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Prevalence and clinical significance of collateral findings detected by chest computed tomography in patients undergoing atrial fibrillation ablation

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Aims Chest computed tomography (CT) scanning is increasingly used as an imaging technique in patients undergoing atrial fibrillation (AF) catheter ablation. Chest CT scans visualize organs other than the heart and collateral findings may be identified incidentally. Our study aims to assess the prevalence and clinical relevance of such collateral findings in patients undergoing AF ablation.

Methods and results One hundred and seventy-three patients (127 males, age 59 ± 10 years) underwent chest CT scan for image integration in AF ablation. Collateral findings from visualized thoracic and upper abdominal organs were collected. Findings that required further investigations or treatment according to current guidelines were considered as clinically significant. A total of 164 collateral findings were identified in 97 (56%) patients, and most patients showed abnormalities of the lungs (67 patients, 39%). Forty-nine (28%) patients had clinically significant findings needing further investigation and 17 (10%) of them required specific treatments, including three cases (1.7 %) of lung malignancy.

Conclusions Chest CT images acquired for integration in AF ablation should be read thoroughly as they may serve as a screening tool for otherwise unrecognized clinically significant conditions of the heart, lungs, or other visualized organs.

Keywords Collateral findings • Incidental findings • Chest computed tomography • Image integration • Atrial fibrillation ablation

Introduction

Atrial fibrillation (AF) is the most common clinically significant cardiac arrhythmia; it carries significant morbidity and mortality, and directs the allocation of sizeable health care resources.[1] According to the current ACCF/AHA/HRS guidelines for AF management,[2] catheter ablation is increasingly used as a therapeutic approach in patients with symptomatic drug-refractory AF.

Atrial fibrillation catheter ablation has undergone considerable technical evolution over the past decade.[3,4] The integration of three-dimensional (3D) electroanatomical mapping systems with pre-acquired images of cardiac anatomy is recognized as a major advancement in the AF ablation technique.[5]

Both computed tomography (CT) and magnetic resonance imaging (MRI) have been employed in this context,[6] as they provide an accurate imaging of pulmonary vein (PV) and left atrial (LA) anatomy with excellent spatial resolution, supplying the necessary anatomic information for successful ablation.

In comparing these techniques, it should be emphasized that multi-slice CT angiography has become a standard non-invasive

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imaging technique to visualize vascular and cardiac anatomy.[7] Moreover, CT is surely more widely available than MRI and is preferred in the evaluation of such structures as the pulmonary parenchyma, mediastinum, and upper abdomen.

The growing number of chest CT scans performed to diagnose coronary artery disease has led to a steep increase in the identification of so-called incidental or collateral findings,[8–15] broadly defined as any finding that is unsuspected or unrelated to the clinical indication for imaging. Some of these findings may explain elements of the patient's clinical presentation, whereas others may reveal subclinical malignant disease, or even remain indeterminate and require further investigation or follow-up.

To date, no systematic data have been published on the prevalence and clinical implications of collateral findings in patients undergoing contrast-enhanced chest CT scan for image integration with electroanatomical mapping in view of an AF catheter ablation procedure. The aim of our study is to assess the prevalence and distribution of clinically significant collateral findings in such patients and to evaluate the impact of those findings on the further clinical management and prognosis of the study population.

Methods

Study population

We enrolled 173 consecutive patients in apparently good health except for AF, who were referred to the Centro Cardiologico Monzino (Milan, Italy) between November 2009 and June 2010 to undergo catheter ablation of AF. All patients had symptomatic documented AF which had proven refractory to at least two anti-arrhythmic drugs. With the intent of estimating the risk for bronchogenic carcinoma, particular attention has been paid to cigarette smoking habit. We defined as 'former smokers' patients who had quit smoking >5 years before the date of enrolment.

Within 24 h prior to the ablation procedure, all patients underwent a transoesophageal echocardiogram to rule out the presence of thrombi in the LA or left atrial appendage (LAA) and a chest CT scan to allow image integration for AF ablation. All patients had provided written informed consent to transoesophageal echocardiogram, contrast-enhanced CT scan, and AF catheter ablation.

Computed tomography scan

Data acquisition

Chest CT angiography scans were acquired using a 64-slice multidetector CT scanner (GE-Lightspeed, General Electric, Milwaukee, WI, USA), with a field of view (FOV) which extended in the *z*-axis from the level of the carina to the diaphragmatic domes. A systematic search of any collateral finding was performed in the FOV. Since a consistent proportion of the patients were in AF at the moment of the exam, CT scan was not synchronized with electrocardiogram (ECG). It was acquired with a slice thickness of 0.625 mm and a slice interval of 0.625 mm. Contrast medium administration consisted of 80–100 mL of 400 mgI/mL agent (Iomeron, Bracco, Milan, Italy) injected through the antecubital vein at 5 mL/s followed by 60 mL of saline chaser using a dual-syringe automatic injector (Stellant, MedRad, Pittsburg, PA, USA). Scan synchronization with contrast material was performed with the bolus tracking technique (SMART PREP, GE, Milwaukee, WI, USA).

Image analysis

All images were transferred to an Advantage Windows workstation (GE Healthcare, Milwaukee, WI, USA) and reviewed by two experienced radiologists. Images were displayed in the original two-dimensional (2D) format in the mediastinal windows (400 W/4°C) and in the 3D or 2D multi-planar reconstruction views. Computed tomography data were recorded onto a CD-ROM in a Digital Imaging and COmmunications in Medicine (DICOM) format, using a soft tissue algorithm.

A first dataset was reconstructed with a small FOV tightly confined around the heart. Thus, images from the contrast-enhanced CT angiography scan were analysed to answer the clinical issue, that is, to evaluate the LA–PV anatomy. A second dataset was then reconstructed with a larger FOV (from the level of the carina through the diaphragmatic domes) and the whole CT scan was analysed to search for cardiac and extra-cardiac abnormalities, such as undetermined nodules, suspected tumours, inflammatory diseases, infections, degenerative, and vascular lesions in the pulmonary parenchyma, mediastinum, breasts, or in the upper abdomen. The presence of collateral findings was investigated by the two radiologists through the original 2D axial images displayed in the mediastinal windows (400 W/4°C), lung windows (1700 W/−50°C), bone windows (2500 W/50°C), and liver windows (200 W/10°C).

Analysis and management of collateral findings

Collateral findings were identified in the chest and upper abdomen. We defined as clinically significant all lesions deemed to require any further medical investigation or follow-up according to current guidelines and consensus papers,[16–18] along with findings that were judged to be important to recognize (such as vascular abnormalities). Non-pulmonary collateral findings were followed up, if indicated, with the appropriate first-line methods, such as ultrasound for kidney and liver lesions, mammography or ultrasound for breast nodules, echocardiography for pericardial effusions, CT angiography for thoracic aortic aneurysms, and so on.

Regarding pulmonary parenchymal lesions, we followed the recommendations from the Fleishner Society[16] to establish if any further investigation was required. In particular, if no previous studies existed to document 2-year stability, a single follow-up chest CT scan was performed at 12 months for lesions <4 mm in diameter only in high-risk subjects (patients with smoking history, previous cancer, first-degree relatives with history of cancer, or other known risk factors). Nodules >8 mm in size were followed up with CT scan at ∼3, 9, and 24 months, or other investigations were performed if appropriate, such as positron-emission tomography (PET), PET-CT, bronchoscopy, or biopsy. Nodules in the 5–8 mm range were managed according to their morphology and patient risk factors, as stated by current guidelines.[16] Moreover, features characteristically associated with benign nodules, such as fat attenuation and diffuse, central, or lamellated calcifications, were also taken into account in order to spare the patient unnecessary radiation exposure from multiple follow-up studies.

Statistical analysis

All variables are reported as mean ± standard deviation. Continuous variables were compared with either Student's *t*-test or the Wilcoxon rank-sum test. Qualitative variables are presented as numbers and proportions and were compared using Fisher's exact test. All *P* values were two sided, and statistical significance was established at $P < 0.05$.

Results

Study population

Table 1 lists the demographic and clinical features of the 173 consecutive patients we enrolled (127 males; mean age 59 ± 10 years). Of these, 112 (65%) had paroxysmal AF, while 61 (35%) had long-standing/persistent AF. At the time of the procedure, 19 (11%) patients were active smokers, 67 (39%) were former smokers, and the remaining 87 (50.3%) patients were non-smokers.

Collateral findings and their impact

All patients successfully underwent contrast-enhanced CT scan without complications. We detected 164 collateral findings in 97 patients (56%). The mean follow-up of the study was 17 ± 5 months. We identified as clinically significant 72 findings in 57 patients (33% of the total population, 59% of the population with collateral findings); of the 173 patients, 49 patients (28%) underwent further investigations and in 17 (10%) this led to therapeutic decisions. Diagnostic work-up included 50 CT scans, 16 ultrasound studies, 3 conventional radiographs, 3 mammographies, 4 MRI studies, 7 PET-CT scans, 5 bronchoscopies with transbronchial biopsy, and 10 provocative cardiac exercise tests. *Table 2* presents the location of incidental findings and *Table 3* summarizes clinically significant findings with the additional work-up and therapeutic consequences they implied.

The additional time spent by the radiologists for the study of collateral findings consisted of a mean of 7 ± 3 min: 2 ± 1 min were needed to reconstruct the second dataset of the chest CT with a larger FOV, while 5 ± 2 min were involved in reading the whole CT to look for all the collateral findings.

On the basis of CT findings, we decided not to proceed with AF ablation in one patient due to a diagnosis of lung cancer, in one patient with inter-atrial shunt, and in six patients due to pneumonia. The procedure was instead merely postponed during the same hospital stay in 10 patients who required provocative tests for suspected myocardial ischaemia. All other patients (90%) underwent a successful AF catheter ablation at the scheduled time.

Table 1 Demographic and clinical characteristics of the patient population

Patients	173 (100)
Age (years)	59 ± 10
Male gender	127 (74%)
Arterial hypertension	84 (49%)
Diabetes mellitus	7 (4%)
Smokers, current	19 (11%)
Smokers, former	67 (39%)
Atrial fibrillation, paroxysmal	112 (65%)
Atrial fibrillation, persistent/long-standing	61 (35%)

Values are *n* (%) or mean ± standard deviation.

Pulmonary collateral findings

Pulmonary abnormalities were found in 67 of 173 patients (39%); 39 (58%) lesions were identified as clinically significant. These included six patients with pneumonic consolidations requiring antibiotics and follow-up with CT or chest X-rays.

A nodule >8 mm in size was found in three patients, in two of whom further investigations (PET-CT, follow-up CT) showed substantial 2-year stability and ruled out malignancy. In the remaining one patient (0.6%), however, the nodule was accompanied by satellite lymphadenopathy and PET-CT, bronchoscopy, and biopsy led to a diagnosis of bronchogenic carcinoma ($T_1N_2M_0$), which was treated surgically (*Figure 1*).

A total of 26 nodules ranging 5–8 mm in size were found in 23 patients (13%). Of these, 8 patients required no further investigation (3 because of previously documented 2-year stability,

Table 2 Organs and structures with collateral findings

Organ/apparatus	Structure	Findings	*n*
Cardiovascular system	Pericardium	Effusion	3
	Coronary arteries	Calcifications	10
	Thoracic aorta	Dilatation	4
	Inter-atrial septum	Inter-atrial shunt and pulmonary vein anomalous connection	1
	Great vessels	Common origin of brachiocephalic trunk and left common carotid artery	1
Lung		Nodules ≤4 mm	29
		Nodules 5–8 mm	26
		Nodules >8 mm	3
		Emphysema/bullae	3
		Hamartomas	3
		Atelectasis	2
		Inflammatory consolidations	4
Airways	Bronchi	Bronchiectasis	4
Pleura		Focal thickening	6
Mediastinum	Lymph nodes	Swelling	23
	Thymus	Thymic remnants	3
Breast		Nodules	3
Spinal column		Vertebral fracture	4
		Haemangiomas	1
		Osteoarthritis	4
Abdomen	Liver	Steatosis	5
		Cysts	5
		Haemangiomas	3
		Focal lesions	3
		Parenchymal calcifications	2
	Kidney	Cysts	5
	Gall bladder	Cholelithiasis	3
	Spleen	Calcifications	1
Total			164

Table 3 Clinically significant collateral findings and their diagnostic/therapeutic consequences

Clinically significant collateral findings	*n*	Findings needing investigations	Type of investigation	Findings needing treatment	Treatment description
Pericardial effusions	3	3	Ultrasound	4	Anti-inflammatory drugs
Coronary calcifications	10	10	Exercise testing	0	
Thoracic aorta dilation	2	2	CT	0	
Inter-atrial shunt and pulmonary vein anomalous connection	1	0		1	Cardiac surgery
Common origin of brachiocephalic trunk and left common carotid artery	1	0		0	
Pulmonary nodules ≤4 mm	4	2	CT	0	
Pulmonary nodules 5–8 mm	26	15	CT, PET-CT, bronchoscopy, biopsy	2	Surgical excision
				2	Antibiotic therapy
Pulmonary nodules >8 mm	3	3	CT, PET-CT, bronchoscopy, biopsy	1	Surgical excision
Pulmonary inflammatory consolidations	6	6	CT, chest X-rays	6	Antibiotic therapy
Hepatic cysts	2	2	Ultrasound	0	
Hepatic haemangiomas	3	3	Ultrasound	0	
Hepatic focal lesions	3	3	Ultrasound	0	
Hepatic calcifications	1	1	Ultrasound	0	
Breast nodules	3	3	Mammography, ultrasound	0	
Vertebral fractures	4	4	MRI	2	Orthopaedic corset
Total	72	58		17	

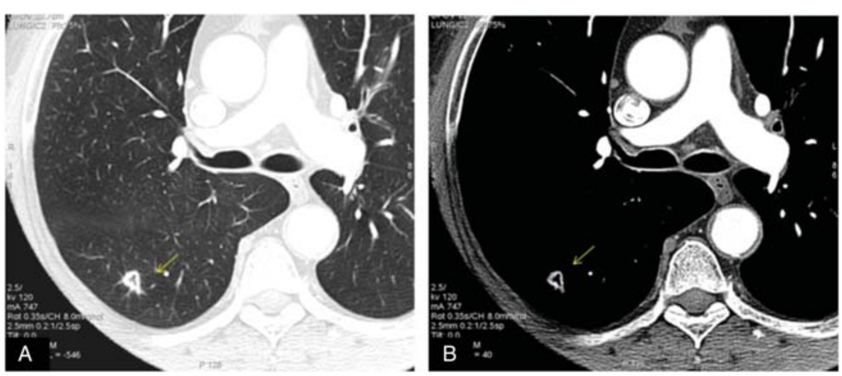

Figure 1 Computed tomography axial windows lung image (*A*) showed irregular, speculated solitary pulmonary nodule (size 9 mm) with central cavitation in the right lower lobe (yellow arrow). The mediastinum windows image (*B*) confirmed the presence of central cavitation. These findings are suspected for malignant nature of the nodule. Three-month follow-up showed the nodule growing and computed tomography-positron-emission tomography confirmed later the malignant nature of the lesion.

5 because of a benign pattern of calcification), while in the other 15 follow-up CT showed nodule stability in 9 patients and nodule change in 6 patients. Of these six, in two patients a diagnosis of pneumonia was established because of nodule growth, development of new densities, and air bronchogram sign; the remaining four underwent PET-CT and bronchoscopy-guided biopsy, so that bronchogenic carcinoma was ruled out in two patients and confirmed by subsequent surgery in the last two.

Nodules ≤4 mm in size were considered as clinically significant in four patients with a history of smoking; of these, two required no further investigation because of previously documented 2-year stability, while in the other two follow-up CT showed nodule stability too.

A total of five lung nodules (three in the 5–8 mm range, two in the ≤ 4 mm in size) were detected in five patients who already had such lesions documented at previous CT studies; in these patients, the chest CT performed for AF ablation allowed us to establish 2-year stability of the nodules and was considered as a follow-up CT, thus sparing the patients further investigations.

Taking smoking habit into consideration, 42 of 58 (72%) nodules were detected in smokers or former smokers and 16 of 58 (28%) in non-smoking patients ($P = 0.01$). Nodules that required follow-up because they were ≥5 mm in size were also significantly more frequent in smokers or former smokers (22 of 29, 76%) compared with non-smokers (7 of 29, 24%) ($P \leq 0.001$).

Extra-pulmonary thoracic collateral findings

Extra-pulmonary thoracic collateral findings were observed in 21 of 173 patients (12%) and were all judged as not clinically significant. They included 6 cases of focal pleural thickening, 4 bronchiectasis, 3 thymic remnants, and 26 swollen lymph nodes, all of which were calcified and <1 cm in diameter.

Breast collateral findings

In three women (7% of the female study population) breast nodules were detected, none of which showed signs of malignancy on mammography and ultrasound. These women continued their follow-up in specialized centres.

Cardiovascular collateral findings

Cardiovascular collateral findings were observed in 19 of 173 patients (11%). Evaluation of coronary anatomy requires ECG synchronization and was therefore possible only in 106 patients (61%) who were in sinus rhythm at the time of CT. In 10 patients CT showed coronary calcification of one or two arteries; all patients underwent a provocative exercise test that excluded stress-induced myocardial ischaemia. Four patients had a dilated thoracic aorta: in two cases the diameter was <4 cm, and no further investigation was deemed necessary, whereas in the other two it was still <5.5 cm and stable on follow-up CT angiography, so that there was no indication to surgery. Three pericardial effusions were treated with anti-inflammatory drugs and shown to have regressed on follow-up echocardiography. A case of inter-atrial shunt and anomalous connection of right superior PV into right atrium was detected; this patient required surgery correction (*Figure 2*). A common origin of the brachiocephalic trunk and left common carotid artery was also detected. Cardiac or aortic features that had already been observed by transoesophageal echocardiogram were not considered as CT incidental collateral findings.

Abdominal collateral findings

Abdominal collateral findings were observed in 27 of 173 patients (16%). The most frequent were liver abnormalities: focal lesions in three patients, haemangioma in three, cysts in five, steatosis in five, and parenchymal calcification in two (*Figure 3*). Nine of these findings required further evaluation with ultrasound. In the three patients with focal lesions ultrasound examination confirmed the lesions as cysts in two patients and as haemangioma in one case. Haemangioma and cysts detected on CT were confirmed by ultrasound. A parenchymal calcification was eventually found to be a haemangioma. All other hepatic lesions, as well as the incidental findings identified in abdominal organs other than the liver, were not clinically significant.

Spinal column collateral findings

Spinal column lesions were discovered in 9 of 173 patients (5%). Of these, four were vertebral fractures, which STIR MRI sequences identified as chronic in two cases (requiring no further action) and recent in the other two. The latter were treated with orthopaedic corset for fracture stabilization.

Discussion

The main result of our study is that contrast-enhanced chest CT imaging allowed detecting clinically significant collateral findings in

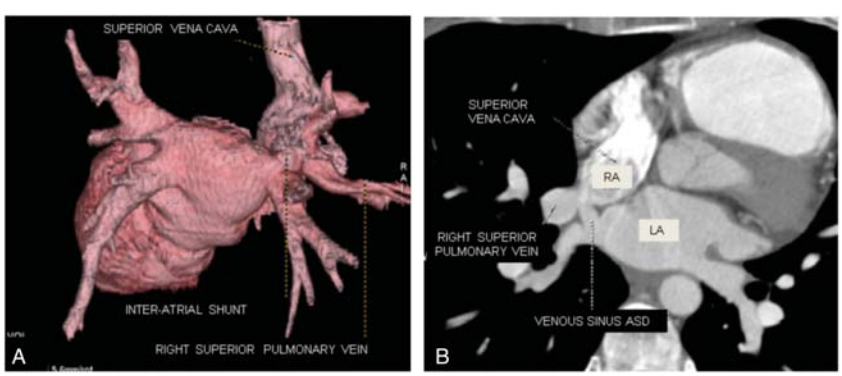

Figure 2 Computed tomography volume rendering reconstruction (*A*) of left atrium, pulmonary veins, and superior vena cava, showing the presence of inter-atrial shunt and anomalous connection of right superior pulmonary vein into right atrium. Multi-planar reconstruction (*B*) confirmed the presence of inter-atrial shunt consistent with venous sinus atrial septal defect and the anomalous connection of superior pulmonary vein into right atrium close to the superior vena cava ostium. ASD, atrial septal defect; LA, left atrium; RA, right atrium.

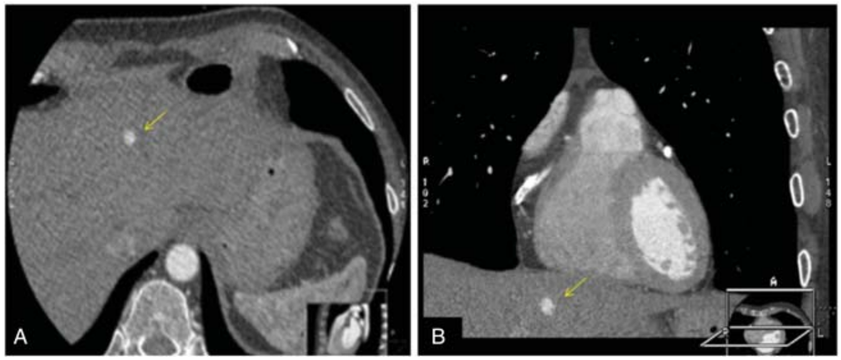

Figure 3 The multi-planar imaging (*A* and *B*) showed a liver focal enhancement (size 5 mm) suspected for angioma (yellow arrow) in segment 4 of the right lobe. The focal lesion was later evaluated with ultrasound, confirming the nature and the localization of the lesion.

about one-third of patients in 'apparently' good health. Of note, in 1.7% of cases, the detection of a collateral finding allowed early diagnosis and treatment of a potentially life-threatening condition such as lung cancer.

Computed tomography studies of the heart are being performed with increasing frequency as the preferred imaging method to plan and perform AF catheter ablation,[5,6,19] but while this entails irradiation of almost the entire chest, only a small FOV focused on the heart is routinely analysed in some detail. However, a larger FOV can be reconstructed from the raw data subjecting the patient to no additional radiation; in this way plenty of information on the pulmonary parenchyma, mediastinum, breasts, spine, and upper abdomen becomes available. A crucial element is the likelihood of collateral findings in these organs and controversies abound as to whether the lungs and chest should be formally reviewed.[20,21]

Several studies elucidated the prevalence of non-cardiac abnormalities in cardiac CT studies, almost exclusively performed for the diagnosis of coronary artery disease.[8–15] Recently, Cademartiri *et al.*[22] in a population of 670 patients undergoing CT scan for suspected coronary artery disease, described collateral findings in 79.4% of patients. Among these findings, 26.9% were classified as non-significant, 66.5% as mild, and 6.6% as compulsory for study; in 12.1% of patients' non-cardiac findings required additional clinical or radiological follow-up. In an another study, Onuma *et al.*[9] reported that 23% of patients had extra-cardiac disease requiring additional work-up, and four cases (0.8%) of malignancy were revealed. Similar previously published studies were carried out on electron beam CT examinations. Horton *et al.*[23] reviewed the scans performed with a small FOV including just a portion of the chest, therefore resulting in a 7.8% rate only of significant findings. In another study by Hunold *et al.*[24] 53% of the study subjects had extra-coronary abnormal findings, but analysis was limited to the mediastinal windows, therefore discarding any possible evidence on pulmonary parenchymal nodules. In summary, the proportion of patients with at least one imaging abnormality requiring further investigation or follow-up varies widely among different studies, but, rather homogeneously, almost half of all collateral findings consisted of suspect pulmonary nodules. Malignancy is revealed in a percentage ranging from 0.2 to 1% of patients.[10,22]

These data are corroborated by our study: over a 17 ± 5 month follow-up we investigated 173 patients, of whom 94 showed collateral findings. Thirty-three per cent of the patients had clinically significant findings, often needing additional work-up and, in three patients, previously undiscovered early-stage bronchogenic carcinoma was diagnosed. In comparison with the relevant literature, in our population a higher incidence (1.7%) of malignancy was observed. This feature is particularly significant if we consider that such an incidental finding has been reported to improve the 10-year survival rate in the 2006 paper by the Early Lung Cancer Action Program Investigators dealing with patients with stage I lung cancer detected on CT screening.[25] The higher prevalence of malignancy in our population is probably due to a systematic analysis of almost all pulmonary parenchyma, including lateral lung fields, which are often excluded from routine cardiac CT scanning.

We discovered no case of ischaemic heart disease in our study, even though it is well known that AF is associated with various cardiovascular diseases, including coronary artery disease.[4] While we observed 10 cases of significant coronary calcifications on CT, a provocative exercise test excluded inducible myocardial ischaemia in all patients. This result might be explained by the fact that a detailed history was collected before considering AF catheter ablation in order to exclude all possible secondary causes of AF as well as relevant co-morbidities. Also, coronary CT imaging is infeasible in patients who are not in sinus rhythm.

Regarding the secondary end-point of our study, incidental findings on the preliminary chest CT scan led us to postpone AF ablation during the same hospital stay in 10 patients and convinced us not to go ahead with the procedure in 8 patients. We should also remark that in no patient CT found intra-atrial thrombosis (a clear indication to postpone ablation), as it was reasonably expected considering that all patients underwent a preliminary transoesophageal echocardiogram to rule out the presence of thrombi in the LA or LAA before CT scanning. Even if transoesophageal echocardiogram may be considered not strictly necessary in patients undergoing cardiac CT scanning, it should be stressed that studies comparing these two techniques are not conclusive and that transoesophageal echocardiogram is nowadays a robust gold standard which, at the moment, cannot be replaced by CT scan.[26]

On the other hand, CT scan is universally considered the gold standard for the visualization of adjacent intra-thoracic structures and vessels[7] and the incidental detection of subclinical organ disease is, as mentioned above, a growing issue.[8–15,22] In the work of Lacomis *et al*.[7] a direct comparison of CT and MRI for characterization of the posterior LA wall suggested that the techniques provided comparable image quality and information but, notably, a suspect pulmonary nodule was identified only by CT scan. Magnetic resonance imaging equipment is surely less widely available than CT equipment, even when considering the most recent CT technology, and MRI is sometimes poorly tolerated by patients, primarily due to the duration and confinement associated with the exam.

One last consideration regarding the likelihood of collateral findings needs to be discussed. When engaging a diagnostic work-up, the risk of unwanted effects carried by each procedure must be taken into account. In this particular case, contrast medium-induced complications (immune-mediated reactions, contrast-induced nephropathy), as well as the lifetime attributable risk of cancer related to exposure to ionizing radiation, represent the main counterpart of diagnosing otherwise unrecognized conditions. For that reason, a risk/benefit analysis on a large population, which takes into account the amount of follow-up examinations required for patients with clinically significant collateral findings, would be worthwhile.

Limitations

We recognize that our study has some obvious limitations. First, the duration of clinical follow-up was relatively short at 17 ± 5 months. As the standard approach to make certain that a low-risk pulmonary nodule is benign is to follow it up to demonstrate stability over at least 2 years, a shorter follow-up time might have led us to underestimate the significance of such extra-cardiac findings. Also, prognostic significance has only been determined indirectly by considering the advantage of an early diagnosis of lung cancer, since the long-time mortality and adverse event rate have not been investigated.

Secondly, technical limitations might have prevented visualization of some clinically relevant collateral findings. For example, because the FOV extended from the diaphragmatic domes to the carina, the pulmonary apexes were left out.

We also recognize that a cost/efficacy analysis was not performed in the present study.

Conclusions

The use of chest CT for image integration in AF ablation may act as a screening tool for otherwise unrecognized clinically significant conditions of the heart, lungs, and other visualized organs. These collateral findings may provide important and potentially decisive information for the clinical management of patients and their survival. For this reason, reading radiologists should interpret chest CT scans for image integration in AF ablation extensively, rather than just in reference to the electrophysiological procedure, as this may avoid delays in the diagnosis and treatment of potentially curable life-threatening diseases.

Conflict of interest: C.T. has served as a member of the advisory board of Biosense Webster and has been a consultant for, and received lecture fees from, St Jude Medical. A.N. has received compensation for belonging to the speakers' bureau for St Jude Medical, Boston Scientific, Medtronic, and Biosense Webster and has received a research grant from St Jude Medical. A.N. is also a consultant for Biosense Webster. L.D.B. is a consultant for Hansen Medical and Biosense Webster. The other authors declare no significant relationships with industry.

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