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Multimodality imaging of left atrium in patients with atrial fibrillation

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ABSTRACT

Atrial fibrillation (AF) is the most common arrhythmia worldwide associated with significant morbidity and mortality and represents a significant health care burden. Goals of AF treatment include prevention of cardioembolic stroke using anticoagulation and device therapy and restoration of sinus rhythm using antiarrhythmic drugs or catheter ablation techniques. A comprehensive assessment of cardiac chamber size and function is often started with echocardiography as a first line diagnostic imaging strategy. Recently, innovations in advanced imaging using cardiac magnetic resonance (CMR) and cardiac computed tomography (CCT) provide a detailed characterization of atrial anatomy and have been shown to accurately exclude thrombus and guide left atrial appendage (LAA) closure or catheter ablation (CA) of atrial fibrillation. Compared to echocardiography, CCT offers an uncompromised spatial resolution and a fast dataset acquisition, with the disadvantages of the need of iodine contrast agent and radiation exposure. CMR, conversely, can rely on very high temporal resolution, the unique feature of tissue characterization and the absence of radiation exposure. However, the main drawbacks of this diagnostic tool are long scan times and low availability. This review will illustrate the vital role of multimodality cardiac imaging in the accurate identification of left atrial, pulmonary vein and LAA size and function, discuss advanced imaging techniques to rule out thrombus and highlight novel CMR and CCT techniques to guide catheter ablation of AF and LAA occlusion.

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia worldwide and is epidemic.[1] AF is a strong, independent risk factor for cardioembolic stroke[2] with a significant impact on morbidity, mortality and health care costs.[1,3] An important AF treatment goal is the prevention of cardioembolic stroke using anticoagulation therapy. Additional goals are sinus rhythm restoration and arrhythmia recurrence prevention using antiarrhythmic drugs.[4]

Some patients present contraindications to anticoagulation therapy.[5] In these cases, percutaneous left atrial appendage (LAA) closure may represent a possible alternative therapy.[4] Furthermore, in order to reduce the recurrence of AF, catheter ablation (CA) is a valuable strategy.[4]

An accurate evaluation of left atrial (LA) size and function provides essential information to the clinician for AF prognosis and treatment. Furthermore, ruling out LA and LAA thrombus is crucial to safely perform electrical cardioversion of AF.

A comprehensive assessment of the LA, pulmonary veins (PV) and LAA structure and function is of unparalleled importance before proceeding to invasive treatments like CA or LAA closure and in patient follow-up after such therapies.

Transthoracic (TTE) and transesophageal (TEE) echocardiography have a large role in the evaluation of patients with AF. However, cardiac computed tomography (CCT) and cardiac magnetic resonance (CMR) are gaining an important role in this field.

The aim of this review is to focus on the additional value of advanced cardiac imaging including CCT and CMR, in the assessment of LA anatomy, in ruling out of LA thrombus and in guiding CA of AF and LAA occlusion (see Table 1).

2. Left atrium size and function

Multimodality imaging is able to provide a complete evaluation of LA anatomy and function in patients with AF including a thorough assessment of PVs and LAA.

Abbreviations: AF, Atrial fibrillation; CA, Catheter ablation; CMR, Cardiac magnetic resonance; CCT, Cardiac computed tomography; DE, Delayed enhancement; DE-MRI, Delayed-enhancement MRI; ED, Effective dose; LAA, Left atrial appendage; MBIR, Model-based iterative reconstruction; PV, Pulmonary veins; TI, Inversion time; TTE, Transthroracic echocardiography; TEE, Transesophageal echocardiography

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Table 1
Advantages and Disadvantages of CCT, CMR and Echocardiography. CCT: cardiac computed tomography, CMR: cardiac magnetic resonance, LA: left atrium, LAA: left atrium appendage, TEE: transoesophageal echocardiography.

	Echo		CCT		CMR	
	Pros	Cons	Pros	Cons	Pros	Cons
Rule out of LA and LAA thrombosis	Gold standard for ruling out of LA and LAA thrombosis Widely used in clinical practice	Semi-invasive procedure (TEE)	High sensitivity	Low specificity (significantly improved by late-phase imaging) Radiation exposure (additional late-phase images required) Iodinated contrast agents use	High diagnostic accuracy	Few studies published on this field Low availability of scanners Claustrophobic patients or presence of CMR unsafe devices
LA ablation	Procedural monitoring (intracardiac echocardiography)	Difficult characterization of pulmonary veins anatomy and extracardiac thoracic structures	Possibility of obtaining merged electro-anatomic map High resolution datasets Ruling out of concomitant coronary artery disease	Radiation exposure Iodinated contrast agents use	Evaluation of atrial fibrosis Possibility of obtaining merged electro-anatomic map	Low availability of scanners Claustrophobic patients or presence of CMR unsafe devices
LAA occlusion	Procedural monitoring Follow up after occluder positioning	Tendency to underestimate LAA diameter Semi-invasive procedure (TEE)	Precise sizing of the occluder device Higher sensitivity than TEE in identifying peri-device leaks	Radiation exposure Iodinated contrast agents use		No available studies evaluating its role in LAA appendage closure

The determination of LA size is of utmost importance for patient risk stratification. Indeed, LA enlargement is an independent predictor of stroke and death among patients with AF[6].

Echocardiography is commonly used as the first non-invasive imaging technique to evaluate LA size as it holds many advantages. Indeed, it is a widely available method, it does not require contrast agents or ionizing radiation and it is less expensive than CMR or CCT.

TTE (Fig. 1 A and B) is the standard approach for assessing LA size. Indeed, with TEE, the entire LA is not fully visualized and therefore it should not be used to assess LA size,[7] unless using a transgastric view.[8]

LA volume determination by TTE using the Simpson's rule or the area-length method is widely used and more accurate than the linear M-mode measurement as LA enlargement is frequently asymmetrical[7,9]. However, 2D measurements compared to CCT and CMR underestimate LA volumes[10] 3D echocardiography derived LA measurements are more accurate than 2D based analysis, resulting in fewer patients with undetected atrial enlargement when compared to CMR[11] and CCT.[12]

CMR is considered the gold standard technique for cardiac chamber evaluation, including LA volumes. CMR does not make any geometrical assumptions when evaluating LA size when determined using the Steady State Free Precession (SSFP) technique. The SSFP sequences are characterized by excellent blood-endocardium contrast and high spatial resolution allowing a better endocardial delineation compared to echocardiography[13–15]. In order to measure LA volumes, the SSFP short axis multi-slice acquisition used to determine left and right ventricle volumes and function is extended to encompass the entire atria.[16] (Fig. 1 C, D). A major advantage of CMR over echocardiography and CCT is its unique ability to characterize tissue. Thanks to specific post-contrast delayed enhancement magnetic resonance images (inversion-recovery-prepared, respiration navigated, ECG-gated, gradient echo pulse sequence with fat saturation), identification and quantification of left atrial fibrosis is feasible.[17,18]

LA size can also be accurately measured by CCT[19] (Fig. 1 E, F). The high spatial resolution of this imaging modality makes it the perfect approach for accurately depicting the anatomy. Principal drawbacks of CCT are the radiation dose (remarkably reduced with the use of new generation scanners) and the requirement of iodine contrast agents. In order to assess the anatomy properly, the imaging acquisition must be performed when a maximal opacification of the left atrium is reached. Although non-gated CT imaging is able to illustrate LA anatomy, ECG gated CT is crucial to minimize motion.

Although not routinely performed in clinical practice, LA function by determination of LA volumes at different times during the cardiac cycle can be obtained using echocardiography[20] and CMR.[21] For this purpose, due to a lower temporal resolution, CCT results are not optimal.[22]

More recently, LA deformation analysis has emerged as a tool for LA function assessment. Speckle tracking echocardiography has been applied to assess atrial function[23] as well as quantitative tissue tracking CMR.[24,25]

3. Pulmonary veins and left atrial appendage

Both CCT and CMR are able to characterize pulmonary vein anatomy, sizing the veins and identifying the presence of anatomical variants (accessory pulmonary veins, common ostium) and abnormalities (anomalous pulmonary venous return) representing an outstanding tool prior to AF ablation.[26,27] The choice between the two modalities for anatomical evaluation of pulmonary veins depends on availability and patient specific contraindications.

In order to correctly size the pulmonary veins, cross sectional orthogonal views for maximal and minimal diameters and area measurements of the ostia are obtained by multiplanar reconstruction CMR and CCT imaging.[26]

Despite TEE is the reference technique used for LAA anatomy and function assessment,[28] CMR and CCT are gaining an important role,

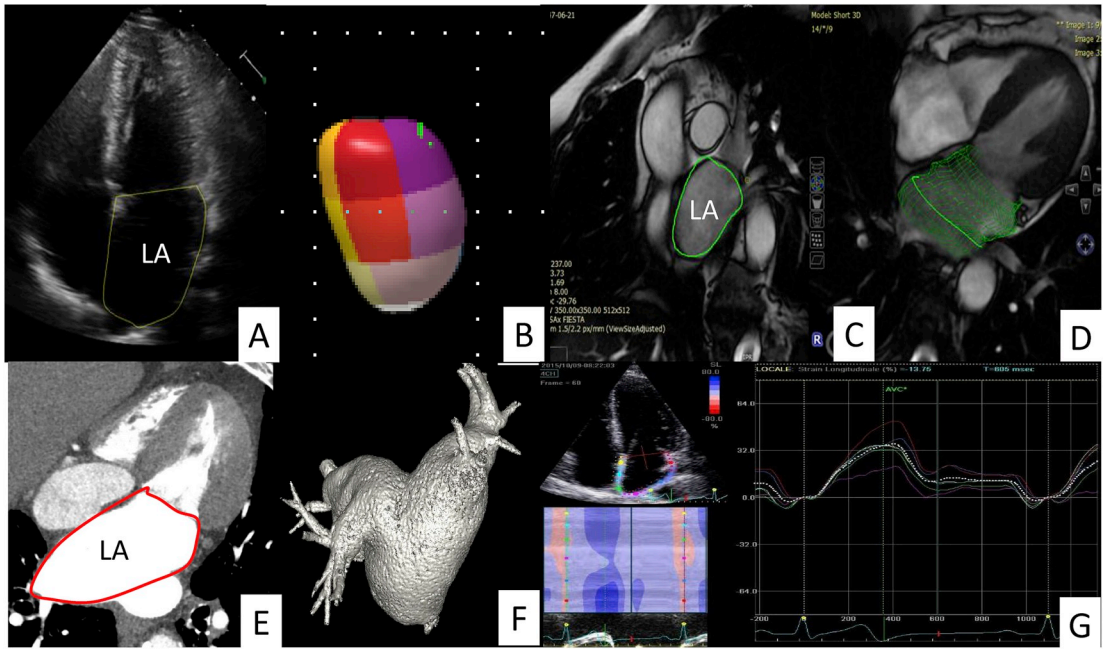

Fig. 1. A. TTE 4 Chamber Long Axis view showing LA area measurement (yellow line). **B.** 3D echocardiography measurement of LA volume. **C.** CMR SSFP cine Short Axis Stack for LA volume measurement and left atrial CMR 3D volume rendering (**D**). **E.** CCT measurement of LA area (red line) **F.** CCT 3D volume rendering of LA. G. Strain with speckle tracking method of a LA. CCT: cardiac computed tomography; CMR: cardiac magnetic resonance; TTE: transthoracic echocardiography; LA: left atrium; SSFP: steady state free precession sequence.

especially before and after interventional procedures. CMR and CCT are able to overcome the limitations of 2D imaging depicting the anatomy of the LAA in its complexity and ruling out the presence of LAA thrombus. Although not commonly performed in clinical practice, CMR offers the possibility of measuring blood flow in the LAA using velocity encoded techniques.[29]

4. Rule out of thrombosis

TEE is considered the gold standard technique for ruling out LA and LAA thrombus and is routinely used in clinical practice before electrical cardioversion and ablation of AF[30] (Fig. 2A).

The prevalence of atrial thrombus before cardioversion despite different treatments with anticoagulants is about 7% and a TEE guided approach may prevent the risk of embolic events.[31]

However, TEE is a semi-invasive procedure and sometimes time-consuming. In addition, compared to CMR and CCT 3D cross-sectional techniques, TEE does not allow an accurate study of the pulmonary veins and of the surrounding thoracic structures. Furthermore, TEE has some absolute (esophageal pathology, active gastrointestinal bleeding) and relative (coagulopathy, previous gastrointestinal bleeding) contraindications.[32,33]

CCT has been proposed as an alternative to TEE in excluding the presence of LA and LAA thrombus. Even though CCT has high sensitivity in detecting atrial thrombosis when validated against TEE, false positive findings have been reported.[34]

Pectinate muscles may be hard to differentiate from thrombi by CCT and blood flow dynamics can contribute to non uniform opacification of LAA blood pool, mimicking the presence of true filling defects. Indeed, LAA filling defects can be due to thrombus or incomplete contrast agents mixing with blood.

However, the use of double phase CCT acquisition with the analysis of late-phase images improves the specificity of the scan in distinguishing sluggish flow from thrombus.[35] According to the results of a meta-analysis encompassing 19 studies for a total of 2955 patients with AF in which CCT diagnostic accuracy was compared to TEE, the use of delayed imaging raised the positive predictive value of standard CCT scanning from 41% to 92%.[36]

Furthermore, the use of ECG gated acquisitions and heart rate control by beta-blocker administration improves the diagnostic accuracy of this technique.[37] In many institutions, in order to rule out LA and LAA thrombus, after obtaining an adequate heart rate control by betablocker administration (preferably HR < 65 bpm), the patient receives an injection of 70 mL of iodinated contrast at 5 ml/s followed by 50 ml normal saline at 5 ml/s using a bolus tracking technique with a region of interest in the descending aorta. Delayed imaging is acquired 15–30 s after the first pass acquisition (Fig. 2B and C).

In a recent study, Mosle et al. analyzed the safety and cost-effectiveness of a CCT-only strategy to rule out thrombus concluding that this approach improves electrophysiology laboratory efficiency, reducing lab utilization time to exclude LAA thrombosis by TEE, without influencing peri-procedural cost or post-procedural stroke risk.[38]

Although the excellent results of this technique in ruling out LAA thrombus, the use of additional late-phase images is associated with an increase in radiation exposure. An additional drawback in the use of CCT in this setting is the mandatory use of contrast agents. Due to these limitations, the use of this diagnostic tool should be reserved to patients with contraindications to TEE or those undergoing an interventional procedure such as AF ablation or LAA closure in which CCT is already performed to accurately depict the anatomy.

The issue of radiation dose related to double acquisition to rule out LAA thrombus may be solved by dual energy computed tomography, a relatively recent result of the rapid advancement in scanner technology. This technology is based on acquiring images at different energy levels enabling the discrimination of different materials on the basis of their attenuation profiles. This approach helps differentiate thrombus from slow flow with a single acquisition.[39,40]

Even though CMR is a well-established technique for ruling out left ventricular thrombus, its use for LAA thrombus detection is less common and few studies have been published on this field. However, as in the case of CCT, CMR can be a favorable diagnostic technique for the detection and assessment of LA and LAA thrombus, with the advantage of avoiding ionizing radiation and iodinated contrast agents.[41] Kitkungvan et al. studied the diagnostic performance of

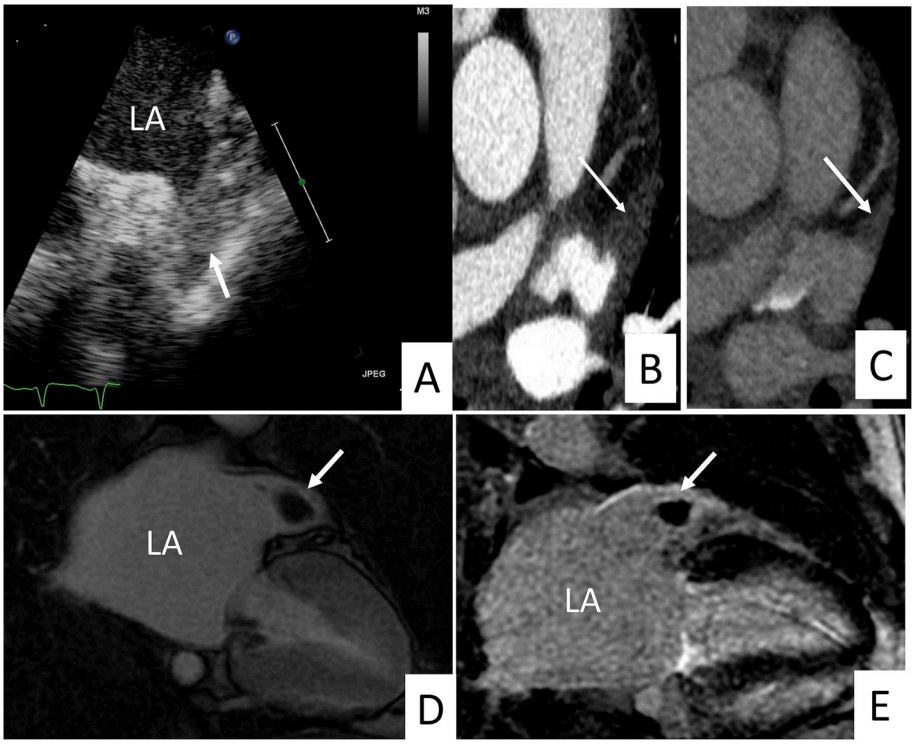

Fig. 2. A. TEE showing LAA thrombus (arrow) **B, C.** Early and delayed post contrast CCT imaging showing LAA thrombus (arrow). **D** and **E.** early (C) and late (D) post contrast T1W CMR images showing LAA thrombus (arrow). CCT: cardiac magnetic resonance; CMR: cardiac magnetic resonance; LA: left atrium; LAA: left atrial appendage; TEE: transesophageal echocardiography.

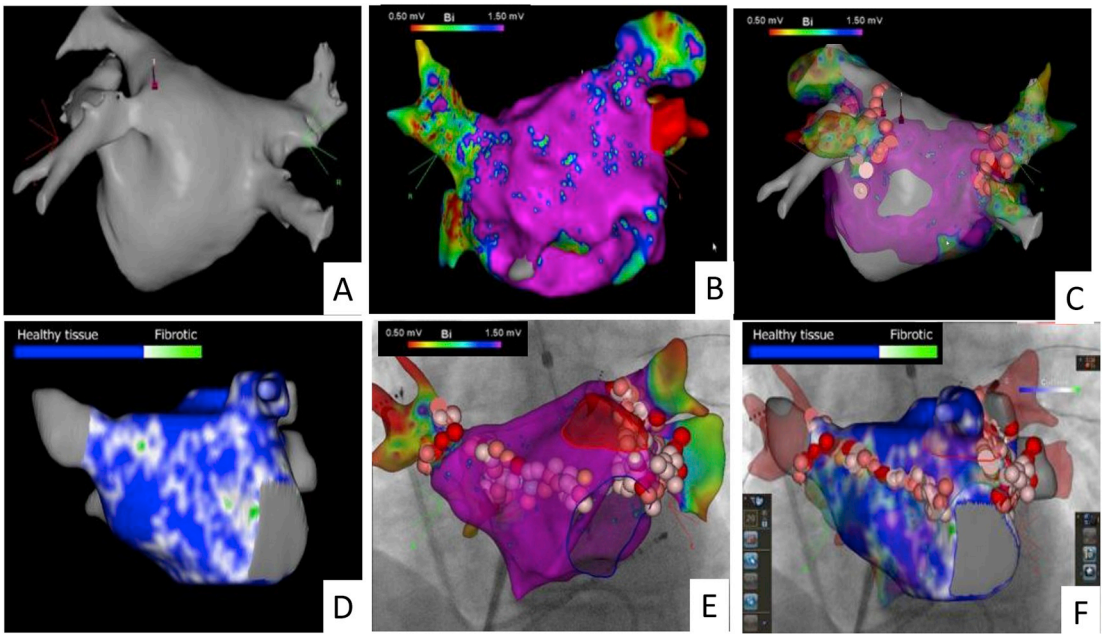

Fig. 3. A. CCT 3D volume rendering of left atrial volume. **B.** 3D electroanatomical mapping of left atrium. **C.** 3D CCT volume and 3D electroanatomical mapping merge. **D.** Left atrial 3D color model of segmented delayed enhancement CMR scan for left atrial fibrosis. **E.** 3D electroanatomical mapping **F.** Left atrial 3D color model of segmented delayed enhancement CMR scan for left atrial fibrosis and 3D electroanatomical mapping merge. CCT: cardiac computed tomography; CMR: cardiac magnetic resonance.

CMR for ruling out LAA thrombus in 261 patients who underwent CMR using TEE as reference standard. The results were promising, and they proposed this technique as a single complete diagnostic study for assessment of pulmonary venous anatomy as well as presence of LA/LAA thrombi. According to the authors, equilibrium phase delayed enhancement (DE) CMR with a long inversion time (TI) of 600 ms (long TI DE-CMR) had a diagnostic accuracy of 99.2%, sensitivity of 100%, and specificity of 99.2% for thrombus detection[42] (Fig. 2D and E).

5. Left atrium ablation

Catheter Ablation (CA) is well-established interventional therapy for restoring and maintaining sinus rhythm in patients with AF. Pulmonary vein isolation, either by radiofrequency or cryoablation is the most common ablation technique.[4] Pulmonary vein isolation is oftentimes sufficient in patients with paroxysmal AF but is often insufficient in patients with persistent and long-standing forms of the arrhythmia. In these more complex patients, different targets in addition to the

pulmonary veins must be identified. These targets usually cluster in specific regions such as the left atrial posterior wall, other thoracic veins (superior vena cava, coronary sinus, vein of Marshall), crista terminalis, interatrial septum and the LAA.[43]

As a result, detailed characterization not only of the pulmonary veins but also the entire LA and its surrounding structures are important to guide the ablation of AF.

3D electro-anatomical mapping systems such as CARTO (Biosense, Diamond Bar, CA, USA) and EnSite NavX (St. Jude Medical, St Paul, MN, USA) provide a 3D anatomical map of the LA and precisely identify the position of the catheter's tip during the procedure (Fig. 3B and E). The CARTO system is a non-fluoroscopic system that uses magnetic technology to determine the catheter location in 3D. The NavX system technology uses an electrical field generated between external patches placed along 3 orthogonal axes on the patient.[44]

3D-electroanatomical mapping facilitates radiofrequency ablation, increases its efficacy and reduces the use of fluoroscopy and radiation dose.[45,46] The role of 3D mapping using cryoablation remains unclear.[47]

The integration of 3D cardiac images into electro-anatomical maps represents a major step forward for the development of ablation procedures designed specific to patient anatomy with more effective therapeutic lesions and an increased safety profile.

For this reason, pre-procedural CCT or CMR imaging has been increasingly used to guide ablation of AF. This process consists of four steps: 1) CCT or CMR scans are performed and datasets are imported in a dedicated workstation to be segmented; 2) the LA is electro-anatomically reconstructed during the procedure; 3) a merge phase in which the two maps of LA are superimposed by landmarks or surface registration to produce a hybrid map; 4) the catheter is navigated into a merged electro-anatomic map.[48]

The image-integration CCT-guided catheter ablation of AF has been shown to be superior to conventional electrophysiological guided ablation with significantly lower recurrence rates of the arrhythmia[49] (Fig. 3A,C).

Moreover, CCT may provide additional information on coronary artery calcification and plaque to diagnose concomitant coronary artery disease. In addition, as CCT is a 3D technique that visualizes thoracic structures that surround the heart, it is able to detect clinically significant collateral findings before the ablation procedure. Perna et al. showed that collateral findings can be detected in up to one-third of patients referred to CCT before CA, allowing the diagnosis and treatment of a potentially life-threatening condition in 1.7% of individuals.[50]

As previously mentioned, radiation exposure from CCT is an important drawback of this modality, and the use of iodinated contrast agents is required. However, continuous technological progress has significantly reduced the patient's radiation exposure. Increased image noise from dose reduction strategies can be reduced by multiple reconstruction techniques offered across all vendor platforms with ability to reconstruct the image at varying level of strength of iterative reconstruction (for example: Image space and sinogram affirmed iterative reconstruction – Siemens Healthcare, Erlangen, Germany; Adaptive iterative dose reduction – Toshiba Medical Systems, Otawara, Japan; iDose4 – Philips Healthcare, Cleveland, OH; Adaptive statistical and model based iterative reconstruction techniques – GE Healthcare, Waukesha)[51]

For instance, CCT with MBIR (model-based iterative reconstruction - VEO, GE Healthcare, Milwaukee, WI -) allows accurate reconstruction of LA anatomy in AF patients undergoing CA with a sub-millisievert effective dose (ED) and comparable success rate of CA as compared to a standard CCT scan protocol.[52,53]

CMR integration with electro-anatomical mapping for AF can be performed with time-resolved contrast-enhanced angiography sequences with low dose of gadolinium or without any contrast by using 3D SSFP in cases of severe renal impairment. Pontone et al. compared CCT versus CMR for characterization of LA anatomy before radiofrequency CA and demonstrated similar freedom from AF with higher radiation exposure in patients undergoing CCT rather than CMR.[48]

Furthermore, the most important asset of CMR over CCT is its ability to perform tissue characterization. There is a strong association between AF and atrial tissue fibrosis. Indeed, atrial fibrosis is essential to perpetuate atrial arrhythmias and leads to increased AF burden.[54] Recently, novel DE-MRI (Delayed-Enhancement MRI) sequences have been developed demonstrating both the presence and extent of atrial fibrosis in patients suffering from AF[17] (Fig. 3D). In the DECAFF (DE-MRI Determinant of Successful Radiofrequency Catheter Ablation of Atrial Fibrillation) multi-center observational study, the extent of LA fibrotic tissue was found to be independently associated with likelihood of recurrent arrhythmia. Specifically, patients were divided, based on the degree of detected fibrosis into 4 stages: stage 1, less than 10% of the atrial wall; stage 2, 10% or greater but less than 20%; stage 3, 20% or greater but less than 30%; and stage 4, 30% or greater. Recurrence of arrhythmia was 69.4% in patients with stage 4 vs 15.3% in patients with stage 1.[18]

Currently, a multicenter trial is ongoing, the DECAFF 2 Study, with the endpoints of assessing efficacy, safety and procedural outcomes of DE-MRI-guided atrial fibrosis ablation (Fig. 3 F).

Although CMR plays an important role in LA and PV imaging before AF ablation, several reasons such as limited availability of scanners, claustrophobic patients or presence of CMR unsafe devices may limit its use in favor of CCT.

6. Left atrial appendage occlusion

LAA occlusion using percutaneous devices may be considered for stroke prevention in patients with AF and contraindications for long term anticoagulant treatment.[4]

An accurate description of the LAA morphology and precise sizing of LAA diameters is of paramount importance before device deployment.

Oversizing of the device could lead to LAA rupture and cardiac tamponade while undersizing is related to incomplete LAA occlusion with residual peri-device blood flow and to possible device migration, dislodgement or embolization.[55]

TEE and angiography are the main techniques currently used for evaluating LAA dimensions before LAA occluder implantation and TEE is routinely used for procedural monitoring and follow up after occluder positioning.[56] However, TEE and angiographic measurements suffer from the inherent limititation of being bi-dimensional techniques and a tendency towards underestimation of LAA diameters with these techniques has been observed.[57,58] 3D TEE has partly overcome these drawbacks.[59]

CCT provides high resolution 3D datasets and is a useful tool to precisely characterize the anatomy of the LAA, size of the occluder device and exclude the presence of thrombus before the LAA occlusion procedure. In addition, CCT is able to identify device malapposition, peri-device leaks and device-related thrombus at follow up.

LAA shape, depth, number and positioning of lobes are accurately depicted by CCT (Fig. 4A and B,C). Cross sectional orthogonal CT views for diameter measurements of the LAA ostium (diameter at the level of the left circumflex) and landing zone (diameter of the LAA 1–1.5 cm distal to the ostium) are obtained using multi plane reconstruction images.[60] In follow up, CCT has higher sensitivity than TEE in identifying peri-device leaks (Fig. 4D), especially during the venous phase, and is able to identify device-related thromboses.[61,62]

The use of CT-derived 3D printing LAA models may increase the accuracy of CCT in sizing the LAA occluders as illustrated by a report from Obama et al. In a series of 24 patients, the authors observed 100% accuracy in prediction of device size, quick and intuitive identification of the landing zone and significant reduction in procedure time and peri-device leak using pre-procedural CT based 3D printing.[62]

CMR can provide a detailed LAA evaluation.[63] However, there are

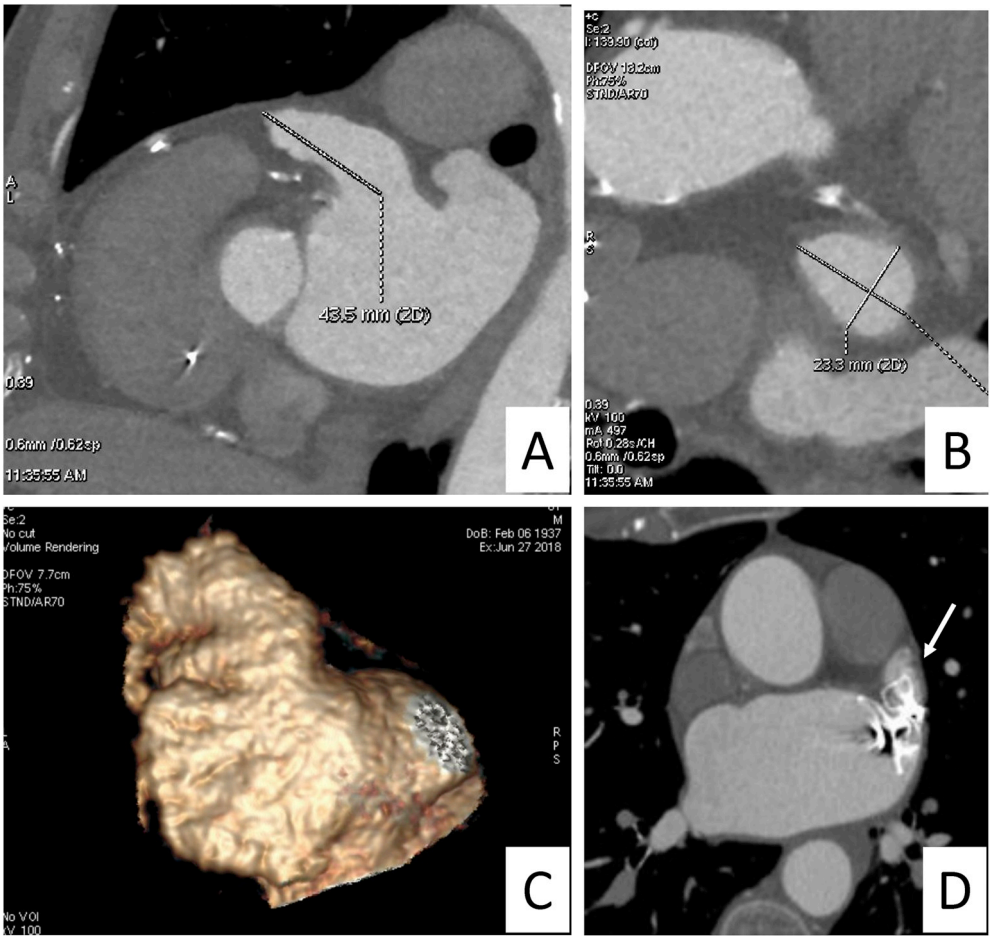

Fig. 4. A and B. CCT measurements of LAA depth **(A)** and ostium diameters **(B) C.** CCT 3D volume rendering of LAA. **D.** Delayed CCT post contrast images showing residual leak in a patient who underwent LAA closure (white arrow). CCT: cardiac computed tomography; LAA: left atrial appendage.

no available studies evaluating its role in LAA appendage closure; this is probably a consequence of higher spatial resolution, speed of scanning and widespread availability of CT.

7. Conclusions

Although echocardiography remains the first-line imaging modality for patients with AF, advanced cardiac imaging represents a valuable tool, especially when an interventional strategy is pursued. CCT and CMR are able to accurately depict the anatomy of LA, pulmonary veins and LAA, including ruling out thrombus, and can be utilized for guiding invasive procedures. The choice between the two modalities relies on the specific procedure, costs, availability and patient specific characteristics.

Conflicts of interest

No relationship with industry and financial associations within the past 2 years that poses a conflict of interest in connection with the submitted article exists.

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