia following catheter ablation.<sup>126</sup> Other studies from the same group have further documented the link between pre-ablation LGE and poor outcomes of AF catheter ablation.<sup>127,128</sup> These results have been confirmed by the multicentre DECAAF trial in which 329 patients prospectively underwent LGE MRI within 30 days before AF catheter ablation.<sup>123</sup> The authors categorized patients into four groups according to the extent of pre-ablation LGE: stage 1 (atrial fibrosis burden <10%), stage 2 (10–20%), stage 3 (20–30%), and stage 4 (>30%). The cumulative incidence of AF recurrence at day 475 after ablation was 15% for stage 1, 36% for stage 2, 46% for stage 3, and 69% for stage 4. These results suggest that the degree of LA fibrosis quantified by LGE CMR might be used to stratify recurrence risk and therefore personalize the therapeutic

strategy to each patient (i.e. to decide medical management vs. catheter ablation, and if so to tailor ablation strategy to LGE imaging).

Atrial fibrosis has also shown to be significantly and independently associated with the risk of LV systolic dysfunction,<sup>129</sup> with LAA-thrombus formation,<sup>130</sup> and with the risk of stroke.<sup>131</sup> A better knowledge about the impact of fibrosis on atrial electrical activity may allow identifying new ablation targets in persistent AF. Several studies have investigated the relationships between LGE CMR and endocardial mapping.<sup>126,132–136</sup> All of those have reported a strong spatial agreement between enhancement areas on LGE CMR imaging and low-voltage regions on electroanatomic maps. In addition, Jadidi et al. have studied the relationships between atrial fibrosis at LGE CMR and electrogram characteristics from high-density mapping in 18 patients with persistent AF.<sup>133</sup> The authors categorized atrial tissue into dense LGE areas, patchy LGE areas, and non-LGE (i.e. normal) areas. They found an inverse relationship between atrial fibrosis and electrogram fragmentation, with more complex fractionated atrial electrograms in patchy and non-LGE areas, and more organized electrical activity in dense LGE areas. These results might have an impact on ablation strategy. Also, the fusion of LGE CMR imaging with body surface ECG mapping might be a promising way to study the relationships between atrial fibrosis and reentrant AF drivers.<sup>137</sup>

#### In regard to the potential role of post-ablation LGE CMR

Hunter et al. have recently concluded that LGE CMR is not yet sufficiently accurate to reliably assess post-ablation lesion distribution.<sup>138</sup> Moreover, LGE imaging does not seem to provide accurate information on the location of pulmonary veins reconnection sites in patients undergoing repeat ablation for AF.<sup>136</sup>

#### Key point 11

*Up to now, there is neither recommendation nor expert consensus on the role of LGE CMR to assist AF ablation procedures. The available data are intriguing enough to warrant further research.*

## 4. Computed tomography (CT)

Cardiac computed tomography (CT) imaging is increasingly being implemented in clinical routine due to advances in technology offering higher spatial and temporal resolution and hence better diagnostic image quality. Indications for cardiac CT imaging extend beyond assessment of CAD and risk stratification to the use in structural heart disease for pre- and post-procedural assessment of patients referred for several percutaneous interventions. More importantly, the increasing use of acquisition modes with prospectively ECG-gated trigger have led to a significant reduction in effective radiation doses compared with retrospective acquisition modes. In a meta-analysis of 3330 patients, the pooled effective radiation dose for prospectively gated examinations was reduced by a factor of 3.5 compared with retrospective gating (3.5 mSv) compared with 12.3 mSv for retrospective gating,  $P < 0.01$ ).<sup>139</sup> While imaging of the pulmonary venous anatomy prior to pulmonary vein isolation is possible using non-gated CT acquisitions, recent advances in CT

scanner technology allow for low-dose ECG-triggered acquisitions with far superior image quality compared with non-gated-exams. Also, imaging of the pulmonary veins is done using the very routine contrast timing used for a usual cardiac CT.

### 4.1 Epicardial adipose tissue (EAT) and AF

In the past decade, there has been growing interest in 'cardiac adiposity' and its relationship to cardiovascular disease. Epicardial adipose tissue (EAT) refers to visceral fat enclosed within the pericardial sac, and in direct contact with neighbouring cardiac structures. Several imaging modalities such as echocardiography, CT, and CMR can be used to quantify epicardial adipose tissue. Owing to its high spatial resolution and true volume coverage of the heart, CT (and potentially CMR) provides an attractive modality to quantify epicardial adipose tissue. An increasing body of evidence has been accumulated, which demonstrates a relationship between EAT and coronary atherosclerosis, cardiovascular outcomes, and heart disease such as AF.<sup>140,141</sup> The association of increased epicardial adipose tissue with cardiac disease remains significant even after correction for weight, body mass index, and traditional cardiovascular risk factors. The mechanisms have not been reliably identified, but metabolic properties of epicardial fat seem to play a role.<sup>140,141</sup> Obesity is increasingly being recognized as a risk factor for the increasing burden of AF.<sup>140,142–144</sup> Whether localized cardiac ectopic fat rather than traditional measures of obesity is more predictive of cardiovascular disease and AF burden has been a field of intensive research over the past years. Currently, quantification of epicardial adipose tissue is not included in recommended algorithms for risk stratification.

#### Key point 12

*Further studies investigating the association atrial arrhythmia and epicardial adiposity are needed. No real clinical impact is demonstrated yet.*

### 4.2 Geometry of LAA: implications for transcatheter closure

Percutaneous interventional closure of the LAA has emerged as an alternative therapy for reduction of embolic stroke in patients with non-valvular AF and contraindications to oral anticoagulation, and has been shown to be comparable with standard warfarin treatment in reducing thrombo-embolic events.<sup>145,146</sup>

Device sizing is based on TOE, angiographic measurements as well as 3D imaging modalities. 3D imaging using CT provides complete volumetric evaluation of the LAA and its spatial orientation to important neighbouring structures, including the MV and the pulmonary veins. Detailed assessment of the ostium of the LAA with its spatial surrounding is essential for correct sizing and procedural success. Several studies using 3D imaging techniques have reported on the morphology of the LAA in a descriptive fashion.<sup>147–150</sup>

Terminology as 'chicken wing', 'windsock', 'cactus', and 'cauliflower' have been used to describe the LAA morphology. Recently, a study classifying LAA morphology based on the assessment of post-mortem specimens as well as CT imaging in patients referred for

LAA occlusion has been published.<sup>151</sup> The authors classified the LAA into three types according to specific anatomical features, and further evaluated the relation between different LAA morphologies to procedural success and difficulties. LAA was classified according to the level of the ostium, thickness, and width of the left lateral ridge, anatomy of the zone extending between the ostium and the left lateral ridge and the distance to the MV.<sup>152</sup> Appendages in close proximity to the 'LA floor' were described from an interventional standpoint to be the most difficult to occlude, due to the difficulty of coaxially aligning the delivery catheter with the long axis of the LAA.<sup>151</sup> This anatomical information can be provided by CT and not totally by TOE or angiography and may alert operators to use a lower septal puncture or a different delivery catheter.<sup>151</sup>

Furthermore, patients with broader left lateral ridge provide an appropriate landing zone for the occluder device in contrast to patients with narrower ones, in whom compromise of the pulmonary veins could be caused by encroaching devices. Moreover, other anatomical considerations increasing the complexity of the procedure include bilobular appendages and appendages with early branching and absence of an adequate 'landing zone'.<sup>151</sup> In addition, the ellipsoid nature of the LAA ostium as well as the complexity of defining the borders of its orifice may lead to discrepancies in ostial measurements using different imaging modalities. CT offers an accurate modality capable of defining the orientation of the LAA and subsequently providing cross-sectional measurements of the LAA ostium strictly orthogonal to its long axis. The use of CT imaging is not limited to pre-procedural planning, assessment of device position, complete occlusion of the LAA and device-related complications such as thrombosis and para-device leak could be assessed by CT.

### 4.3 CT imaging before and after catheter ablation

#### *Morphological considerations*

Catheter ablation with pulmonary vein isolation is an established treatment option for symptomatic patients with drug-refractory paroxysmal or persistent AF.<sup>11</sup> Detailed anatomy of the LA pulmonary veins and neighbouring structures can be easily provided using CT imaging and is important for procedural planning and to help minimize the risk of complications.<sup>153,154</sup> The number of pulmonary veins, pattern of branching, ostial morphology and measurements, and more importantly anomalous pulmonary vein variants, accessory pulmonary veins, or anomalous pulmonary venous drainage can be easily identified by CT compared with other modalities such as TOE and ICE.<sup>154–157</sup> Spontaneous echo contrast was more commonly diagnosed with ICE ( $P < 0.01$ ). ICE imaging is an alternative to TEE for visualization of the LAA and RAA during catheter ablation procedures.<sup>158</sup>

All the more, 3D reconstructions depicting the complex LA and pulmonary venous anatomy provide important information that may guide the operator in catheter selection and approach for the procedure (Figures 9 and 10).<sup>154</sup> While TOE remains the gold standard for the detection of LAA thrombi prior to ablation procedures, several studies have shown a high diagnostic accuracy of CT to detect LAA thrombi. An adequate scan algorithm with a late pass scan has to be performed. The diagnostic accuracy for detection of LAA thrombi was reported to be 99% in a meta-analysis of studies using delayed imaging protocols.<sup>159</sup> These modified scan algorithms improve the diagnostic accuracy of thrombus detection, which is

usually hampered in early scan phases by delayed contrast filling of the LA appendage in patients with AF.

However, according to the expert consensus statement for catheter and surgical ablation published in 2012, the use of cardiac CT to exclude thrombi of the LAA in patients with high risk of stroke is not recommended.<sup>160</sup> Furthermore, spatial orientation of the LA and the pulmonary veins to the oesophagus can be easily identified and is beneficial in risk reduction of lethal complications such as atrio-oesophageal fistula caused by high-energy application during ablation procedures.<sup>153,154</sup> Pulmonary vein stenosis is nowadays an infrequent, yet known complication following catheter ablation procedures.<sup>161,162</sup> In patients with symptoms suggestive of pulmonary venous obstruction, serial CT assessment of pulmonary veins allows for detection or exclusion of stenosis.<sup>154</sup> Due to the wide variation in pulmonary venous anatomy, acquisition of a pre-procedural scan for comparison purposes is important especially to detect cases with only mild-to-moderate stenosis that may progress with time.

#### *Integration of CT anatomy and electro-anatomical mapping*

The introduction of 3D electro-anatomical mapping systems has led to a new era in catheter ablation procedures. Data acquired from electrical mapping of the left atrium are used to render a 3D geometrical map of the left atrium. However, these maps are operator-dependent and are subject to anatomical inaccuracies.<sup>163</sup> Technological advances has allowed for fusion of pre-procedural CT images either direct into fluoroscopy or into electro-anatomical mapping systems providing 3D depiction of individual patient anatomy.<sup>163</sup> The static nature of the CT images as well as the time lag between CT acquisition and the ablation procedure with subsequent change in volume status and potentially rhythm status are acknowledged limitations for such fusion modalities. Furthermore, data evaluating patient outcomes' after catheter ablation procedures with and without integration of pre-procedural CT anatomical data are controversial.<sup>163–167</sup> Whether the use of such fusion technologies translate into better patient outcomes remains questionable and need to be assessed in future prospective studies (Figure 10).

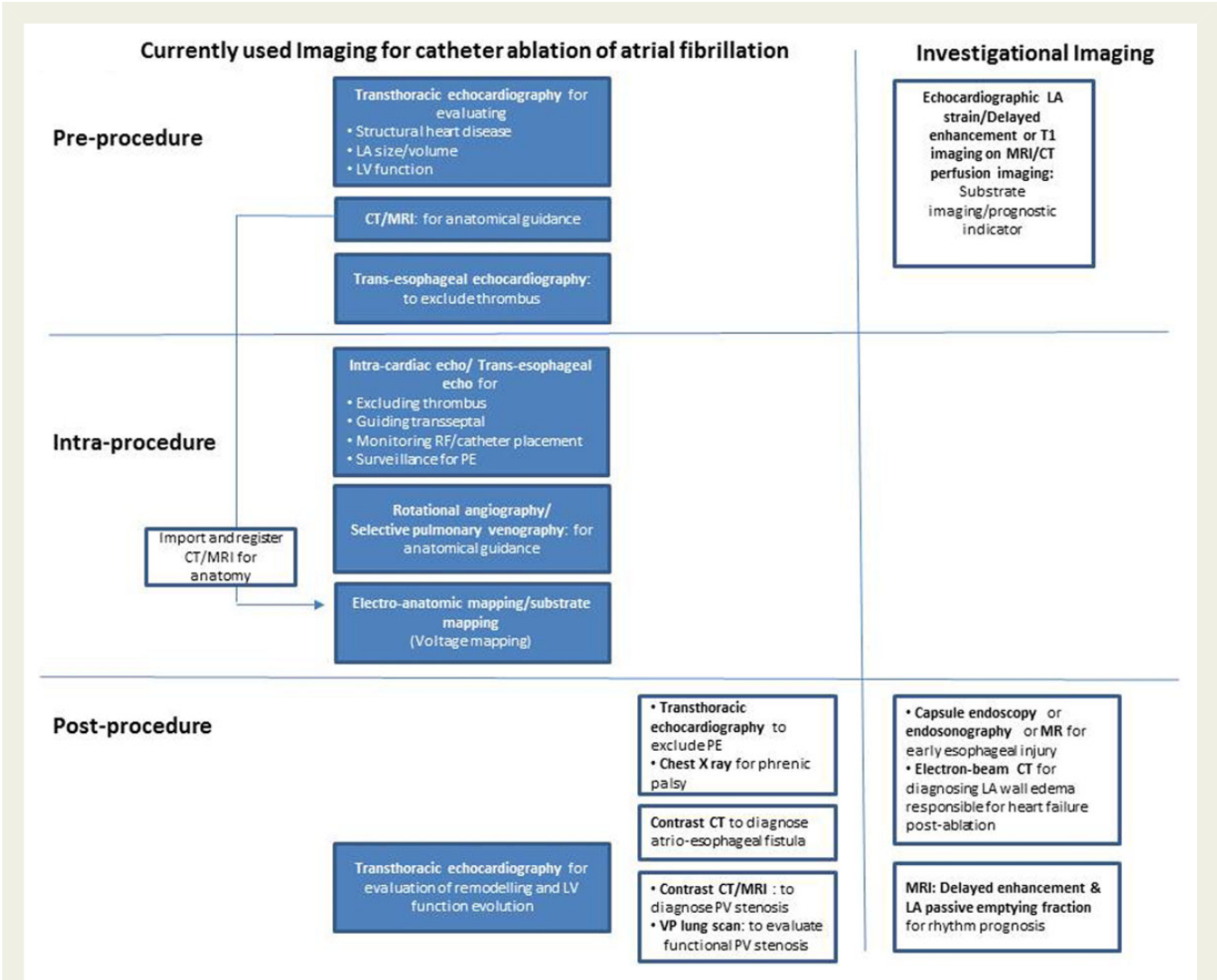
## D. Specificity of the imaging assessment of AF patients

### 1. Cases of the valvular heart diseases

#### 1.1 MV disease

Echocardiography plays an essential role for the diagnosis and follow-up of patients with MV disease and AF, guiding both the timing and the type of intervention.

It is well known that valvular heart diseases, and particularly those involving the MV, are associated with AF;<sup>168</sup> however, the precise rate of association of AF and organic MV disease has been variably reported with a relationship between LA size and the incidence of the arrhythmia. In the largest series reported in patients with degenerative mitral regurgitation (MR), AF was a common complication if patients were managed conservatively, occurring at a linearized rate of 5% per year and the risk increased with advancing age.<sup>169</sup> The onset of AF was independently associated with an increased risk of adverse cardiac death and HF. Indeed, AF is considered a risk factor of



**Figure 9** Algorithm of the role of imaging modalities in the process of AF ablation.

worse outcome in patients with either mitral stenosis or regurgitation and is considered as a possible indication for intervention even in asymptomatic patients (classes IIa and IIb, level of evidence C).<sup>170,171</sup> Additionally, AF is associated with a certain degree of functional MR due to annular dilatation and loss of atrial contraction, which is mild or moderate in most of the cases and secondary to the arrhythmia and the associated cardiac remodelling.<sup>172</sup>

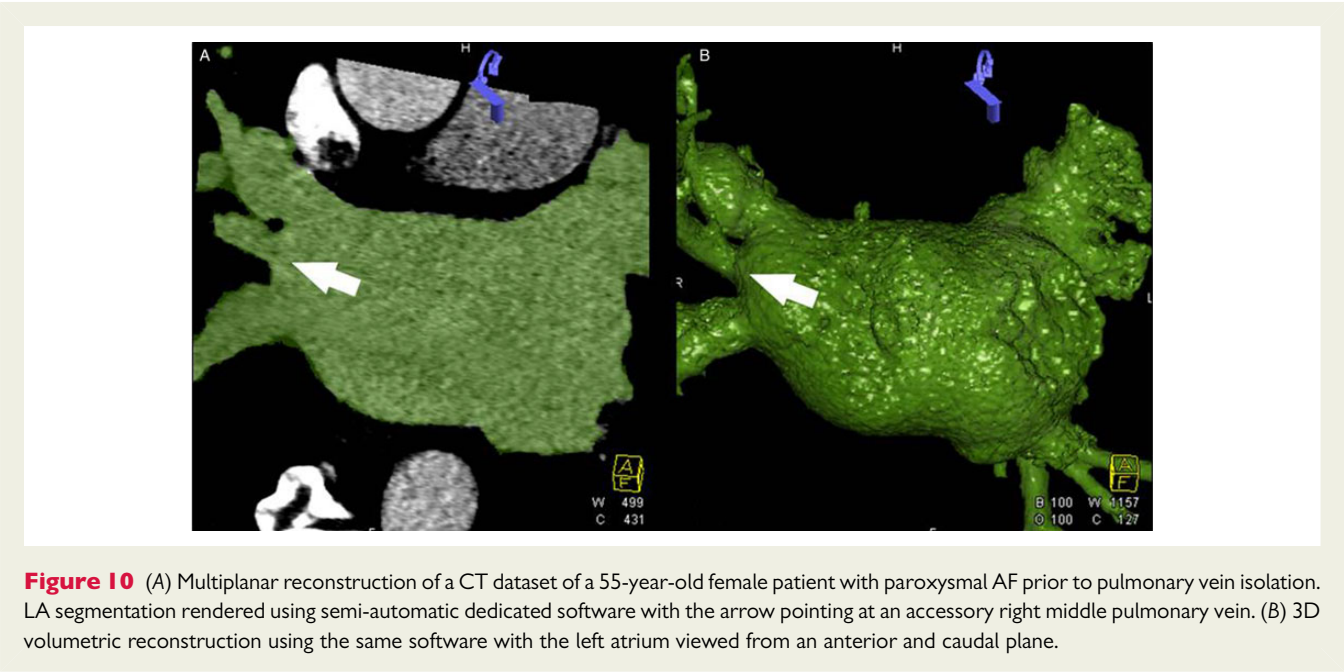
The main contributions of cardiac imaging in patients with MV disease and AF are summarized in Table 3. Echocardiography remains the imaging technique of choice to quantify MV dysfunction. Mitral stenosis severity is typically quantified either by the use of the pressure half-time formula or direct planimetry, with severe stenosis being considered in estimated valve areas of <1.5 cm<sup>2</sup>; other methods such as flow convergence or PISA and quantitative Doppler can also be used. The addition of transvalvular pressure gradients calculated with CW Doppler contributes to the diagnosis. The main limitation of area estimation and gradient calculation among patients with AF is the variability in the R–R cycle due to the different ventricular rate response as well as high heart rates. The former can be

minimized by averaging several cardiac cycles (at least 5) in patients with variable R–R lengths; the latter is more difficult to overcome but one has to keep in mind that transvalvular gradients increase with tachycardia due to shortening of the diastolic time and not necessarily due to more severe valve stenosis; valsalva manoeuvre or pharmacological treatment to reduce ventricular rate response (ideally <80 bpm) might be of help to improve the accuracy of Doppler-echo-based measurements. Three-dimensional echocardiography planimetry has shown the best agreement with invasive methods to determine the stenotic MV area.<sup>173</sup> Although a few studies have shown its potential use to estimate mitral stenosis severity, MSCT and MRI studies are rarely used for this only purpose (Table 3).

In patients with AF, quantification of MR with the PISA method based on 2D echo is recommended and widely used, like in other conditions. A more detailed review of the different methods to quantify MR is reported elsewhere.<sup>174</sup>

Echocardiography also provides information about the morphology of the valve which is essential to evaluate the suitability for





**Figure 10** (A) Multiplanar reconstruction of a CT dataset of a 55-year-old female patient with paroxysmal AF prior to pulmonary vein isolation. LA segmentation rendered using semi-automatic dedicated software with the arrow pointing at an accessory right middle pulmonary vein. (B) 3D volumetric reconstruction using the same software with the left atrium viewed from an anterior and caudal plane.

**Table 3** Contribution of cardiac imaging in patients with AF and MV disease

	TTE	TOE	MSCT	CMR
Quantification of mitral valve dysfunction	+++ includes 3DTTE	+++ includes 3DTTE	–	+
Functional anatomy of the MV: suitability for repair (percutaneous or surgical)	++ includes 3DTTE	+++ includes 3DTTE	+ Calcium	+/–
Haemodynamic impact of MV dysfunction (ventricular volumes and function)	++ includes 3DTTE	+	+	+++
Evaluation of LA size, geometry, function and fibrosis	+++ includes 3DTTE and strain	+ includes 3DTTE	+	+++
Rule out complication of AF and MV disease: LAA thrombus	–	+++	++	++
Guiding intervention: percutaneous or surgical	+ includes 3DTTE	+ includes 3DTTE	–	–

Relative contribution of each technique: – none, + useful, +++ most useful.  
AF, atrial fibrillation; LA, left atrial; LAA, LA appendage; MV, mitral valve; TTE, transthoracic echocardiography; TOE, transoesophageal echocardiography; MSCT, multi-slice computed tomography; CMR, cardiac magnetic resonance.

percutaneous balloon valvuloplasty. In this sense, 3D echocardiography provides a unique comprehensive analysis of the whole geometry of the valve and has been shown to be feasible and useful in the assessment of residual stenosis and regurgitation before, during, and after a percutaneous balloon valvuloplasty procedure.<sup>72,175,176</sup>

1.2 Aortic valve disease

In guidelines, atrial arrhythmias are not proposed as significant events that might impact the treatment strategy. The prevalence of AF is lower in aortic valve disease than in MV diseases. In Rennes surgical database, according to more than 4000 patients assessed for aortic valve replacement, about 10% are in arrhythmia before

surgery and about 15% will have atrial arrhythmia episode in the early post-operative period. These have more co-morbidities, an history of renal failure, stroke, etc.; thus, they have an higher EuroSCORE. In PARTNER A (40%) and in FRANCE-2 (25.5%) the prevalence of arrhythmia is higher than in surgical cohorts.<sup>177–179</sup>

AF is more prevalent in low-flow, low-gradient, preserved LVEF patients. That is in part related to the co-morbidities but it is important to keep in mind that this arrhythmia complicates the assessment of the severity of the aortic stenosis (AS) as it would complicate the assessment of the degree of aortic regurgitation. The ventricular irregularity requires averaging several consecutive gradients and the calculation of the effective orifice area is complicated as well except if the continuous Doppler tracing provide a

clear trace of the LV outflow tract flow and a clear trace of the trans aortic valve flow.

Interestingly, in the years following the surgery, about 40% will present an atrial arrhythmia episode. Also it has been reported by Pilgrim et al.<sup>180</sup> that in patients with a severe AS, independent prognostic markers for death were: body mass index  $\leq 20$  kg/m<sup>2</sup>, diabetes, peripheral vascular disease, and AF, in addition to pulmonary hypertension. Therefore, in the population of patients proposed for a percutaneous treatment of the AS, the prevalence of atrial arrhythmia is greater than in surgical cohort.<sup>181</sup> AF has an independent prognostic value independently of the quality of the aortic prosthetic valve implantation.<sup>182</sup> For the TAVI population, Stortecky et al. reported that AF is associated with a two-fold increased risk of all-cause and cardiovascular mortality among patients undergoing TAVI at 1-year follow-up.<sup>181</sup>

### 1.3 Right heart valve disease

Data in the literature are scarce, but in patients with AF, there is a progressive increase in the RA size and pressure. That leads to an enlargement of the tricuspid annulus. Contemporarily, elevated LA pressure might increase the RV afterload. All these phenomena may lead to a functional tricuspid regurgitation that will increase by participating in this vicious cycle.<sup>183</sup>

## 2. Detection of myocardial ischaemia in patients with AF

### 2.1 Stress echocardiography

As coronary disease and AF can coexist, patients with AF are often referred for stress echo to assess myocardial ischaemia or viability, in the context of existence of symptoms of angina or HF. In the absence of such symptoms, there is no evidence to support the use of stress echo for the assessment of aetiology of new onset AF.<sup>184</sup> More so, AF can develop during stress echo as a complication of the test<sup>185</sup> in patients with or without a history of paroxysmal AF.

*The assessment of wall motion abnormalities in AF patients: reliable or not?*

AF can impact regional LV-systolic function assessment, resulting in both false-positive and false-negative results. Furthermore, in AF, the heart rate may rise excessively at low workload, during either dobutamine stress echo or exercise echo, resulting in low sensitivity of the test, with higher likelihood of false-negative results, which does not seem to alter the prognostic value of the test.<sup>186</sup>

False-positive results may be due to LV systolic dyssynchrony induced by tachycardia-related aberration with bundle branch block morphology of ECG complexes and consequent delayed myocardial activation resulting in delayed contraction. More so, even in the absence of aberration, extreme tachycardia may simply make the interpretation of results difficult, despite the use of heart rate synchronization in between stages on the stress echo template, restricting both the specificity and the sensitivity of the test. Particularly, if the cardiac cycle assessed is preceded by a short cardiac cycle, implying short diastole resulting in limited LV cavity filling and consequent limited contraction in the cardiac cycle assessed, the limited endocardial excursion makes it more difficult to detect regional wall motion abnormalities.

The beat-to-beat variation of the cardiac cycle length results in specific pitfalls. The beat-to-beat variation renders the recognition

of regional wall motion abnormalities during the test difficult. To overcome this, image acquisition should avoid both extremely short and extremely long cardiac cycle length, selecting a cardiac cycle which is representative of the actual average heart rate.

### 2.2 The choice of the stressor

With appropriate precautions, any stressor can be generally used successfully and safe in AF. The stress echo report should mention the workload achieved and declare the low sensitivity of the test in case of early termination due to excessive tachycardia.

Occasionally, the patients present for a dobutamine or exercise stress echo with tachycardia at rest, because of discontinuation of heart rate-limiting drugs.<sup>185,187</sup>

In this case, the test may be rearranged on heart rate-limiting drugs. Dobutamine and exercise echo have a lower sensitivity when performed without discontinuation of heart rate-limiting drugs. Alternatively, adenosine or dipyridamole stress echo may be performed using myocardial contrast echocardiography-based myocardial perfusion assessment<sup>188,189</sup> to improve the diagnostic value of the test compared with assessment of regional wall motion only.

### 2.3 Nuclear cardiology techniques

In recent years, the functional relationship between the occurrence of AF and the presence and extent of myocardial ischaemic heart disease has been investigated.<sup>190</sup> However, the existence of a pathophysiological interaction between these two affections has not been conclusively demonstrated.<sup>191,192</sup>

Independently of the presence of CAD, a consistent association among AF and the development of significant alterations of myocardial blood flow regulation at myocardial perfusion imaging (MPI) has been suggested.<sup>190–192</sup> As a matter of fact, the presence of AF has been shown to be significantly associated with relevant alterations of global myocardial perfusion at cardiac-PET, as indicated by increased coronary vascular resistances and diminished resting and hyperaemic perfusion.<sup>190</sup> This behaviour might explain angina-like symptoms and diminished physical peak performance during AF.

Similarly, AF has been reported to significantly affect regional myocardial perfusion heterogeneity at SPECT, diminishing MPI accuracy in identifying the presence of ischaemia.<sup>191,192</sup> These perfusion abnormalities, only partially related to SPECT-related technical limitations, i.e. unreliable gating, suggest a strong interaction between AF- and MPI-related diagnostic efficacies.

In a recent study, Gimelli et al.<sup>193</sup> demonstrated that, despite the overall strict correlation between the presence and extent of CAD and myocardial perfusion and contractile impairment, the presence of AF may significantly impact myocardial perfusion imaging accuracy in detecting significant coronary luminal narrowings. This deleterious association is independent from patients' clinical and functional variables, suggesting the existence of a causal link between AF and impaired MPI diagnostic accuracy.

In this study the presence of AF associated with a significantly lower accuracy in detecting CAD that may depend on the type of stress test used, pharmacological vs. exercise.

According to present and previous reports,<sup>194,195</sup> the choice of the vasodilator stress test might be preferable in order to maintain diagnostic accuracy and avoid false-negative results.

**Key point 13**

*In patients with suspected ischaemic heart disease, the presence of AF may substantially impair MPI accuracy in detecting significant CAD. The interaction between AF- and MPI-related diagnostic power was limited to patients submitted to an exercise stress protocol and was related to a substantially lower exercise duration and overall cardiac workload than in patients with sinus rhythm. Therefore, while in the presence of AF a particularly careful evaluation of patients' clinical characteristics and ability to exercise seems mandatory, the use of a vasodilator stress-test might be preferred.*

## E. Multi-modality imaging (MMI) approach for AF-treatments

### 1. Catheter ablation imaging

#### Pre-ablation

TTE is performed prior to an ablation procedure at the minimum to detect or evaluate structural heart disease, measure the LA size or volume, and assess systolic LV function (Figure 10).<sup>196</sup>

Since an LA thrombus is a definite contraindication for an AF ablation procedure, pre-procedure TOE is commonly performed to exclude an LA thrombus, and in many centres for all patients. Consensus guidelines recommend a TOE if

- the patient has been in AF for 48 h or longer or
- for an unknown duration but without effective continuous anticoagulation for at least 3 weeks prior.

Performance of a TOE in patients who are in sinus rhythm at the time of ablation or correctly treated by anticoagulants is not mandatory but is considered a useful additional precaution.<sup>160</sup>

Pre-procedure contrast-injected CT or CMR is used in many centres in order to evaluate LA and pulmonary veins size and anatomy with precision. These image sets are then used for anatomical guidance during the procedure.

#### Intra-procedural imaging

During the ablation procedure, TOE or ICE may be used to confirm the absence of an LA thrombus before introducing catheters into that chamber, to guide and confirm safe transseptal access to the LA (typically in case of difficult or unusual anatomy or in the presence of inter-atrial septal occlusion devices), to guide and monitor catheter placement at desired sites in the LA and at the LA–PV junction, to confirm occlusive placement of cryo-balloon catheters at PV ostia and to maintain continuous surveillance for and provide early warning of a developing pericardial effusion.

Echocardiographic screening is part of the evaluation of every patient presenting with hypotension, breathlessness, chest discomfort, and/or symptoms of low cardiac output after catheter ablation of AF.<sup>197</sup> TTE screening for pericardial effusion after even uncomplicated catheter ablation of AF is performed in some labs.

If a pericardiocentesis is performed, periodic TTE are performed to monitor response to, or to screen for re-accumulation of

pericardial fluid and/or timing of re-starting anticoagulation. After discharge, a post-procedure Dressler-like syndrome, atrial tachycardia in the setting of LV dysfunction or volume overload, and diastolic atrial dysfunction (oedema after extensive atrial ablation) may all be part of the differential diagnosis of breathlessness and echocardiography has a key role in allowing the correct diagnosis and optimal treatment.

#### Intra-cardiac echocardiography

The technique has been used for more 10 years but still remain confidential despite its great advantages as the decrease in use of the fluoroscopy. The use of intra-cardiac echo can increase the safety of transeptal puncture. It remains an expensive tool (2500€ the ICE catheter) that has been studied and demonstrated useful.<sup>198–203</sup> Its future is perhaps the new 3D probes that have been developed, but no clear validation of their value for guiding the treatment has been published (Figure 11).

**Key point 14**

*Echocardiographic examination of pericardial effusion after catheter ablation should only be performed based on symptoms and clinical signs (i.e. drop in blood pressure).*

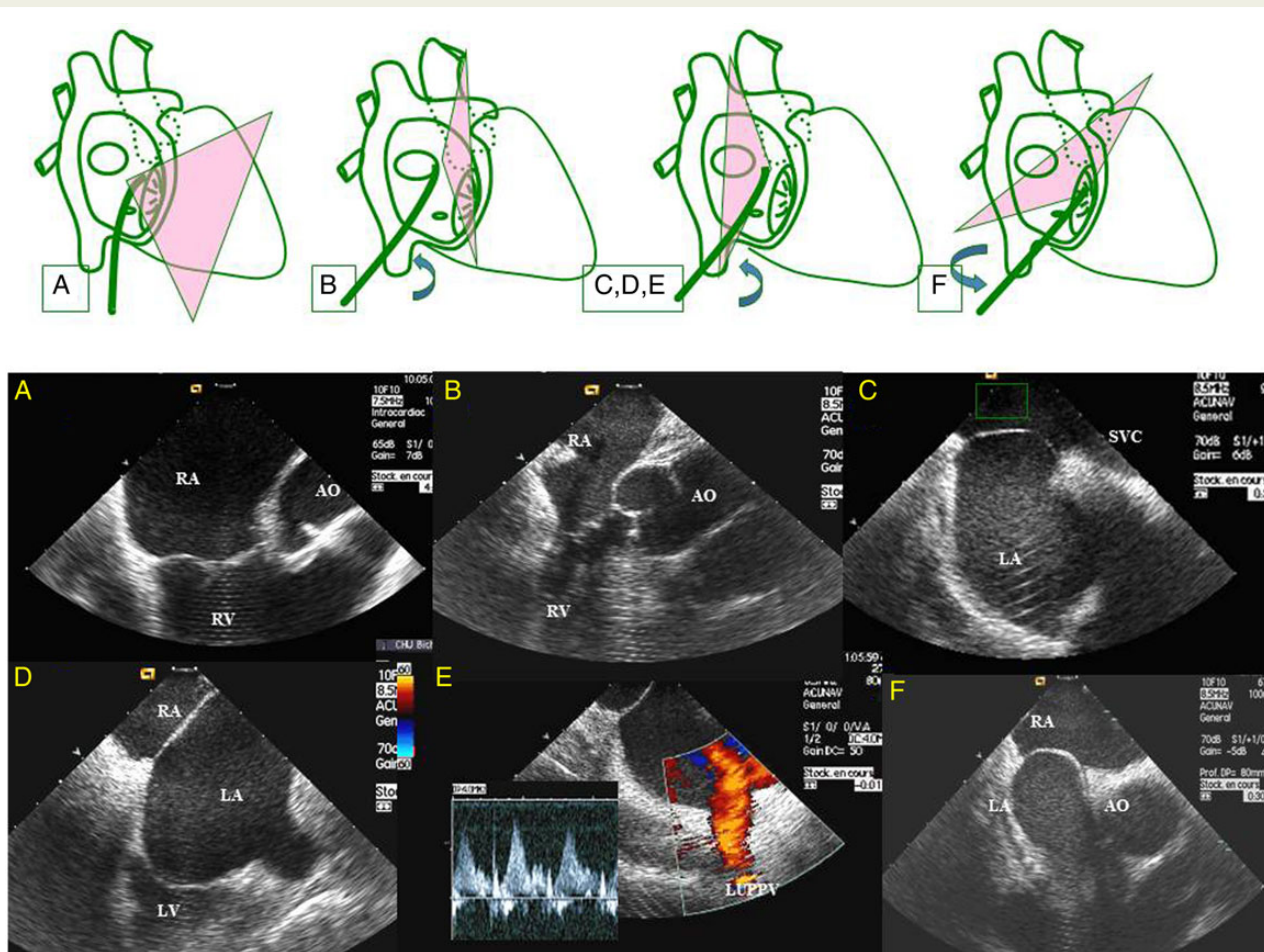
#### Post-procedural imaging for prognosis and diagnosis of the rare complications

In patients with pre-existing reduced LVEF and HF syndromes, it is useful to perform TTE to monitor the evolution of LV function. New parameters such as LA strain have been shown to predict the rhythm outcome but may also provide prognostic rhythm information following ablation.<sup>204,205</sup>

The occurrence of fever and/or a neurological deficit a week to 3 weeks after the procedure can result from an atrio-oesophageal fistula formation and hence must not be ignored. A contrast-injected thoracic CT scan is required to exclude the diagnosis. Electron beam tomography has been described to visualize the LA oedema associated with HF after extensive atrial ablation and both CT as well as MR imaging may be useful to assess pericardial pathologies.<sup>206</sup>

The onset of cough, haemoptysis, and dyspnoea weeks after the procedure should suggest the possibility of pulmonary vein stenosis and again a contrast-injected thoracic CT scan is typically diagnostic.<sup>161,202,207</sup> Routine CMR or CT for pulmonary vein stenosis 3–6 months after an ablation procedure is no longer advised but may be useful when using a new ablation device or technology or in centres beginning to perform AF ablation procedures. A ventilation-perfusion lung scan may be useful to screen for PV stenosis if CT and CMR are unavailable or to provide functional corroboration of the severity of the narrowing.<sup>208,209</sup>

LGE CMR, T1 imaging, or CT perfusion imaging are all being evaluated for their ability to recognize atrial fibrosis and/or scar and may be useful in patients with a recurrence after ablation to evaluate the underlying scar and help develop an optimal management strategy including planning repeat ablation. LA passive emptying fraction evaluated by CMR may also provide prognostic information related to rhythm outcomes.<sup>210</sup>



**Figure 11** Examples of the views that can be obtained by ICE. The septum, the veins can be precisely analysed.

The value of LAA morphological characteristics determined by TOE but also CT or MR imaging as predictors of thrombo-embolic events is currently under evaluation.<sup>211–214</sup>

Simple chest radiography may, of course, be of help to detect pulmonary infection and/or broncho-aspiration. Post-procedural dyspnoea due to phrenic palsy can be easily detected under fluoroscopy by a ‘sniff test’.

## 2. Imaging in devices: LAA occluder

In patients with stroke of embolic origin, it is important to search for a cardiogenic source of thromboembolism. Thromboembolism typically arises from a clot in LAA in AF patients. Local therapeutic alternatives to systemic anticoagulation involving surgical or percutaneous exclusion of the LAA have been developed. Occlusion of the LAA using less invasive percutaneous, catheter-based methods has been described since 2002.<sup>20</sup> Preliminary studies of PLAATO and WATCHMAN<sup>215,216</sup> systems specifically designed for this purpose has been completed. Both systems deploy a device that is placed in the LAA through puncture of the interatrial septum.<sup>152</sup>

Imaging plays an important role in this procedure, which is important for the LAA pre-procedural and peri-procedural assessment of

the LAA and for follow-up. The LAA can occasionally be visualized with TTE but usually requires TOE, ICE, MRI, or CT<sup>23,217</sup> (Figure 12).

### Pre-procedural imaging

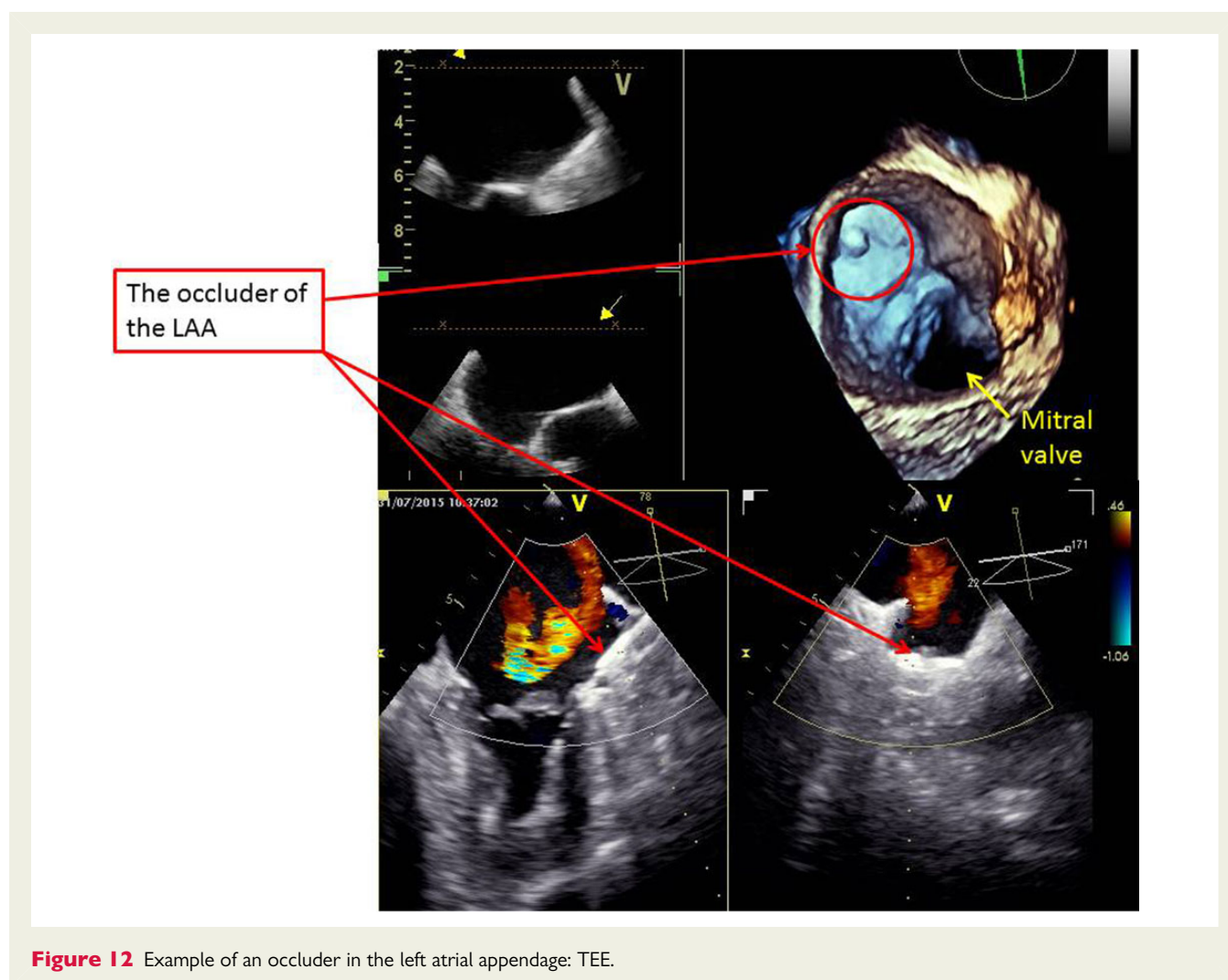
Pre-procedural echocardiography is used to screen suitable candidates and to define the LAA morphology and dimension. It is very important to confirm the absence of LAA thrombi prior to LAA occlusion. The presence of mobile thrombi is a contraindication for the procedure. However, LAA cannot be fully examined by TTE. In most patients, the LAA can be adequately visualized using TOE. That is why, TOE is claimed to be superior to TTE, and it is considered the reference technique for the detection of thrombi in the LAA as well as examination of the anatomy and functions of the LAA before procedure.<sup>24</sup>

CMR seems to be another valuable visualization tool for the LAA occluder implantation, which allows visualization of LAA and selection of the optimal LAA occluder size. CT scanning is an alternative to ascertain the LAA anatomy, including its orientation and orifice size in peri-procedural period.

### Post-procedural imaging and follow-up

Post-procedural echocardiography is important in the surveillance and monitoring of long-term outcomes. TTE is performed prior





**Figure 12** Example of an occluder in the left atrial appendage: TEE.

to discharge specifically to confirm device position and to exclude pericardial effusion and thrombus around the device. It should also confirm normal MV function and exclude LV dysfunction. Echocardiographic surveillance is currently recommended at 1 and 6 months, and annually post-procedure. TOE is the preferred imaging modality, although TTE may rarely be suitable in those individuals with good echocardiographic windows. Alternatively, post-procedural imaging to assess device position, peri-device residual flow in the LAA, and thrombus formation on the device consists of chest X-ray or CT. CMR is hampered by device artefacts.<sup>218,219</sup>

The timing of a follow-up TOE varies between institutions. Most operators use early or follow-up echocardiographic findings, i.e. the absence of large residual flow into the LAA or thrombus, as a guide for prescribing antithrombotic drugs.<sup>220</sup>

## F. Areas for future researches

The prevalence of AF and still its complex management requires new approaches. Current guidelines are population-based. The next ones might become more patient-based (what is characterizing

an Afib in a patient and what are the risks and consequences associated with that specific Afib). That means that for each individual, the physician would be able to determine thanks to echocardiography, CMR, and other techniques (including non-invasive electrical mapping), how choosing between rate control and dedicated treatment of the arrhythmia. It would be valuable also to be able to guide the clinician in the sometimes challenging choice with regard to the best anticoagulation regimen.

The ablation techniques have become increasingly sophisticated and are already taking advantage of imaging techniques but one can expect that the electro-mechanical coupling could be best assessed and the treatment strategy individualized according to the presence of low strain or extensive LGE.

High-frequency ultrasound imaging and new faster CMR sequences would probably allow a much better description of the anatomical and histological properties of the atria (Figures 13–15).

Catheter ablation of AF without fluoroscopy is becoming feasible and merits further attention. The 3D ICE is a new opportunity that has to be tested. CMR is probably a valid alternative approach to fluoroscopy.<sup>221,222</sup> Catheter ablation under real-time MRI guidance could be successfully carried out as a new technique.<sup>223</sup>

Combination of advanced imaging techniques for simultaneous tissue and catheter visualization, monitoring of ablation, and assessment of the ablation lesions may be potential advantages over conventional electrophysiology in the future (pre-operative planning of the treatment, less invasive and individualized treatment and at the

end, non-invasive confirmation of the efficacy of the delivered treatment).

Summary of the key messages

Key point 1: Measuring LA biplane volume, using either the area–length or the discs formula indexed by body surface area (BSA) is the method currently recommended for LA size quantification. A normal LA volume is defined as <34 mL/m<sup>2</sup>.

Key point 2: an echocardiographic examination is recommended for every patient with AF to assess cardiac structure and function. An estimate of the degree of atrial remodelling is important (value of indexed LA volume). In addition, echocardiography can help to assess the risk of LAA thrombus.

Past studies have used the theoretically simple measurement of LA diameter using the para-sternal, long-axis M-mode approach. Nowadays, LA-indexed volumes should be preferred.

Key point 3: TOE is the most reliable test to rule-out the presence of an LAA thrombus before cardioversion of AF in non-anticoagulated patients and in patients with past diagnosis of LAA thrombus.

Key point 4: The absence of randomized study or large registry demonstrating the prognostic value of imaging techniques in AF patients is nevertheless a real weakness for echocardiography and other imaging techniques.

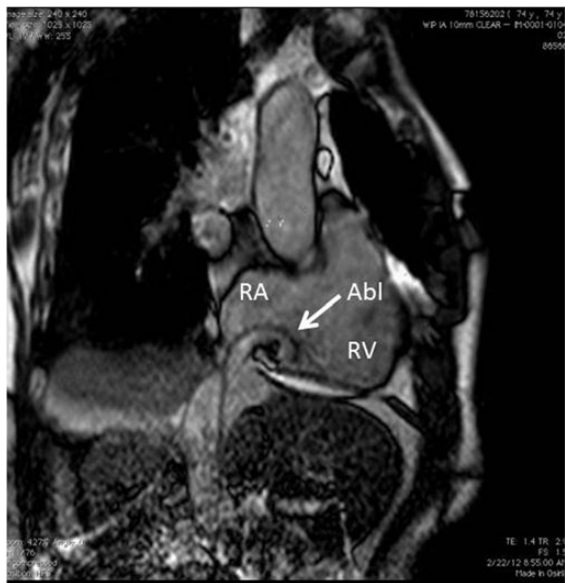


Figure 13 MRI interventional suites—passive tracking of an ablation catheter (ABL) positioned along the right atrial isthmus. RA, right atrium; RV, right ventricle.

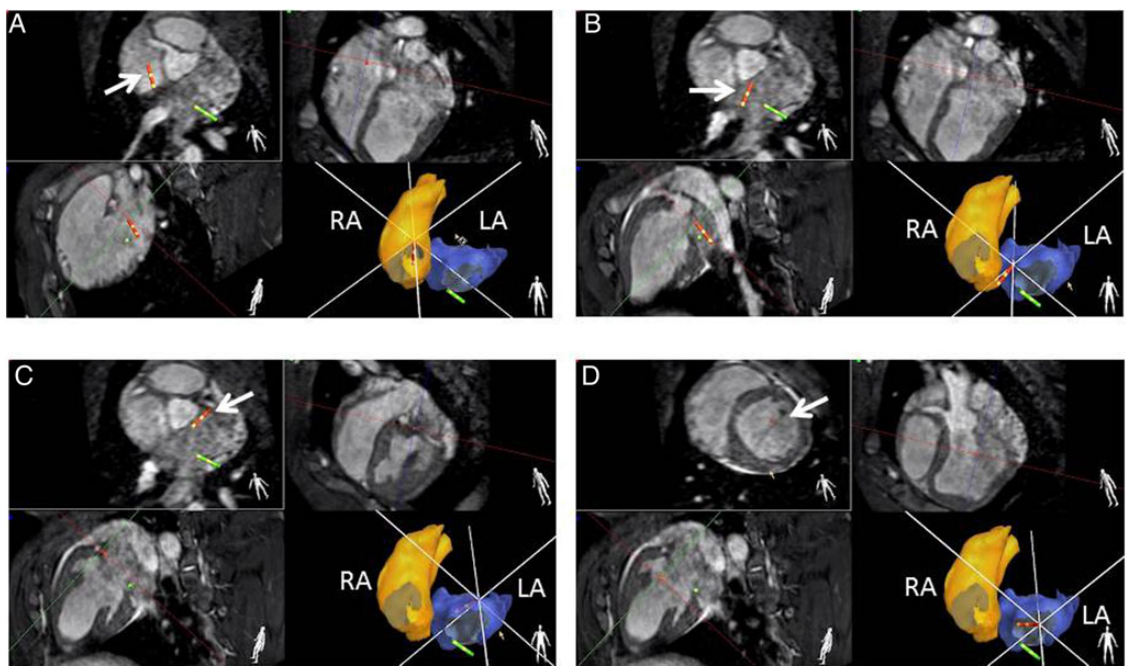
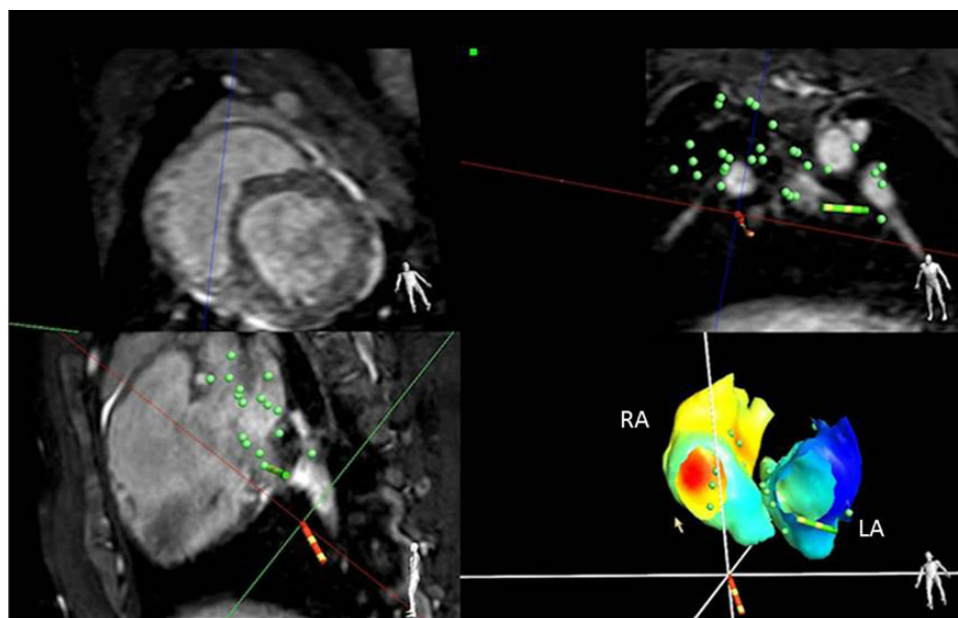


Figure 14 Active tracking of two electrode catheters positioned in the right atrium (RA; 1) and coronary sinus (CS; 2). The sequence A–D depicts the transseptal access of catheter 1 into the left atrium (LA).



**Figure 15** Bi-atrial colour-coded activation map obtained in an interventional 1.5 T MRI. RA, right atrium; LA, left atrium.

**Key point 5:** In AF, the LV systolic dysfunction might be totally or at least partially related to some degree of tachycardia-induced cardiomyopathy. Usually in tachycardia-induced cardiomyopathy, the LV is weakly or not enlarged.

**Key point 6:** In AF, the comprehensive assessment of LV diastolic function and filling pressures required a combination of several parameters. Mitral annular early diastolic velocity by pulsed tissue Doppler is a marker of LV diastolic dysfunction, and septal  $e' < 8$  cm/s has a reasonable accuracy to identify LV delayed relaxation.

**Key point 7:** The normal range for 2DE RA volume index is  $25 \pm 7$  mL/m<sup>2</sup> in men and  $21 \pm 6$  mL/m<sup>2</sup> in women.<sup>40</sup> RA volume  $> 30$  mL/m<sup>2</sup> represents for sure a pathological enlargement of the RA.

**Key point 8:** (1) The LA lateral wall strain can be reliably imaged and is not constrained by other cardiac chambers and may be used as the best surrogate of LA wall fibrosis by CMR. (2) An LA strain (in systole)  $< 30\%$  indicates significant alteration of LA reservoir function, which predicts poor outcome.

**Key point 9:** LA should be measured from the R-wave of the ECG in AF. The beginning of the P-wave should be preferred in sinus rhythm.

**Key point 10:** Assessment of LA volumes by 3D echocardiography will have to be implemented in clinical practice. It is still not available widely, but it has been demonstrated as really valuable. Like LV volume by 3D echocardiography, it has been proposed as superior to the 2D approach that remains the standard approach.

**Key point 11:** Up to now, there is neither recommendation nor expert consensus on the role of LGE CMR to assist AF ablation procedures. The available data are intriguing enough to warrant further research.

**Key point 12:** Further studies investigating the association atrial arrhythmia and epicardial adiposity are needed. No real clinical impact is demonstrated yet.

**Key point 13:** In patients with suspected ischaemic heart disease, the presence of AF may substantially impair MPI accuracy in detecting significant CAD. The interaction between AF- and MPI-related diagnostic power was limited to patients submitted to an exercise stress protocol and was related to a substantially lower exercise duration and overall cardiac workload than in patients with sinus rhythm. Therefore, while in the presence of AF a particularly careful evaluation of patients' clinical characteristics and ability to exercise seems mandatory, the use of a vasodilator stress-test might be preferred.

**Key point 14:** Echocardiographic examination of pericardial effusion after catheter ablation should only be performed based on symptoms and clinical signs (i.e. drop in blood pressure).

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## IMAGE FOCUS

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# Cardiac amyloidosis: an unusual cause of low flow–low gradient aortic stenosis with preserved ejection fraction

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Both low flow–low gradient aortic stenosis (LFLG AS) despite preserved ejection fraction (EF) and cardiac amyloidosis (CA) can be observed in elderly patients with left ventricular (LV) hypertrophy, apparently normal LV systolic function but severe longitudinal dysfunction. We report a case of a patient in whom the pattern of LFLG AS was associated with and related to an associated CA.

An 84-year-old man with hypertension and permanent atrial fibrillation (AF) was referred for congestive heart failure. Electrocardiogram revealed AF and left bundle branch block. Echocardiography found an increased LV wall thickness (Panel A, Supplementary data online, Videos S1 and S2). EF was 72%. Global longitudinal strain was  $-10.5\%$ , with longitudinal dysfunction predominating in the basal segments with apical sparing (Panel A). Aortic valve was heavily calcified (see Supplementary data online, Videos S3 and S4) with an LFLG AS pattern (mean gradient = 32 mmHg, stroke volume index = 35 mL/m<sup>2</sup>, indexed aortic valve area = 0.38 cm<sup>2</sup>/m<sup>2</sup>) (Panel B). High brain natriuretic peptide level (582 ng/L) and elevated kappa light chains (29.5 mg/L) were observed. <sup>99m</sup>Tc-HMDP scintigraphy showed severe cardiac uptake (Panel C). Valve calcium score was high (3925), suggesting severe AS (Panel D). However, associated CA was suspected because of the echocardiographic and strain patterns, and was confirmed by endomyocardial biopsies.

This case illustrates that:

- (1) CA can be associated with and considered as a potential explanation for LFLG AS with preserved EF.
- (2) This diagnosis should be raised in AS patients presenting with suggestive echocardiographic findings.
- (3) Multimodality imaging plays an important role in the assessment of patients with both AS and CA.

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

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