Multimodality imaging to guide cardiac interventional procedures

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Imaging and atrial fibrillation: the role of multimodality imaging in patient evaluation and management of atrial fibrillation

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ABSTRACT

Atrial fibrillation (AF) is the most common cardiac arrhythmia, and is associated with an increased risk of cardiac morbidity and mortality. In this review, the role of multimodality imaging in the evaluation and treatment of AF is discussed in two main parts. First, an overview of the initial assessment of an AF patient is provided, including the role of different imaging techniques. Conditions that are associated with AF (coronary artery disease, heart failure, valvular heart disease and left ventricular hypertrophy), and the assessment with various imaging modalities will be reviewed. Furthermore, left atrial size assessment and the screening for thrombus formation are addressed. Second, the role of imaging in the invasive treatment of AF with catheter ablation is reviewed. Issues that should be considered before the procedure including contra-indications and pulmonary vein and left atrial anatomy will be discussed. Furthermore, the integration of different imaging modalities during catheter ablation is explored. Finally, an overview of the role of imaging in the follow-up of patients treated with catheter ablation will be provided.

INTRODUCTION

Atrial fibrillation (AF) is the most commonly encountered arrhythmia, and its prevalence increases with advancing age. The prevalence of AF in the general population is estimated to be 0.4 to 1% (1). Importantly, AF is associated with an increased risk of cardiac morbidity and mortality (2). The 'Euro Heart Survey on Atrial Fibrillation' that included 5333 AF patients from 35 European countries, demonstrated that the evaluation and treatment of AF is associated with considerable costs (3). Therefore, continuous efforts are made to optimize the evaluation and treatment of AF patients (4).

The treatment of AF patients depends on various factors including but not limited to the type of AF, age and co-morbidity. These issues should therefore be evaluated in the initial assessment of a patient presenting with AF. In daily clinical practice, a 'rhythm control' strategy using anti-arrhythmic drugs is chosen in the majority of the patients (5). However in a large proportion of patients, anti-arrhythmic drugs fail to control AF. In these patients, the invasive treatment of AF with catheter ablation is a good option (6). The cornerstone of catheter ablation procedures is the electrical isolation of the pulmonary veins (PVs), since these are the main source of triggers initiating AF (7). In this review, we will explore the role of various imaging techniques in the evaluation and treatment of patients with AF. The manuscript will focus on relevant questions for daily clinical practice. The role of imaging in both the initial assessment of AF patients, and the invasive treatment of AF patients with catheter ablation will be reviewed.

CLINICAL EVALUATION OF PATIENTS WITH AF

Since the prevalence of AF is steadily increasing, an ever-growing number of patients in the outpatient clinic will present with AF. In the following paragraphs, we will focus on the role of imaging while answering the question *'What should be evaluated in patients presenting in the outpatient clinic with AF?'*

First, important factors associated with AF should be evaluated. A large number of (clinical) conditions, including structural heart disease, hypertension, surgery, hyperthyroidism and drugs are associated with AF. In order to diagnose these clinical conditions, medical history, physical examination and blood tests are often sufficient. However, other conditions associated with AF require (non-invasive) imaging for appropriate assessment. One of these conditions is underlying structural heart disease. Hence, an important question in the initial clinical evaluation of an AF patient is: *'Is there any underlying heart disease present?'* Subsequently, the question arises: *'Which imaging techniques can be used to detect the underlying heart disease?'*

Underlying heart disease

In the clinical evaluation of patients with AF, it is essential to evaluate underlying structural heart disease that may cause, or is associated with AF. Since the presence of 'true' lone AF is controversial, a potential reversible cause of AF (such as myocardial ischemia) should be excluded in the first assessment of a patient presenting with AF. In the Euro Heart Survey on Atrial Fibrillation, 90% of the AF patients had at least one associated medical condition (5). Most frequently, hypertension (up to 66%), coronary artery disease (up to 36%), heart failure (up to 49%), and valvular heart disease (up to 40%) was present. The prevalence of structural heart disease was highest in patients with persistent or permanent AF.

In daily clinical practice, conventional transthoracic echocardiography is most often used to detect underlying heart disease (5). However, other imaging modalities may provide important information that cannot be obtained with echocardiography. In the following paragraphs, the various cardiac conditions associated with AF, and the different imaging modalities to assess these conditions will be discussed.

Coronary artery disease The presence of coronary artery disease should be assessed in patients presenting with AF. Large cohort studies have reported a high prevalence of coronary artery disease among patients with AF (8). In 2768 patients with first detected AF, the incidence of coronary ischemic events was 31 per 1000 person-years (9). Furthermore, it has also been suggested that AF may be the first manifestation of cardiac ischemia (10). Typically, a stepwise approach starting with the evaluation of individual risk factors and exercise stress tests is applied when screening for coronary artery disease. However, non-invasive imaging modalities may have incremental value over traditional risk factors (11).

Various imaging modalities are available for the assessment of coronary artery disease in patients with AF. Conventional angiography remains the gold standard for detection of significant coronary artery stenosis. In recent years, non-invasive assessment of coronary artery disease with multi-slice computed tomography (MSCT) has become available. This technique enables non-invasive detection of significant coronary artery stenosis with a high sensitivity and specificity (12). It should be noted however that the diagnostic accuracy of MSCT may be limited in patients with AF during data acquisition (13). In addition, MSCT still is limited by higher radiation exposure as compared with conventional angiography. New techniques, such as the use of dose modulation during scanning may reduce radiation exposure. In a recent study, the presence of coronary artery disease was evaluated with MSCT in 150 patients with AF and 148 patients with similar age, gender, symptomatic status and pretest likelihood, but without a history of AF (14). Interestingly, a higher prevalence of obstructive coronary artery disease was noted in the AF patients, compared with the non-AF patients (41% in AF patients vs. 27% in non-AF patients, p=0.01). However, more studies are needed to fully appreciate the role of MSCT in the screening for coronary artery disease in AF patients.

Nuclear myocardial perfusion imaging provides information on the presence of ischemia, a surrogate marker for coronary artery disease; the diagnostic accuracy of nuclear perfusion imaging to detect significant coronary artery stenoses is high (15). It has been shown that nuclear imaging has similar diagnostic accuracy for detection of coronary artery disease in asymptomatic patients with AF as compared with patients without AF (16). Abidov et al. have demonstrated the prognostic value of ischemia detection with single-photon emission computed tomography in 384 AF patients and 15.664 patients without AF (17). The cardiac death rate was 6.3% per year in the AF patients with mildly abnormal myocardial perfusion scan, compared with 1.2% per year in the non-AF group with similar perfusion findings. This finding further underlines the importance of screening for coronary artery disease in AF patients.

Heart failure The presence of left ventricular (LV) systolic dysfunction or heart failure should be assessed in AF patients. The close relation between AF and heart failure has been well appreciated (18). In the Euro Heart Survey on Atrial Fibrillation 135 patients (5%) developed new onset heart failure during 1-year follow-up, while 314 patients (24.7%) experienced worsening of existing heart failure (5). Conversely, the Framingham Heart study demonstrated a 4.5-fold to 5.9-fold increased risk for the development of AF in men and women with LV systolic dysfunction (19). The exact pathophysiologic mechanism underlying the association between AF and LV dysfunction is only partially understood, but includes electromechanical factors, cellular and extra-cellular changes, and neurohumoral modulation (20).

For the assessment of LV systolic function, conventional two-dimensional transthoracic echocardiography is typically used. Using standard apical images, LV volumes can be assessed and subsequently LV ejection fraction can be calculated (21). Although conventional echocardiography is most frequently used in daily clinical practice, the accuracy of this technique largely depends on the operator and LV morphology. Therefore, in general magnetic resonance imaging (MRI) is considered the gold standard for assessment of LV volumes. However, it should be noted that pacemakers still are a contra-indication for cardiac MRI. In addition, gadolinium for delayed-enhancement MRI should not be used in patients with severely impaired renal function, due to the risk of nephrogenic systemic fibrosis. Nuclear imaging and MSCT can also be used for the assessment of LV function (12), but these techniques are associated with radiation. Novel real-time three-dimensional echocardiography allows accurate assessment of LV volumes and systolic function (22), and good agreement between this technique and MRI has been reported (23). However, more studies on the accuracy of this technique in patients with AF are needed.

Valvular heart disease Another condition that is associated with AF is valvular heart disease. In the Euro Heart Survey, about 20% of AF patients had valvular heart disease, with the highest prevalence among patients with persistent or permanent AF (5). Most often, mitral valve disease is present, resulting in elevated left atrial (LA) pressures and subsequently in a higher susceptibility to AF.

Transthoracic echocardiography is typically used for the assessment of valvular disease in patients with AF. It allows a comprehensive anatomical and functional evaluation of the different valves. Recently, the feasibility of both MRI (24) and MSCT (25) to assess valvular heart disease have been demonstrated. However, in daily clinical practice conventional echocardiography remains the technique of choice to assess valvular heart disease in AF patients.

LV hypertrophy The presence of LV hypertrophy should be evaluated in the initial assessment of AF patients. Long-lasting hypertension may result in LV hypertrophy and may expose the LA to elevated pressures. Since hypertension may be present in up to 66% of patients presenting with AF (5), screening for LV hypertrophy is essential. In 1924 patients of the Framingham Heart Study, increased LV wall thickness was one of the predictors for the development of AF over a 7.2-year period (HR 1.28 per 4-mm increment, 95% CI, 1.03 to 1.60) (26). Importantly, it has been suggested that antihypertensive therapy targeted at regression or prevention of LV hypertrophy may reduce the incidence of new-onset AF (27).

In addition to conventional criteria using electrocardiography, various imaging modalities can be used for the screening for LV hypertrophy in AF patients. In daily clinical practice, transthoracic echocardiography is most frequently used. Using standard echocardiographic images, LV wall thickness and LV mass can be assessed (21). However, three-dimensional imaging techniques such as MRI may provide a more accurate quantification of LV hypertrophy (28). Real-time three-dimensional echocardiography may overcome the limitations of conventional echocardiography and may be comparable with MSCT and MRI for assessment of LV hypertrophy (22).

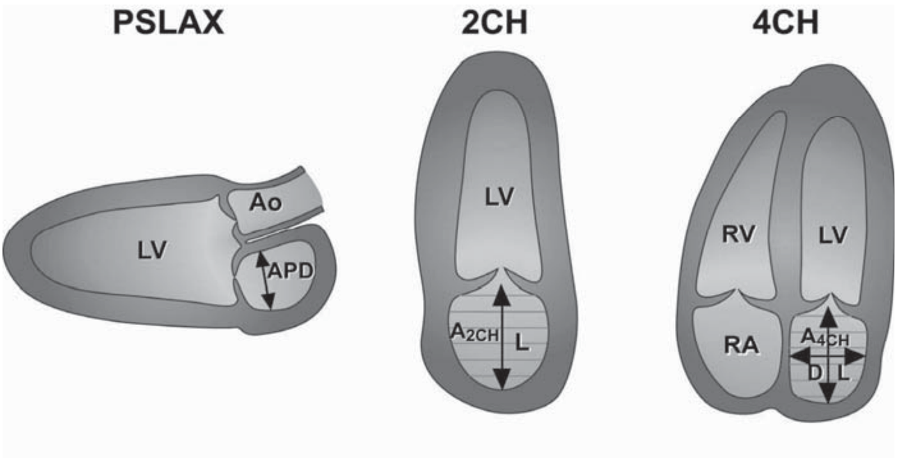
Left atrial size

In addition to underlying structural heart disease, LA size should be assessed in the initial evaluation of patients with AF (1). In particular LA dilatation, as a marker of LA remodeling, should be identified. The association between AF and LA remodeling is well appreciated (29), but it remains controversial whether AF causes LA dilatation, or rather is its consequence. It has been demonstrated that LA size is a strong predictor of cardiovascular events in patients with lone AF, independent of age and clinical risk factors (30). Therefore, LA size should be assessed in the initial evaluation of AF patients, but the question is: *'How should LA size be assessed?'*

Magnetic resonance imaging still is considered the gold standard for quantification of LA size. Its three-dimensional character and high spatial resolution allow accurate assessment of the LA. Typically, the modified Simpson's rule is applied, using LA areas from subsequent cross-sectional images (31). However, MRI is limited by the relatively time-consuming data acquisition and cumbersome data analysis. Therefore, in daily clinical practice, MRI is not often used for the assessment of LA size. Similarly, MSCT allows three-dimensional assessment of LA size, with high spatial and temporal resolution (32). The modified Simpson's rule and simplified linear methods can be used to quantify LA size (33). MSCT however, is not routinely used for assessment of LA size, because of radiation exposure and the need for contrast agents.

Transthoracic echocardiography is widely used for assessment of LA size in daily clinical practice. In randomized clinical trials and large cohort studies, linear methods such as the M-mode derived LA diameter are typically used for LA size assessment because of the good reproducibility. However, it has been well recognized that the M-mode derived LA diameter may underestimate true LA size (34). In particular when LA dilatation is present, resulting in an asymmetric shape of the LA, linear methods are not the preferred method. Instead, LA volumes should be assessed for quantification of LA size (21).

Various methods are available for quantification of LA volumes using transthoracic echocardiography (Figure 1). The ellipsoid method and biplane area-length method use various LA diameters and/or areas to calculate LA volumes, assuming that the LA has an ellipsoid shape (35). The modified biplane Simpson's rule using planimetry is considered the most accurate method and is most frequently used. Good agreement between the biplane area-length method and the biplane Simpson's rule has been demonstrated (36). However, all these methods still use geometric assumptions and are operator dependent. Real-time three-dimensional echocardiography allows more accurate assessment of LA volumes (Figure 2) (22). In addition, because



Method	LA volume =
Cube	$4/3\ \pi\ (APD/2)^3$
Ellipsoid	$4/3\ \pi\ (APD/2)(D/2)(L/2)$
Biplane area-length	$8/3\ \pi\ [(A_{2CH})(A_{4CH})/L]$
Modified Simpson's rule	Summation of discs

Figure 1. Using transthoracic echocardiography, various methods are available to assess LA size. The standard parasternal long-axis view (PSLAX) and the apical 2-chamber (2CH) and 4-chamber (4CH) views are used to assess LA diameters and LA area (using planimetry). Subsequently, LA volume can be calculated with the different equations. APD, D, L = LA diameter; A_{2CH} = LA area on 2-chamber view; A_{4CH} = LA area on 4-chamber view.

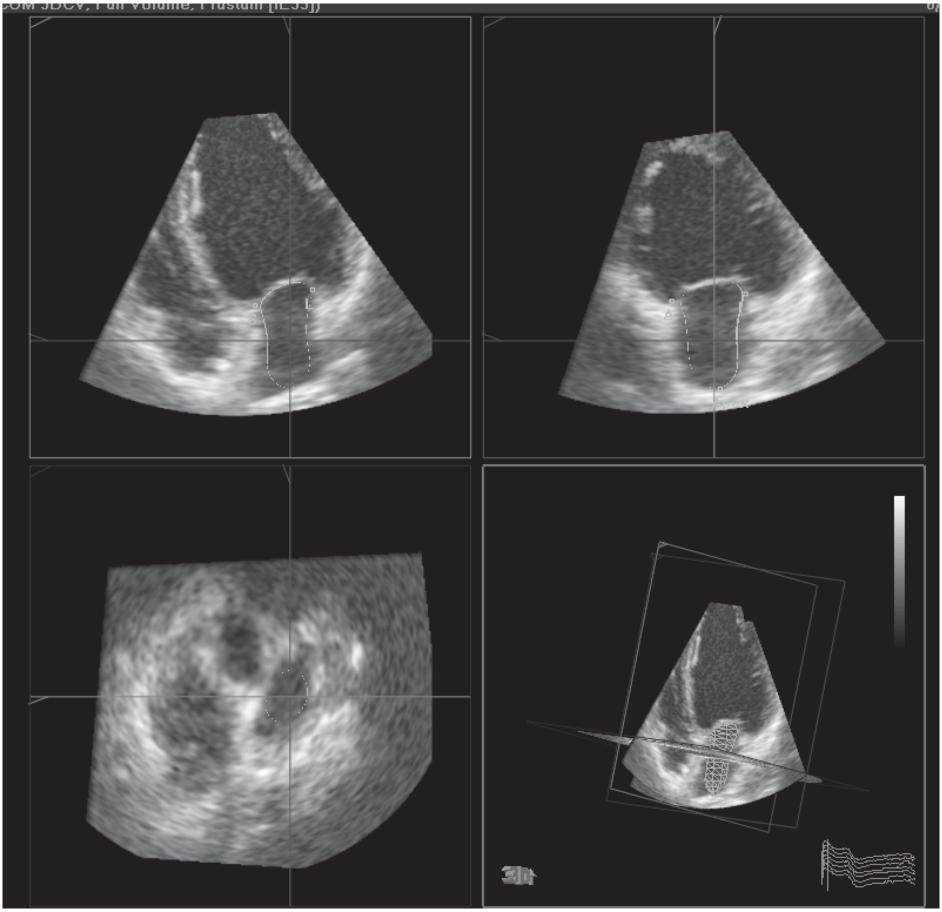


Figure 2. Real-time three-dimensional echocardiography for the assessment of LA volumes. Automatic border detection can be applied to the apical 4-chamber and 2-chamber view (upper panels) for quantification of LA volumes.

of its semi-automatic character, resulting in high reproducibility, real-time three-dimensional echocardiography is of great value in the follow-up of AF patients (37).

Left atrial thrombus

In addition to underlying structural heart disease and LA size, the presence of thrombus should be assessed in selected patients presenting with AF. Although there are various sources of embolism in patients with ischemic stroke, the majority of strokes occurring in patients with AF can be attributed to the presence of thromboembolism in the LA (1). Therefore, screening for thrombus formation is of critical importance, in particular in patients undergoing cardioversion or catheter ablation for AF. The question arises: *'Which imaging technique should be used for the screening for LA thrombi?'*

Conventional transthoracic echocardiography can be used to assess LA dilatation and severe LV dysfunction, both associated with the presence of LA thrombi and stroke (38,39). However, this technique has only moderate sensitivity and specificity for the detection of LA thrombi (40). In contrast, transesophageal echocardiography has a very high sensitivity and specificity for detection of cardiogenic sources of thromboembolism (41). In addition, spontaneous echo contrast and reduced LA appendage flow velocity, associated with LA thrombus formation, can be assessed with transesophageal echocardiography. Importantly, it has been demonstrated that the use of transesophageal echocardiography may result in less hemorrhagic complications after cardioversion, compared with a conventional strategy using anticoagulation prior to cardioversion (42).

Non-invasive three-dimensional imaging techniques such as MRI and MSCT have also been used for the detection of thrombi in the LA and LA appendage. However, both techniques have low inter-observer agreement, and moderate sensitivity and specificity compared with transesophageal echocardiography (43,44). Therefore, at present transesophageal echocardiography is still considered the gold standard for the detection of thrombi in the LA and LA appendage in patients with AF (1).

PATIENTS WITH AF UNDERGOING CATHETER ABLATION

After the initial assessment as described before, a tailored treatment strategy should be planned for each AF patient. Radiofrequency catheter ablation is a good therapeutic option when at least one anti-arrhythmic drug has failed (1). A recent study including 1404 AF patients undergoing PV isolation demonstrated that 78% of patients with paroxysmal AF and 67% of patients with non-paroxysmal AF ($p<0.001$) maintain sinus rhythm after a single catheter ablation procedure (45). Although various ablation strategies exist, the majority of approaches target electrical isolation of the PVs (6). In the following paragraphs, the question *'What is the role of imaging in catheter ablation for AF?'* will be answered. Before the procedure, during the actual ablation and during follow-up various imaging modalities play a different role (Table 1). The different processes and the preferred imaging modalities will be reviewed in the following paragraphs.

Pre-procedural issues: Contra-indications and assessment of anatomy

The first step in the work-up of a patient referred for AF ablation is to exclude any contra-indication. The most important is to rule out the presence of LA thrombi. In particular in patients with persistent AF, or patients who are in AF at the time of the procedure, this is of critical importance (6). As discussed previously, transesophageal echocardiography is considered the gold standard for detection of LA thrombi. In addition, extreme LA dilatation and long-lasting permanent AF are relative contra-indications for AF ablation, since these conditions are associated with a low

Table 1. The role of imaging in AF ablation

Process	Imaging modality	Comment
Before catheter ablation		
Assessment of LA / LAA thrombus	TEE	Considered gold standard for detection of thrombi
Assessment of LA size and anatomy	TTE	Most often used in daily clinical practice
	RT3DE	New technique allowing accurate assessment of LA volumes
	MSCT or MRI	Allow three-dimensional assessment of LA volumes and specific anatomic features. Considered gold standard for assessment of LA volumes
Assessment of PV anatomy	MSCT or MRI	Provide detailed three-dimensional information on PV anatomy as a 'road-map to ablation'
During catheter ablation		
Positioning catheters	Fluoroscopy	Standard imaging modality in the electrophysiology laboratory. Enables visualization of catheters and devices.
Transseptal puncture	ICE	May enhance safety of transseptal puncture by direct visualization of inter-atrial septum and puncture needle
Visualization of LA and PVs	Fluoroscopy	New rotational angiography technique accurately identifies PV anatomy and PV diameters
	ICE	Allows real-time assessment of PV ostium, but underestimates PV diameter
	Mapping system	Provides real-time electroanatomic information, and guides ablation. Limited by the use of reconstructed anatomy
Image integration	Fluoroscopy & MSCT / MRI	Combines real-time fluoroscopy with detailed LA and PV anatomy from MSCT or MRI
	Mapping system & MSCT / MRI	Combines electroanatomic map with detailed LA and PV anatomy from MSCT or MRI
	Mapping system & ICE	Combines electroanatomic map with real-time anatomic information from ICE
Follow-up after catheter ablation		
Assessment of PV stenosis	MSCT or MRI	Preferably, these three-dimensional techniques are correlated with pre-procedural images for detection of PV stenosis
Detection of pericardial effusion	TTE	Routine echocardiography should be performed before discharge and during follow-up
Esophageal injury	MSCT or MRI	Should be performed when atrio-esophageal fistula is suspected
Assessment of LA size and function	TTE	Conventional method for detection of LA volumes and function
	RT3DE	Three-dimensional assessment of LA volumes allows detection of LA reverse remodeling
	MSCT	Three-dimensional assessment of LA volumes allows detection of LA reverse remodeling
	MRI	Preliminary studies demonstrate feasibility of LA scar detection with gadolinium enhanced MRI

ICE = intracardiac echocardiography; LA = left atrium/atrial; LAA = left atrial appendage; MRI = magnetic resonance imaging; MSCT = multi-slice computed tomography; PV = pulmonary vein; RT3DE = real-time 3-dimensional echocardiography; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

probability of successful outcome (46). Therefore, LA size assessment should be performed routinely, as described in the previous section. After exclusion of any contra-indication, LA and PV anatomy should be assessed, since the PVs are the main target during the ablation procedure. Therefore, an important question is: *'How can LA and PV anatomy best be assessed?'*

From anatomical studies it has become apparent that LA and PV anatomy is highly variable (47). Typically, four separate PVs are present: two right-sided and two left-sided PVs. Large *in vivo* studies using MSCT and MRI scanning have demonstrated that a single PV ostium on the left side or an additional right-sided PV are the most common variations (Figure 3) (48,49). These anatomical variants may be present in up to 30% of patients, and may affect the planned ablation strategy. In general, three-dimensional imaging techniques such as MSCT and MRI are used for assessment of PV anatomy. Using three-dimensional reconstructions and cross-sectional images, these techniques provide the most detailed information on PV anatomy.

In addition to the number of PVs, the exact diameter and shape of the PVs should be assessed. Knowledge on PV diameter may be very helpful, especially for new ablation strategies

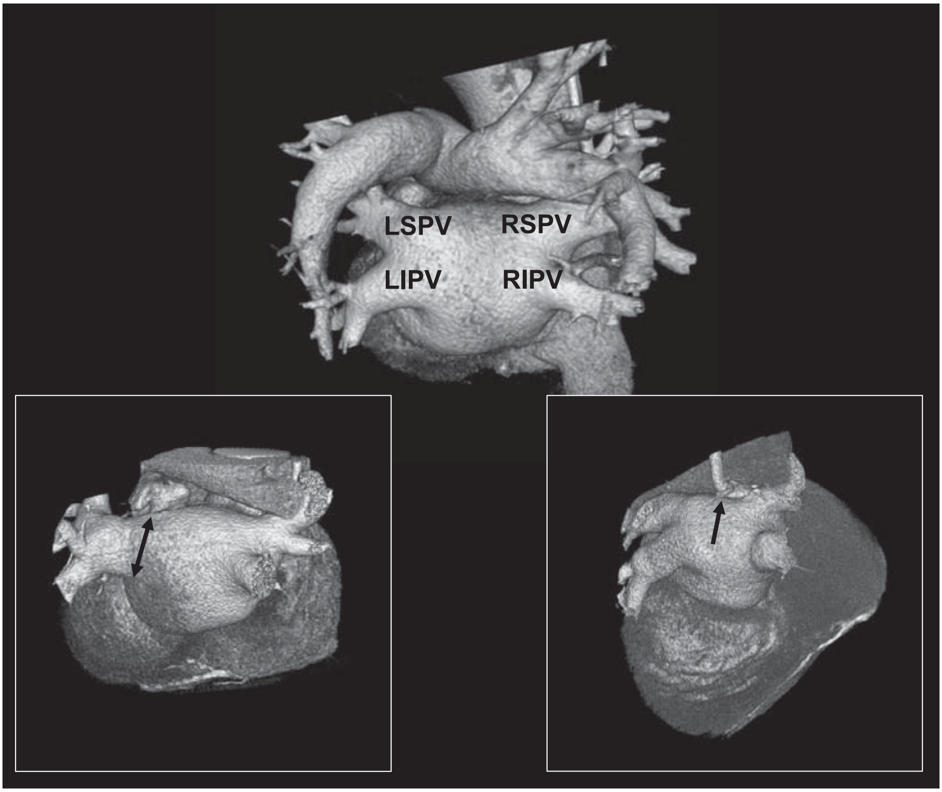


Figure 3. Three-dimensional volume-rendered reconstructions of MSCT images are created to assess LA and PV anatomy. Normal PV anatomy includes four PVs draining separately into the LA (upper panel). Variations of PV anatomy include a single (or 'common') ostium of the left-sided PVs (lower left panel, black double-arrow), and an additional right-sided PV (lower right panel, black arrow). LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

using balloon-catheters (50). In addition, comparison of PV diameters at baseline and during follow-up allows detection of PV stenosis after catheter ablation (51).

Finally, specific anatomical features of the LA, such as the LA appendage, variations in LA roof anatomy and the 'Coumadin ridge' between the left-sided PVs and the LA appendage, can be assessed prior to the ablation procedure (52). Surrounding structures that may be important during catheter ablation can be identified including coronary veins, coronary arteries and the course of the esophagus (25,53). For these issues, MSCT and MRI are the preferred imaging modalities (6).

During catheter ablation: visualization of structures and image integration

During the actual catheter ablation procedure, mapping and ablation catheters are introduced into the LA after a transseptal puncture. This is typically performed under fluoroscopy guidance, but intracardiac echocardiography can be used to better visualize the inter-atrial septum and puncture needle (54). After gaining access to the LA, the exact location and anatomy of the PV ostia is determined, and the position of the mapping/ablation catheters in relation to them. For this purpose, various imaging modalities are available.

Fluoroscopy is the most widely used imaging technique in the electrophysiology laboratory. However, correct visualization of cardiac structures may be limited with fluoroscopy alone. In recent years, a new application of conventional fluoroscopy has been introduced: rotational angiography uses a C-arm flat-panel fluoroscopy system and contrast medium to create three-dimensional images of the LA and PVs (55). It has been demonstrated that this technique correctly identifies PVs and provides PV diameters that correlate well with those derived from pre-procedural acquired MSCT images (56).

Intracardiac echocardiography can be used in addition to fluoroscopy to visualize the PVs. This technique provides real-time images of the PVs and neighboring structures. In addition, it may be very helpful in avoiding complications during the ablation (57). A limitation of intracardiac echocardiography is its two-dimensional character. As a result, PV diameters may be underestimated as compared with three-dimensional imaging techniques (58,59).

Electroanatomic mapping systems may also be used in addition to fluoroscopy. These systems provide on-line electrophysiologic data, and allow tracking of mapping/ablation catheters and annotation of ablation points (60). A limitation of electroanatomic mapping systems however is the use of reconstructed anatomy. Finally, three-dimensional imaging techniques such as MSCT and MRI can provide very detailed information on LA and PV anatomy. However, scanning is performed before the ablation procedure, and therefore these techniques cannot provide real-time images.

Although the various imaging modalities all provide important information during the catheter ablation procedure, each technique has its own limitations. Integration of the different modalities may overcome the limitations of each separate modality. Hence, the question is: *'Is it possible to integrate different imaging modalities during AF ablation?'*

In recent years, various image integration systems have been introduced, allowing integration of different imaging modalities. Dedicated software has been developed to integrate biplane fluoroscopy and MSCT or MRI images (61). Angiographic reconstructions of the LA and PVs from fluoroscopy and three-dimensional volume rendered reconstructions from pre-procedural acquired MSCT or MRI images are merged with the use of calibration, translation and rotation processes. Several studies have demonstrated the feasibility of this new technique and its value during AF ablation (62,63).

In the past years, large clinical experience has been obtained with the integration of electroanatomic maps and three-dimensional techniques such as MSCT and MRI (64). This image integration strategy uses algorithms that minimize the distance between the reconstructed anatomy from the electroanatomic map and the MSCT or MRI image (65,66). Importantly, it has been demonstrated that the use of image integration may improve the outcome of the ablation procedure (67). In a cohort of 290 patients (145 patients with image integration, 145 patients with conventional mapping and ablation approach), the AF-free survival rate was significantly higher in patients with image integration (Figure 4) (68). However, this finding was not confirmed in a smaller, randomized study: single procedure success after 6 months follow-up was similar in patients with image integration and conventional mapping approach (50% vs. 56%, p=0.65) (69). More randomized controlled trials are needed to fully appreciate the role of integration of electroanatomic maps and MSCT or MRI images in catheter ablation procedures, and the impact on procedure/ fluoroscopy times and outcome. Nonetheless, image integration facilitates AF ablation by combining on-line electrophysiologic and detailed anatomic information.

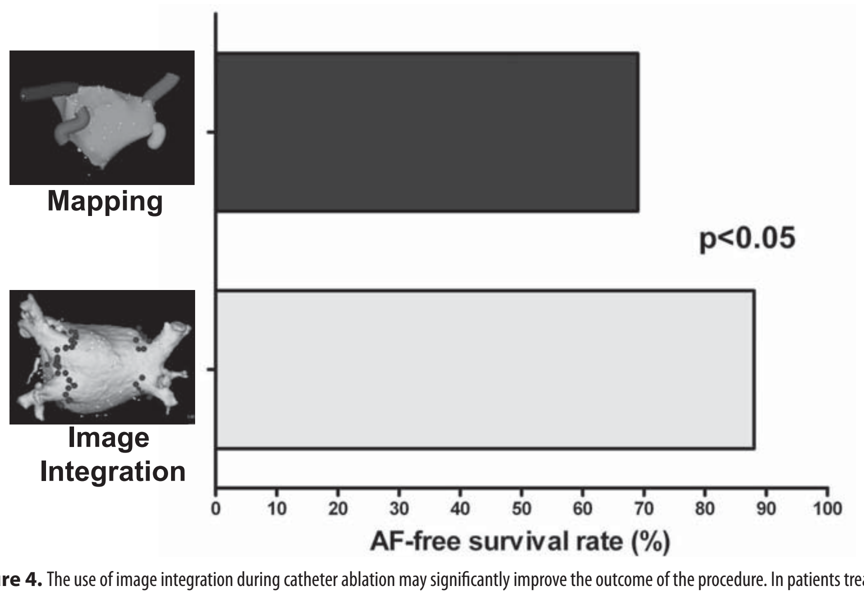


Figure 4. The use of image integration during catheter ablation may significantly improve the outcome of the procedure. In patients treated with catheter ablation using image integration, the AF-free survival rate was significantly higher compared with patients who were treated with conventional electroanatomic mapping alone (AF-free survival rate 88% vs. 69%, $p<0.05$). Adapted from Della Bella et al., reference 68.

More recently, integration of intracardiac echocardiography, electroanatomic mapping and MSCT has become available (70) (Figure 5). With the use of an intracardiac echocardiography probe that is tracked by the electroanatomic mapping system, a real-time electrophysiologic and anatomic reconstruction of the LA and PVs is created. Subsequently, it is integrated with MSCT images, adding detailed anatomic information. Although it is a promising strategy, more studies are needed to appreciate the role of this new technique and its effect on the outcome of catheter ablation for AF.

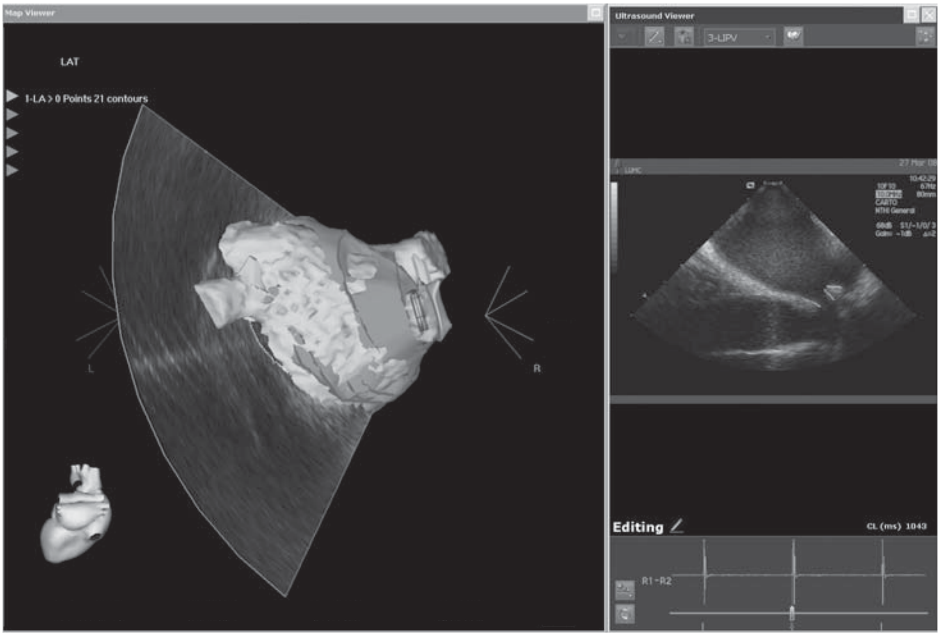


Figure 5. The feasibility of the integration of electroanatomic mapping, intracardiac echocardiography and MSCT has recently been demonstrated. A dedicated intracardiac echocardiography probe provides real-time anatomic images that are integrated with pre-procedural acquired MSCT images. On the ECG-gated intracardiac echocardiography images, the anatomy of the LA and PVs can be annotated, creating a three-dimensional shell (right panel). Subsequently, the three imaging modalities are integrated with dedicated algorithms (left panel).

Follow-up issues: assessment of complications and evaluation of LA function

Immediately after the procedure and during follow-up, patients should be screened for complications. A large survey revealed that serious complications occur in up to 6% of patients (71). Therefore, it is important to know: *'Which complications can be expected and how can they be assessed?'*

Pulmonary vein stenosis is one of the most frequently occurring complications of AF ablation (6). Fortunately, the prevalence is decreasing due to more proximal ablation strategies. Asymptomatic PV stenosis may occur in up to 19% of patients, whereas symptomatic PV stenosis requiring intervention occurs in less than 1% of patients (72). Conventional invasive angiography assessing PV diameters may be used for the detection of PV stenosis. However, three-dimensional imaging techniques such as MSCT or MRI are recommended for accurate assessment of PV stenosis (73).

Severe pericardial effusion or cardiac tamponade is another serious complication after AF ablation. In a recent meta-analysis with 70 studies including approximately 15.500 AF patients, cardiac tamponade was reported in up to 5% of the patients (median from all studies 1%) (72). During the procedure, invasive blood pressure measurement, fluoroscopy, and transthoracic echocardiography are helpful tools to detect pericardial effusion. In addition, intracardiac echocardiography can be used during the procedure (74). Conventional transthoracic echocardiography is the preferred imaging modality for screening during follow-up (6).

Finally, injury to the esophagus may occur after ablation, since the esophagus has a close relation with the posterior LA wall and PVs. A rare but severe complication is an atrio-esophageal fistula (75). MSCT or MRI should be performed when this complication is suspected (6).

In addition to the detection of complications, the effects of catheter ablation on cardiac function may be assessed during follow-up. It has been demonstrated that AF ablation has favorable effects on LV systolic function in patients with heart failure (76). In contrast, in patients with preserved LV systolic function, LV ejection fraction does not change after successful catheter ablation (77). However, it may be that LV ejection fraction is not a sensitive marker to detect subtle changes in LV systolic function. Recently, it has been demonstrated that global LV systolic strain does improve in patients with preserved LV systolic function who maintain sinus rhythm after catheter ablation (78). In contrast, patients who had recurrence of AF did not show a significant improvement in LV systolic strain.

Furthermore, since extensive ablation in the LA may result in scar formation and subsequently in changes in LA anatomy, one could wonder: *'What is the effect of catheter ablation on LA size and function?'* As previously described, there is a strong association between AF and LA enlargement. Interestingly, it has been demonstrated that restoration of sinus rhythm may result in reversal of LA enlargement (29). Several studies have demonstrated a decrease in LA volumes after successful catheter ablation (79-81). Typically, transthoracic echocardiography is used for the follow-up of LA volumes. However, three-dimensional techniques may provide more accurate information, as previously described. With the use of real-time three-dimensional echocardiography, it has been shown that LA maximum volume decreases in patients who maintain in sinus rhythm during follow-up (82). Similarly, LA reverse remodeling has also been demonstrated with MSCT (32) and MRI (83).

Furthermore, AF ablation may affect LA function. Three distinct phases can be distinguished in LA function: LA reservoir function (during ventricular systole), LA conduit function (during early ventricular diastole) and LA booster pump function (during late ventricular diastole). In general, LA function parameters are derived from trans-mitral flow patterns using Doppler echocardiography. However, using real-time three-dimensional echocardiography the different phases in LA function can be derived from LA volumes throughout the cardiac cycle. Marsan et al. demonstrated that LA booster pump function significantly improves in AF ablation patients who maintain sinus rhythm during follow-up (Figure 6) (37).

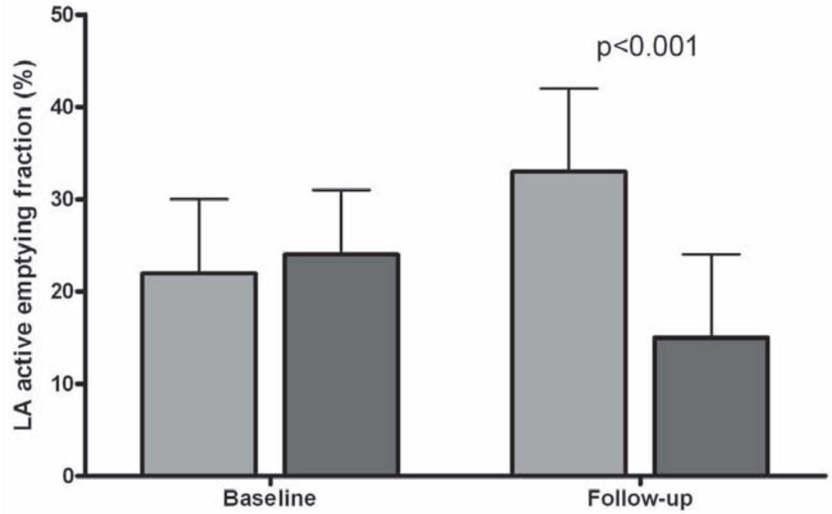


Figure 6. Left atrial active emptying fraction (representing LA active function) improves in patients who maintain sinus rhythm during follow-up (green bars). In contrast, a deterioration of LA active emptying fraction is noted in patients who have recurrence of AF during follow-up (red bars). Adapted from Marsan et al., reference 37.

With the use of tissue Doppler echocardiography, LA strain and strain rate can be assessed. These parameters represent myocardial mechanical function, allowing quantification of LA segmental function (84). Schneider et al. used this technique to assess LA function in 118 patients undergoing AF ablation (85). After 3 months follow-up, an improvement in the different LA functions was noted, but only in patients who maintained sinus rhythm during follow-up.

Finally, the feasibility of LA scar assessment with gadolinium enhanced MRI has recently been demonstrated. In 53 patients undergoing AF ablation, MRI images were acquired before the procedure and after 3 months follow-up. Interestingly, the extent of LA scar as assessed with MRI was a strong predictor of freedom from AF during follow-up (OR 18.5, 95% CI 1.27 to 268, p=0.032) (86). However, more studies are needed to appreciate the role of LA scar assessment with MRI in the follow-up of AF ablation patients.

CONCLUSIONS

Multimodality imaging plays an important role in the initial assessment of AF patients, and during subsequent invasive treatment with catheter ablation (Figure 7). An important issue to consider in the first evaluation of AF patients is the presence of any underlying heart disease that is associated with AF: coronary artery disease, heart failure, valvular heart disease and LV

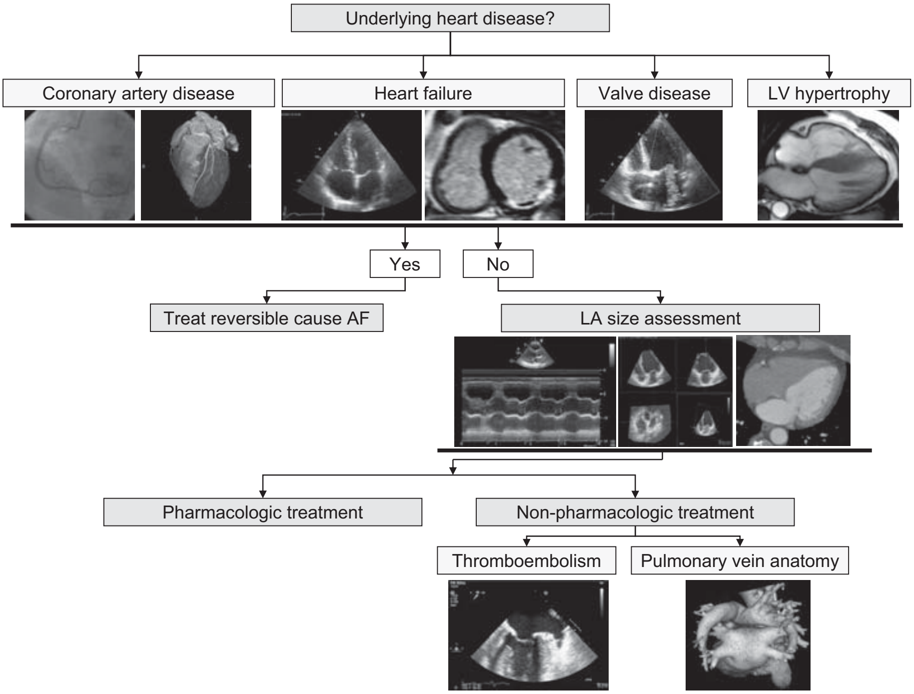


Figure 7. Multimodality imaging plays an important role in the evaluation of AF patients, and in the management of AF. Various modalities are available for screening for underlying heart disease causing AF. For LA size assessment, various methods are available; three-dimensional imaging techniques provide the most accurate estimation. In particular in the non-pharmacologic treatment of AF, imaging plays an important role in patient selection and guidance of the procedure. See also text for explanation.

hypertrophy. Any (reversible) underlying disease that causes AF should be treated first. Furthermore, LA size should be assessed in the initial evaluation of AF patients. For the routine assessment of LA size transthoracic echocardiography is the technique of choice. Preferably, LA volumes are assessed for estimation of LA size.

After the initial assessment of the AF patient, a treatment strategy is chosen (pharmacologic vs. non-pharmacologic). Multimodality imaging is of particular value in the non-pharmacologic treatment of AF. In patients undergoing electrocardioversion or catheter ablation, LA thrombi should be excluded with transesophageal echocardiography. Before catheter ablation, PV anatomy should be evaluated, preferably with three-dimensional imaging techniques such as MSCT or MRI. During the actual ablation procedure, different imaging modalities are available for visualization of cardiac anatomy. New dedicated systems allow integration of the various modalities, further facilitating catheter ablation procedures. After the ablation procedure, imaging plays an important role in the detection of complications. Finally, the effects of the catheter ablation procedure on LA size and function can be assessed with various imaging modalities.

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