

Collateral findings during computed tomography scan for atrial fibrillation ablation: Let's take a look around

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Abstract

The growing number of atrial fibrillation catheter ablation procedures warranted the development of advanced cardiac mapping techniques, such as image integration between electroanatomical map and cardiac computed tomography. While scanning the chest before catheter ablation, it is frequent to detect cardiac and extracardiac collateral findings. Most collateral findings are promptly recognized as benign and do not require further attention. However, sometimes clinically relevant collateral findings are detected, which often warrant extra diagnostic examinations or even invasive procedure, and sometimes need to be followed-up over time. Even though reporting and further investigating collateral findings has not shown a clear survival benefit, almost all the working groups providing data on collateral findings reported some collateral findings eventually coming out to be malignancies, sometimes at an early stage. Therefore, there is currently no clear agreement about the right strategy to be followed.

Key words: Collateral findings; Incidental findings; Incidentalomas; Cardiac computed tomography; Image integration

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Core tip: Several cardiac computed tomography (CT) scans are performed worldwide in order to better delineate left atrial anatomy before atrial fibrillation (AF) ablation. A thorough examination of the entire field of view often discovers cardiac or extra-cardiac collateral findings, which might represent potentially malignant diseases. Early detection of such diseases may guarantee a curative treatment. Our objective is to consolidate the current literature about collateral findings detected at cardiac CT before AF ablation and to highlight the potential

implications of systematically reporting and following up such findings.

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IMAGE INTEGRATION IN ATRIAL FIBRILLATION ABLATION

Cardiac computed tomography (CT) is being increasingly required for a large amount of indications, such as coronary artery disease, congenital heart disease, and detection of intracardiac thrombi^[1]. It is also frequently performed among patients undergoing atrial fibrillation (AF) catheter ablation, in order to achieve three-dimensional reconstruction of the left atrium (LA), which is crucial for pre-procedural planning of the ablation strategy and accurate intra-procedural catheter navigation, especially in complex cardiac anatomies^[2-4].

Pulmonary vein (PV) isolation has become a cornerstone in the treatment of AF, and may represent a first-line therapy in selected cases^[5-8]. However, complicated LA or PV anatomy can make it extremely difficult to access some areas, thus contributing to suboptimal success rates and hindering the successful application of this technique^[9,10]. Moreover, it has been ascertained that PV anatomic variations are fairly common^[11-13]. Knowledge of the conventional pulmonary venous anatomy, as well as of anatomic variants, is crucial for preprocedural planning and safer catheter navigation. Fluoroscopy alone cannot differentiate between PVs, LA and surrounding structures. On this proposal, cardiac CT has gained acceptance, among cardiac electrophysiologists, as the preferred radiological investigation in order to precisely delineate LA and PV anatomy, because of its better diagnostic gain on intrathoracic organs and vessels as compared to other investigations, such as intracardiac echocardiography^[14]; moreover, cardiac CT is more widely available than magnetic resonance, requires shorter scanning times and is better tolerated by patients^[2-4,15]. These characteristics made cardiac CT the gold standard exam for image integration in AF ablation.

Cardiac CT performed for AF ablation is a chest CT angiography scan acquired using multidetector CT scanners with a field of view (FOV) which usually extends vertically from the level of the carina to the diaphragm. CT scan is generally not electrocardiographically (ECG)-gated, since a consistent part of the patients may be in AF during the examination. The absence of ECG-gating is the main difference between cardiac CT scan performed for AF ablation and for coronary artery disease, since

synchronization with the ECG is necessary in order to investigate coronary arteries. Scan synchronization with the contrast medium is often performed with the bolus tracking technique, that is, injecting a bolus of radio-opaque contrast media into the patient *via* a peripheral vein, tracking the volume of contrast within a region of interest, and then following it with the CT scanner after it reaches that region. After imaging the left atrium, it is possible to build a volume rendering three-dimensional image of the structures of interest, which is imported in the electroanatomical mapping system workstation and segmented using an image processing software, in order to better distinguish the left atrium from the surrounding structures. Once the segmentation process is complete, the three-dimensional representation of the left atrium is displayed in the electroanatomical mapping system and is superimposed to the three-dimensional electroanatomical map created by the operator; the electroanatomical map and the CT image are aligned to each other in order to allow the operator to move the mapping catheter within the three-dimensional representation of the left atrium.

Image integration between the cardiac CT scan (performed before the ablation) and the electroanatomical LA map (obtained intraprocedurally), allows the operator to have a detailed roadmap of the actual patient's anatomy available during the ablation procedure. This is crucial for anatomic definition of ablation targets and precise catheter navigation throughout complex anatomies, as well as for limiting collateral damage to adjacent structures, such as the esophagus (lowering the risk of atrio-esophageal fistula)^[16]. This technique is particularly useful while ablating difficult targets, such as the ridge of Marshall between the left-sided PVs and the left atrial appendage, in order to avoid ablating either inside the appendage (risk of perforation) or too deep inside the PVs (risk of PV stenosis) (Figure 1). Image integration systems have been shown to reduce procedural and fluoroscopy times, and even improve procedural outcomes, thus justifying their increased procedural costs^[17-19].

COLLATERAL FINDINGS DETECTED BY CARDIAC CT FOR AF CATHETER ABLATION

Cardiac CT scan usually details only a small FOV strictly around the heart, although almost the entire chest is irradiated during image acquisition. A larger FOV is then available from the unprocessed data to examine the neighboring structures, such as lungs, breasts, mediastinum, spine, and upper abdomen, with no additional X-rays exposure. While examining the entire FOV of a cardiac CT, it is frequent to encounter cardiac or extra-cardiac collateral findings (CFs) during the imaging study (Figures 2 and 3). The term "collateral finding" reflects an incidentally discovered mass or lesion, detected by CT, magnetic resonance imaging, or other imaging modality, which is not related to the primary objectives of the

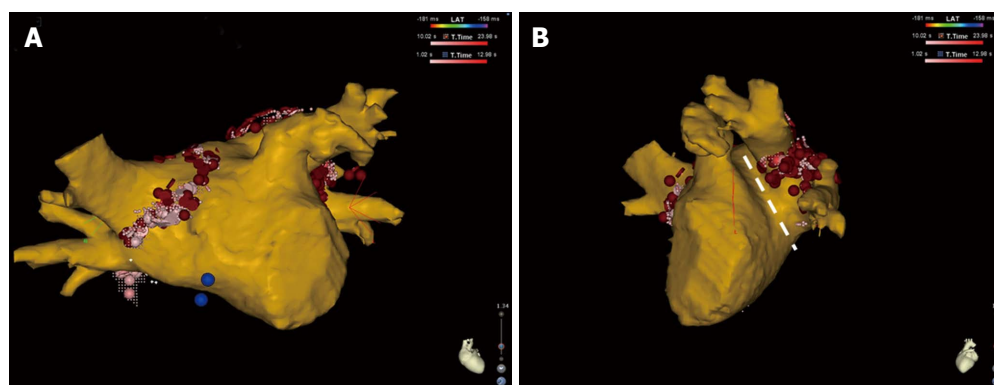


Figure 1 Antero-posterior (A) and left lateral (B) view of three-dimensional reconstruction of the left atrium and pulmonary veins after merging the cardiac computed tomography with the electroanatomical map created with the Carto 3 system (Biosense Webster, Inc., Diamond Bar, CA, United States). Note the ablation tags (red dots) placed around the pulmonary vein ostia on the computed tomography reconstruction. In the left lateral view, the narrow ridge between the left-sided pulmonary veins and the left atrial appendage can be appreciated (white dashed line).

examination; CFs are also called “incidental findings” or “incidentalomas”^[20]. A collateral finding is considered “clinically significant” when its detection warrants further investigations or therapeutic measures, or causes a change in the patient management. Most encountered extra-cardiac CFs pertain to the lungs, particularly small (< 4 mm) pulmonary nodules. Other frequently met CFs are degenerative spine disease, aortic disease, swollen mediastinal or hilar lymph nodes, liver lesions.

On this basis, several working groups reported about the prevalence and clinical significance of such CFs during cardiac CT scans. The early reports mostly referred to CT studies performed in order to diagnose coronary artery disease, which is the main indication for cardiac CT scan^[21-25]. The reported prevalence of CFs during 4 electron beam CT studies ranged between 7.8% to 53%, with 4.2% to 11% of scanned patients needing follow-up examinations; this wide range of prevalence can be explained by different technologies and definition of CFs used in those studies^[26-29]. Along with the expanding indications for AF catheter ablation, there has been a parallel growth in the request of cardiac CT to depict LA and PV anatomy for image integration. As a consequence, some studies reporting CFs detected before AF ablation have been published (Table 1)^[30-35].

Wissner *et al.*^[30] studied 95 patients undergoing PV isolation between 2003 and 2007 with a 16-slice and subsequently 64-slice multidetector scanner, covering an area from above the clavicle to diaphragm, and found that 53% of patients had either cardiac or extracardiac CFs. Most CFs were extracardiac (78 out of 83), and more than half (46 out of 83) were pulmonary. Fifteen patients (16%) needed additional tests, and 6 of them (6.8%) had therapeutic implications due to the detection of unexpected findings. One patient (1.1%) had an adenocarcinoma of the lung diagnosed, which was treated surgically^[30].

Sohns *et al.*^[31] performed 64-slice multidetector CT of the chest and upper abdomen in 158 patients for identification of PV anatomy. They looked for extracardiac CFs only. A total of 198 extracardiac CFs were detected

in 72% of patients, and 31% of patients had at least one clinically significant or potentially significant finding. Lung cancer was diagnosed in 2 patients (1.3%)^[31].

The same group assessed the incidence of both cardiac and extracardiac CFs among an extended population of 224 AF patients. In 91% of patients an average of 3.2 cardiac findings per patient were discovered, while 619 extra-cardiac findings (2.8 per patient) were detected in 80% of patients. Thirty-two percent of the 619 extracardiac findings were classified as “clinically significant”, including 2 cases of previously unknown cancers (esophageal and pulmonary, respectively; 0.9% of patients) and a newly diagnosed aortic dissection. The authors explained the relatively high incidence of extra-cardiac findings with the detailed image and the advanced age of their patients^[32].

Schietinger *et al.*^[33] reached analogous conclusions, finding extra-cardiac CFs in 69% of patients, the majority being pulmonary, and clinically significant CFs in 24% of patients at ECG-gated multidetector CT for PV evaluation.

Martins *et al.*^[34] described a lower prevalence of CFs among 250 consecutive patients (23%). Half of the 76 CFs were pulmonary, including 2 lung cancers (0.8% of patients) and 2 pulmonary fibroses. Several findings led to specific disease management, but no focused follow-up was performed in order to get information about the impact of reviewing the entire FOV on patients’ outcome^[34].

Our group enrolled 173 patients referred for catheter ablation of AF. Fifty-six percent of the patients had at least one CF, and 33% had clinically significant CFs warranting further follow-up or investigations. In 10% of them, the detection of a CF led to therapeutic decisions. Three cases of bronchogenic carcinoma were eventually diagnosed (1.7% of the study population)^[35]. After publication of the study, two more cases of bronchogenic carcinoma were diagnosed during further follow-up chest CTs performed in patients with incidentally detected pulmonary nodules (unpublished data). All lung cancers detected among our patients were at a relatively early stage; therefore, curative treatment was possible in all the cases.

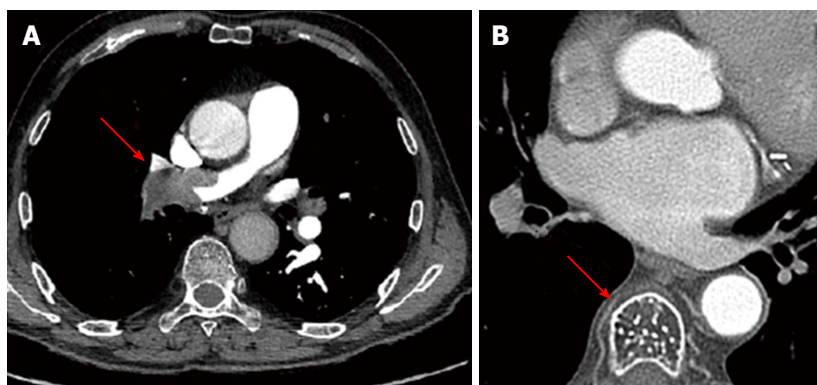


Figure 2 Examples of collateral findings detected with the preprocedural cardiac computed tomography. A: Pulmonary thromboembolism involving principal branch of right pulmonary artery (red arrow); B: Classic “polka dotted” appearance due to the thickened vertebral trabeculae, highly suspicious for vertebral hemangioma (red arrow).



Figure 3 Examples of collateral findings detected with the preprocedural cardiac computed tomography. A: Ostium primum atrial septal defect (red arrow); B: Abnormal dilated vessels (red arrow) diagnostic for pulmonary arteriovenous malformation located in the lower lobe of the right lung.

In summary, the proportion of patients with CFs is very high among the reported studies of cardiac CT performed for AF catheter ablation. Incidental findings requiring further investigations or follow-up are also quite frequent. Rather consistently, almost half of all collateral findings are represented by pulmonary nodules. Malignancy is diagnosed in a percentage ranging from 0% to 1.7% of patients.

REPORTING AND FOLLOWING UP COLLATERAL FINDINGS: AN OPEN DEBATE

Because of the large diffusion of AF catheter ablations, an increasing number of cardiac CT is being performed worldwide. The number of reported CFs is increasing, due to the growing number of cardiac CT performed and to the improved spatial resolution of the CT scanners. The main problem in reporting CFs is the subsequent flow of further investigations and procedures that are performed in order to rule out potentially deleterious pathologies. On the one hand, one should always keep in mind that in some cases, the detection of an early stage malignant disease might allow appropriate treatment and

prolong or save a patient's life. However, to date robust data regarding the potential clinical benefits of reporting and following-up CFs is still lacking, and it has not been shown that reporting CFs may change the course of the disease or prolong survival, especially in the case of metastatic cancers or pathologies with an unpredictable natural history. The risk of undesirable effects carried by additional procedures, such as contrast medium-induced complications or the lifetime risk of ionizing radiation exposure-related cancer, must be kept in mind as well. This hinders the development of a widely accepted approach to such findings^[36]. As a consequence, there is still disagreement about the appropriateness of reviewing and reporting extra-cardiac CFs during cardiac CT studies^[37,38].

Once a CF is reported, there is also uncertainty about the decision to follow-up such findings over time. Some CFs are promptly deemed insignificant, that is, they do not require any additional examination. The dilemma about CFs follow-up arises when so-called “clinically significant collateral findings” are detected. While the anxiety for medico-legal implications from underreporting incidental findings would lead to describe and follow-up any lesion that is found in the FOV, some concern has been raised about increased financial burden in front of

Table 1 Studies about collateral findings detected at cardiac computed tomography performed for atrial fibrillation ablation

Ref.	n of pts	Mean age (yr)	Smoking history	Scanner	FOV	Collateral Findings, n (% of patients)	Cardiac (n)	Extra pulmonary (n)	Clinically significant	Malignancies
Wissner <i>et al</i> ^[30]	95	62 ± 10	45 %	16- and 64-slice	Above clavicle to diaphragm	83 (53 %)	5	46	16 % of patients	1 (1.1 %)
Sohns <i>et al</i> ^[31]	158	NR	NR	64-slice	Supraaortic region to the heart base and upper abdomen	198 (72 %)	NR	47	31 % of patients	2 (1.3 %)
Sohns <i>et al</i> ^[32]	224	64 ± 10	38 %	64-slice	Supraaortic region to the heart base and upper abdomen	1343	724	77	32 % of extracardiac findings	2 (0.9 %)
Schietinger <i>et al</i> ^[33]	149	55.9 ± 11	47 %	16-slice	Aortic arch to diaphragm	110 (69 %)	NR	70	24 % of patients	0 (0 %)
Martins <i>et al</i> ^[34]	250	55.2 ± 9.6	NR	64-slice	20-25 cm centered on the heart	58 (23 %)	3	38	NR	2 (0.8 %)
Casella <i>et al</i> ^[35]	173	59 ± 10	50 %	64-slice	Carina to diaphragmatic domes	164 (56 %)	14	74	33 % of patients	3 (1.7 %)

FOV: Field of view; NR: Not reported.

an unclear benefit while pursuing this strategy.

American guidelines on coronary artery imaging recommend a systematical review of extracardiac structures within the FOV during a CT scan, especially when risk factors for cancer exist^[39]. Missing a malignant cancer, especially in a potentially curable stage, would have deleterious consequences for the patient, as well as potential medico-legal implications for the radiologist. The Fleischner Society and the American College of Radiology provided some recommendations about how to manage incidentally detected small pulmonary nodules^[40] and abdominal incidentalomas^[41].

The Early Lung Cancer Action Project evaluated 1000 asymptomatic smokers aged at least 60 years, finding pulmonary nodules in 23% of the patients; 12% of these patients with noncalcified pulmonary nodules had lung malignancies, which were mostly non detectable on chest radiography^[42].

Nevertheless, it is still unclear whether the strategy of examining the entire FOV and reporting all CFs would be beneficial for the patients' clinical outcome. In fact, reporting all CFs translates into additional follow-up with potential further radiation exposure, increased costs and patients' anxiety, and sometimes, invasive procedures are needed in order to complete the follow-up. Most of those CFs are eventually found to be benign and have little or no clinical influence on patients' health. A large study provided a cost analysis of following-up such findings after CT scan for the screening of coronary heart disease^[37]. Among 966 patients, 41.5% had extracardiac CFs. Additional diagnostic examinations required extra costs of 83.035 United States dollars. The authors concluded that reporting CFs did not provide a clear mortality benefit because CFs were not an independent predictor of noncardiac death. However, the authors did not report whether patients with a diagnosis of malignancy received life-saving or life-prolonging interventions, therefore it is not advisable to draw conclusions about difference in mortality between patients with and without CFs. Moreover, they used a too short mean follow-up (18 mo) to evaluate the course of potentially slow-progressing diseases. Sohns *et al*^[32] estimated additional costs as high as about 42.543 United States dollars (190 United States dollars per patient) for subsequent diagnostic examinations (excluding invasive procedures) of incidentally detected extra-cardiac findings at cardiac CT before AF ablation. A clear clinical benefit was achieved in 1.1 % of patients, however the authors did not attempt to investigate the potential clinical implications of such strategy.

Larger studies are warranted to understand the real impact on patients' outcome of CFs follow-up. In particular, a study randomizing patients with CFs to either further investigations or no follow-up would answer this question, if ethically viable.

In our opinion, on the basis of the potential detection of early stage cancers, until large studies analyze the cost-benefit ratio of such approach in a real-world scenario, the full set of abnormalities that are visible in the entire FOV should be reported, for ethical reasons. Obviously, once CFs are reported, smoking history, previous cancer, presence of first-degree relatives with history of cancer, or other known risk factors should be taken into account in the decision-making process of further follow-up.

CONCLUSION

The large number of cardiac CT performed for AF catheter ablation and the improved spatial resolution of modern CT scanners generates a huge number of serendipitously

detected collateral findings (mostly extracardiac). Collateral findings are very frequently detected during cardiac CT studies, and a consistent proportion of them may require further investigations or follow-up. The optimal strategy to manage CFs is still debated, since most CFs are eventually found to be benign at the end of a diagnostic process which implies an increased financial burden and, in some cases, even some clinical risks for the patient. Moreover, a real clinical benefit of incidentally detecting malignant diseases has not been demonstrated. However, the risk of missing an early stage malignant disease should be considered while deciding whether reporting and following-up CFs or not. Almost all the studies published so far reported some malignant cancers, which could be treated after being serendipitously diagnosed by cardiac CT. We therefore advise a thorough inspection of the entire irradiated FOV, as well as a strict cooperation between cardiologists and radiologists for a comprehensive examination of cardiac CTs, in order to avoid missing important diseases in the examined FOV.

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