REVIEW ARTICLE

Non-coronary Applications of Cardiac Computed Tomography

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SUMMARY

Multidetector row computed tomography coronary angiography (MDCTCA) has been incorporated in the diagnostic algorithm of patients suspected of coronary artery disease due to its significant negative predictive value. In addition, due to volume acquisition and ECG-cardiac gating, the MDCTCA can simultaneously perform submillimeter reconstructions in all possible angles and at different time positions within the cardiac cycle. This produces a favorable scenario for functional and morphological evaluation, and offers a wide range of possible noncoronary applications; most of them can be evaluated during the study of coronary arteries without requiring additional radiation or contrast agents. The ability of the method for simultaneous evaluation of morphology and function allows a comprehensive approach to a broad spectrum of conditions within the same study.

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Key words > Diagnostic imaging – Perfusion – Viability – Tomography – Ventricular function

Over the past five years, multidetector row computed tomography coronary angiography (MDCTCA) has positioned as a non-invasive diagnostic method to conventional coronary angiography (CAG), particularly in patients with intermediate pretest probability. Multicenter trials have shown not only the high diagnostic accuracy of MDCTCA for detecting coronary artery stenosis but also a performance similar to that of CAG to predict revascularization.1,2 Its high diagnostic accuracy and its almost 100% negative predictive value have led to include MDCTCA in the diagnostic algorithm of patients with suspected coronary artery disease.

In paralell, due to volume acquisition and ECG-cardiac gating, the MDCTCA can perform submillimeter reconstructions in all possible angles and at different time positions within the cardiac cycle. This produces a favorable scenario for functional and morphological evaluation, and offers a wide range of possible noncoronary applications.3,4 Besides, the kinetics of iodinated contrast is similar to that observed with paramagnetic contrasts (gadolinium) in magnetic resonance imaging (MRI), allowing the evaluation of perfusion and myocardial viability.5-7

This article discusses the noncoronary applications of cardiac MDCT that can be performed during the same conventional acquisiton of coronary arteries and without increasing the dose of effective radiation or contrast volume (Table 1).

Global and segmental ventricular function

The acquisition through retrospective ECG-cardiac gating allows for accurate assessment of myocardial function. Volume calculation is usually performed using the Simpson's method, after the manual tracing of endocardial borders. Thus, ejection fraction, end-diastolic and end-systolic volumes, and myocardial mass can be estimated and are quite consistent with MRI, which is the reference standard.8,9 Moreover, there is an excellent correlation between cardiac MDCT and two-dimensional echocardiography for regional wall motion assessment, with 96% of similar segment classification, corresponding to a kappa of 0.82 (Figure 1).[10]

The feasibility to perform functional assessment with a significant reduction of effective radiation dose should be emphasized, which is not detrimental to quality. This is possible by using an acquisition technique through retrospective ECG-cardiac gating with tube modulation, which significantly lowers the effective radiation dose by reducing the exposure out of the optimal diastolic window (used for the assessment of coronary arteries) (see Table 1).11

Characterization of myocardial infarction, perfusion at rest, and myocardial viability

For several decades, myocardial perfusion images are considered the reference standard for prognosis and decision making in patients with coronary artery disease.12 Over the past 30 years, myocardial perfusion has been a territory dominated by single photon emission computed tomography (SPECT), a fact supported by strong evidence; this is an indication that prognosis is related to the presence of ischemia induced by stress or drugs.13-15 However, there are limitations inherent to these methods, such as radiation dose, the limited availability of PET

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and the attenuation devices.13 More recently, the study of myocardial perfusion with cardiac MRI was rapidly imposed as a highly accurate method for the assessment of ischemia, with results equivalent to those of SPECT.16-19

In myocardial infarction, as a result of microvascular obstruction and capillary density reduction, the images obtained during the passage of the contrast agent (gadolinium) through the left ventricle show hypodense areas corresponding to infarcted regions due to the delayed arrival of the contrast agent at the infarct core. Similarly, by increasing the volume of distribution and the contrast washout time, infarcted regions present a characteristic delayed contrast enhancement.16-19 One of the main features of MRI is that it enables to differentiate between transmural and subendocardial infarctions, being transmurality a determining factor in predicting functional recovery.20

The field of MDCTCA encouraged the research for noncoronary applications of this method. One of the biggest arguments against this technique has been that assessment is purely anatomical, even though great effort has been made to overcome such limitation by concomitant assessment of myocardial perfusion.5,7,21-25 The pathophysiologic support of this concept is similar to that of MRI gadolinium dye, because both contrast media have similar kinetics. Therefore, there is a conceptual congruency between the methods regarding the assessment of myocardial viability and perfusion.

Several ex vivo and in vivo studies have validated the use of cardiac MDCT for myocardial viability and perfusion assessment. In short, since images are acquired when the contrast agent is passing through the left ventricle, hypoperfused areas present a typical hypoattenuation, which enables the measurement of Hounsfield units in infarcted and remote myocardium. Besides, increased volume of distribution causes delay in contrast washout, producing delayed enhancement of the infarcted area (Figure 2).7,21-27 Both patterns are highly reproducible and have been widely validated in studies on animals and in clinical trials, showing good correlation with the SPECT and MRI, even though the contrast-noise ratio is significantly better with the second one.28

The ability to differentiate between dysfunctional but viable myocardium and necrotic myocardium has important clinical implications, both in prognosis

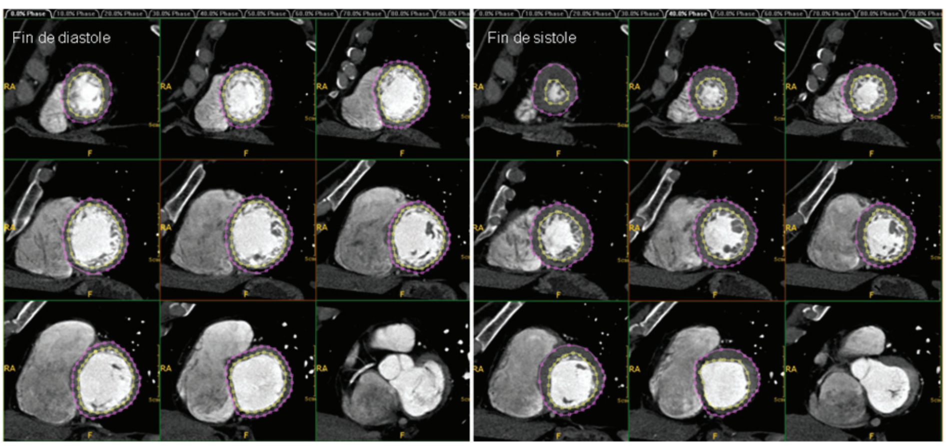

Fig. 1. Regional wall motion assessment [short axis from base to tip, at end of diastole (left) and end of systole (right)], showing akinesia and significant reduction of inferobasal thickening. Assessment of volumes, ejection fraction and myocardial mass.

Table 1. Noncoronary applications of cardiac MDCT during the same study of coronary arteries with retrospective (radiation throughout the cardiac cycle) and prospective (selective end-diastolic radiation only) ECG- cardiac gating.

ECG-cardiac gating:	Retrospective	Prospective
Assessment of coronary arteries	X	X
Ventricular morphology and function8-10	X	O
Rest myocardial perfusion5,7,21-25	X	X
Stress myocardial perfusion* 5,39-40	X	X
Assessment of sequelae of infarction21-27,29,30	X	X
Late contrast enhancement (viability)** 7,21-27	X	X
Detection of masses and sources of embolism30,62,64,65	X	X
Congenital heart diseases69-71	X	-
Assessment of pericardium72-73	X	X
Assessment of valvular heart diseases42-51	X	O
Assessment of pulmonary veins59	X	X
Evaluación de seno coronario y venas coronarias52-54,68	X	X

* Study feasible by the additional administration of contrast agent.40
** Study feasible by additional scanning.

and in determining the most appropriate treatment. A clinical application emerging from the delayed enhancement MDCT is the early assessment of myocardial viability immediately after primary angioplasty (PCTA). A recent trial developed this concept in patients with STEMI, in which cardiac MDCT was performed immediately after a PCTA without administration of contrast agent; the study showed that half of the patients had delayed myocardial enhancement, even though the objectives of door-to-balloon time and the optimal epicardial result (TIMI 3) were achieved. Also, despite no significant differences in events at six months have been observed, the presence of delayed enhancement was associated with poor micorvascular flow, greater enzyme elevation, worse ventricular function and greater incidence of complications during hospitalization.27 Finally, the same MDCT studies with delayed enhancement can identify the presence of microvascular obstruction, an independent predictor of post-AMI events, such as hypoattenuated regions within an area of contrast enhancement.26,29

In addition, cardiac MDCT can accurately assess the characteristics of chronic myocardial infarction, as well as its sequelae.

The complications include greater prevalence of apical mural thrombus observed with CT compared with other methods (Figure 3), possibly attributed to the great spatial resolution and ability to assess the total cardiac volume.30

Moreover, the characterization of chronic myocardial infarction with MDCT revitalized the concept of lipomatous metaplasia in AMI. Although the deposits of myocardial adipose tissue are hystopathologically and even macroscopically easy to detect, until 1997 there are records of descriptions about fat infiltration in myocardial infarctions.31 Recently, Su et al demonstrated the presence of adipose tissue in 84% chronic myocardial infarctions evaluated.32 What is more, a MRI study that utilized specific sequences to detect fat, identified adipose tissue in 78% infarctions of more than six months.33

MDCT can easily differentiate between air, water, fat, and bone, with fat values close to -100 Hounsfield units. Therefore, it is not surprising that studies to characterize the infarction by MDCT have been carried out in recent years. These studies confirmed that infarcted tissue is composed mainly of adipose tissue, although the levels of attenuation found (higher than those of pericardial fat) may indicate an interposition of adipose tissue, fibrosis and myocardial fibers in the infarction (Figure 4).30-32,34 These results challenge the long-established concept of myocardial scar (from Latin cicatrix), which means a scab resulting from the formation and contraction of fibrous tissue.

The high prevalence of adipose tissue in AMI makes it possible to identify chronic myocardial infarction even without contrast agent injection, as it was demonstrated in a recent study which reported 66% sensitivity and 100% specificity of the coronary calcium score to detect chronic myocardial infarction (Figure 4).30

It should be mentioned that due to the hardening of the X-ray beam, which usually affects the inferobasal segments, it is common to observe a soft myocardial hypoattenuation that simulates hypoperfused areas, although such device can be easily differentiated by experienced observers.35

Anatomical and functional assessment for the detection of ischemia

Recently, two major invasive studies that assessed the coronary blood flow reserve (DEFER and FAME) stressed the importance of functional assessment by showing that revascularization of patients with intermediate lesions does not result in a significant clinical benefit if stenosis does not restrict the flow during stress.36,37 Following this approach, Meijboom et al demonstrated that both coronary angiography and MDCTCA have poor correlation with coronary blood flow reserve (r of -0.30 and of -0.32, respectively), with a diagnostic accuracy of 67% and 71%, respectively.38 These findings raise a challenge for non-invasive diagnostic methods and encourage the search for a tool that allows for simultaneous assessment of the coronary anatomy and physiological significance of coronary lesions.

As described above, the MDCTCA allows for an accurate assessment of rest myocardial perfusion. Besides, cardiac MDCT can also assess adenosine stress myocardial perfusion.5,39 This has been demonstrated in a canine model of left anterior

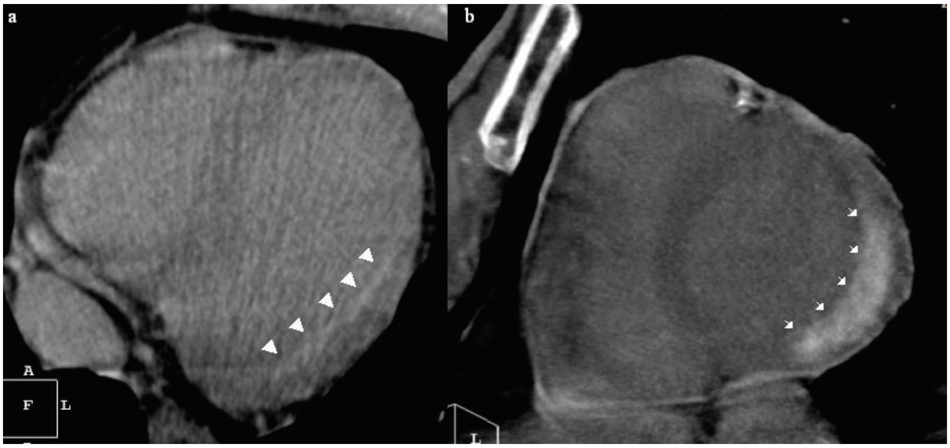

Fig. 2. Sequelae of subendocardial (panel **a**) and transmural (panel **b**) infarction, detected immediately after primary angioplasty by cardiac CT scan without contrast or heart rate monitoring (late contrast enhancement administered during intervention). Reproduced with the authorization of Rodríguez-Granillo GA et al.[27]

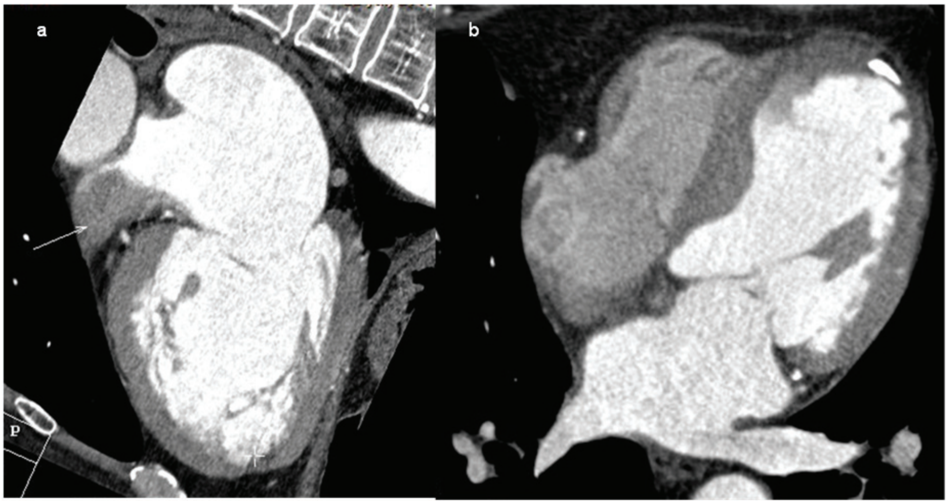

Fig. 3. Left atrial appendage thrombus (panel **a**, arrow). Apical mural thrombus, with significant parietal thinning and partial calcification (panel **b**).

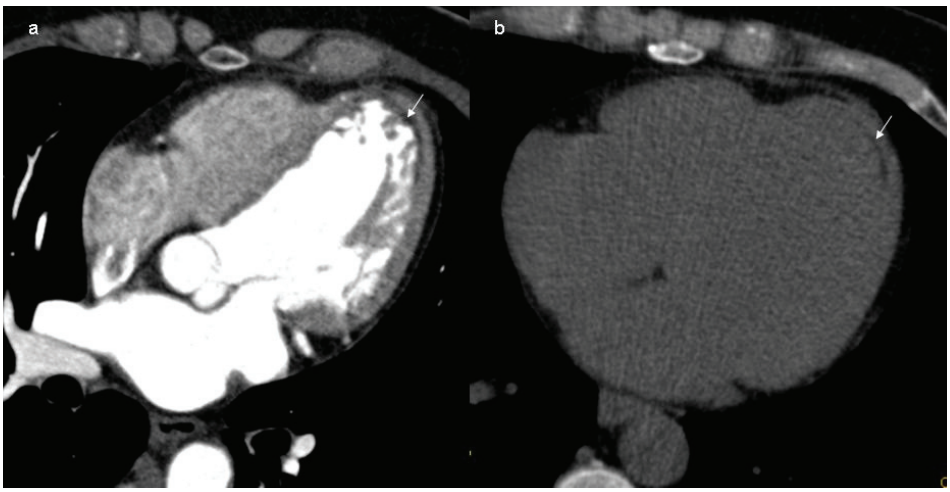

Fig. 4. Sequelae of previous myocardial infarction. There is a hypodense (not perfused) subendocardial area in the contrast study (panel **a**). Lipomatus metaplasia is confirmed with the attenuation values of fat density in conventional acquisition for calcium scoring (panel **b**).

descending artery stenosis, in which myocardial blood flow during adenosine infusion was 2.54 ± 0.93 mL/g/min in territories with stenosis and 8.94 ± 5.74 mL/g/min in remote myocardium ($p < 0.05$), with a signal density of 92.3 ± 39.5 HU in territories with stenosis, and 180.4 ± 41.9 HU in remote myocardium ($p < 0.001$).5

More recently, Blankstein et al demonstrated the feasibility of simultaneously performing (sequentially, during the same procedure): 1) adenosine stress perfusion; 2) rest myocardial perfusion; 3) coronary artery assessment (during rest perfusion); and 4) post-contrast late enhancement at 7 minutes. This combination of studies was carried out with an effective radiation dose (ERD) of 12.7 mSv, the same ERD that was observed in the SPECT. Considered in isolation, and using the detection of stenosis >50% with coronary angiography as reference standard, stress-rest cardiac MDCT perfusion imaging showed a sensitivity and specificity of 79% and 80%, respectively, while in SPECT, it was 67% and 83%, respectively. Using the detection of stenosis >70% with coronary angiography as reference standard, stress-rest cardiac MDCT perfusion imaging showed a sensitivity and specificity of 86% and 68%, respectively, while in SPECT, it was 73% and 73%, respectively.40

It should be pointed out that this study included a high-risk population with high prevalence of previous infarction (35%), revascularization (38%), diabetes (32%), hypertension (88%), dyslipidemia (85%) and obesity (41%).40

This simultaneous anatomical and functional assessment is even more relevant to patients with difussely calcified coronary tree, in which the positive predictive value of MDCTCA is lower due to a considerable number of non-analyzable false-positive segments.

Assessment of valvular heart diseases

While it is possible that the echo-Doppler will still be indefinitely the reference standard for the assessment of valvular heart diseases because of high reliability and low cost, both the cardiac MRI and MDCT are alternative methods that can evaluate different parameters associated with the severity of certain valvular heart diseases.

Estimation of transvalvular gradients is not possible with cardiac MDCT; however, the high spatial resolution of MDCT allows for accurate evaluation of valve anatomy and geometry, valve ring, and subvalvular apparatus, as well as for performance of valve planimetry and the accurate estimation of valve areas (Figure 5).42-46

By performing an accurate morphological

evaluation at different times within the cardiac cycle, the MDCT is an alternative for the estimation of aortic valve stenosis.43-46 Many authors explored the accuracy of the method for the quantification of the aortic valve area (AVA) by planimetry. Among these authors, Pouleur et al showed a strong correlation between MDCT-derived AVA with MRI-derived (r=0.98, P<.001) and the TEE-derived (r=0.96, P<.001).47 Similarly, the number of cusps and the degree of calcification can also be accurately assessed.

While there is no direct way to quantify regurgitant volume or estimate flow rates, recent studies showed that the incomplete coaptation of the valves by MDCT has a sensitivity of 72% and a specificity of 97% to detect aortic regurgitation, and a sensitivity and specificity of 100% and 95%, respectively, to detect acute aortic regurtigation.48

Mitral regurgitation is more difficult to assess with cardiac MDCT; however, the anatomy of the valves, the subvalvular apparatus, the ring and the chordae tendineae can be assessed. However, it is worth mentioning a recent study that evaluated patients with mitral regurgitation by echocardiography, MRI, and MDCT. In that study, Guo et al used the systolic volume of the left and right ventricles to calculate the regurgitant volume and fraction, and did not find any significant difference between MRI and MDCT, with an important correlation between the methods and with echocardiography.49

A recent study that utilized transesophageal echocardiography (TEE) as reference standard showed a high diagnostic accuracy of MDCT to evaluate aortic and mitral valve stenoses, a moderate accuracy to evaluate aortic regurgitation and mitral valve prolapse, and a poor correlation with TEE for mitral regurgitation.50

The same group demostrated the ability of MDCT to assess, with accuracy and reproducibility, the opening angle, ring diameter, and function of the mechanical valve prostheses.51

The use of percutaneous mitral annuloplasty to treat patients with severe mitral regurgitation has increased in recent years. This procedure involves placing a device in the coronary sinus to reduce the mitral annulus. Cardiac MDCT can visualize the relationship among coronary sinus, circumflex artery and mitral annulus, as well as measure the diameters of those structures (Figure 6a). This is important in order to avoid complications (circumflex artery occlusion) and predict success (distance between coronary sinus and mitral annulus).52-54

In contrast, cardiac MDCT does not seem to be a good option to assess pulmonary and tricuspid valves. This is because the targets of the contrast injection are usually the left chambers, whereas the little contrast remaining in the right chambers, if present, usually has a non-homogeneous distribution. In case the assessment of the right chambers is necessary, the geometry of the injection bolus will have to be adjusted to a slower flow.

In recent years, there has been a true increase in the number of percutaneous aortic valve replacements (PAVR).55 Patient screening and selection of the type and size of the prosthesis are crucial to the success of PAVR. In particular, tortuosity, calcification, and minimal luminal diameter of femoral and iliac arteries, and the aorta, are determining factors when choosing patients and path. Of course, these characteristics will not be observed by cardiac MDCT but by angiotomography of the aorta or the lower limbs, or by ultrasound. Instead, the size of the prosthesis is determined by the aortic annulus diameter at the insertion of the sigmoid arteries. This information, as well as the evaluation of other predictors of success such as the degree and distribution of calcification, number of cusps, sinus height, diameter of the aortic root, diameter of the sinotubular junction, distance from the annulus plane to the coronary ostiums, may be characterized with accuracy and reproducibility by cardiac MDCT. It has also been described that basal septal hypertrophy, identified by cardiac MDCT, can interfere in the delivery and positioning of the prosthesis, and can predispose valve migration.55

Planning of electrophysiological studies and detection of sources of embolism

Radiofrequency ablation is a therapeutic strategy increasingly used to treat refractory atrial fibrillation, instead of conventional treatment; its aim is to eliminate ectopic foci originated in pulmonary veins, or to electrically disconnect them.56-58 The success of that procedure is largely due to the accurate visualization of the ostiums. Being a two-dimensional technique, fluoroscopy is limited for this purpose. Thus, cardiac MDCT is increasingly used to assess the anatomy of pulmonary veins and detect thrombus in the left atrium prior to radiofrequency ablation in patients with atrial fibrillation.59

Besides, cardiac MDCT has proved to be superior to transthoracic and transesophageal ECG regarding the evaluation of the left atrium size, an important predictor of the recurrence of atrial fibrillation following ablation.60

Simultaneously, the localization of the esophagus and its relation with the left atrium and pulmonary veins can reduce the risk of thermal injury, although the intraprocedural esophagram is slightly more accurate.61

In a comparative study with intracardiac echocardiography, the MDCT showed higher sensitivity to detect additional branches of pulmonary veins, whereas the intracardiac echocardiography underestimated ostial diameters. Since appendage thrombus can be ruled out (Figures 4 and 6b) in the same study (and with no radiation, contrast agent or additional costs) in which the anatomy of pulmonary veins is assessed, several studies were carried out with that purpose, using the transesophageal echocardiography as reference standard, and identified a MDCT sensitivity of 83% and specificity of 91% to detect atrial thrombi, in a total of 475 patients.62-64

The most recent study that assessed the ability of cardiac MDCT to detect sources of embolism in 137 patients with ischemic stroke using TEE as reference standard, detected an overall sensitivity, specificity, positive predictive value, and negative predictive value of 89%, 100%, 100%, and 81%, respectively. It is worth mentioning that there were no false-positive results in that study, whereas the eight false-negative results detected were associated with low-risk sources of embolism (five patent foramen ovale and three atrial septal aneurysm).65

Fig. 5. Normal aortic valve (panel **a**). Severe aortic stenosis, with diffuse calcification of the noncoronary leaflet free edge (panel **b**).

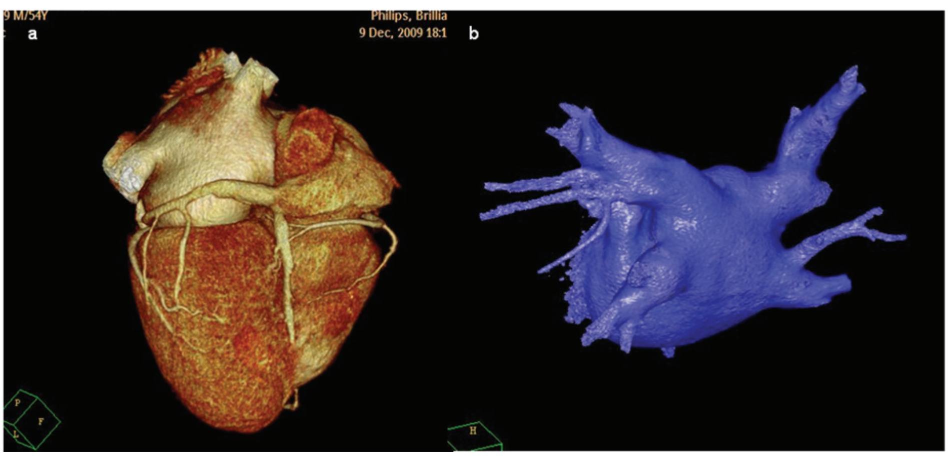

Fig. 6. Visualization of the coronary sinus and its tribute veins, and assessment of the relationship between the mitral annulus and coronary sinus (panel **a**). In panel **b**, there is a three-dimensional reconstruction of the left atrium and pulmonary veins, very useful for planning radiofrequency ablation procedures.

Guide to cardiac resynchronization therapy

Resynchronization therapy, increasingly used in patients with heart failure refractory to treatment with conduction alteration, consists of the insertion of the transvenous electrode into a tributary vein of the coronary sinus, so as to reduce the level of ventricular dyssynchrony. In experienced centers, the rate of success ranges between 88% and 95%, and it largely depends on the ability to catheterize the coronary sinus and the absence of appropriate branches.66, 67 It is therefore expected that the previous knowledge of coronary venous anatomy be useful to guide those procedures.

In this context, cardiac MDCT can accurately evaluate the anatomy of the coronary sinus and its tributary veins.68 Furthermore, MDCT can simultaneously evaluate the integrity of the underlying myocardium, thus preventing the electrode from being inserted into nonviable myocardial areas.

Other applications

In recent years, the use of cardiac MDCT for diagnosis and follow-ups of congenital heart diseases has increased, although it is of little application. In

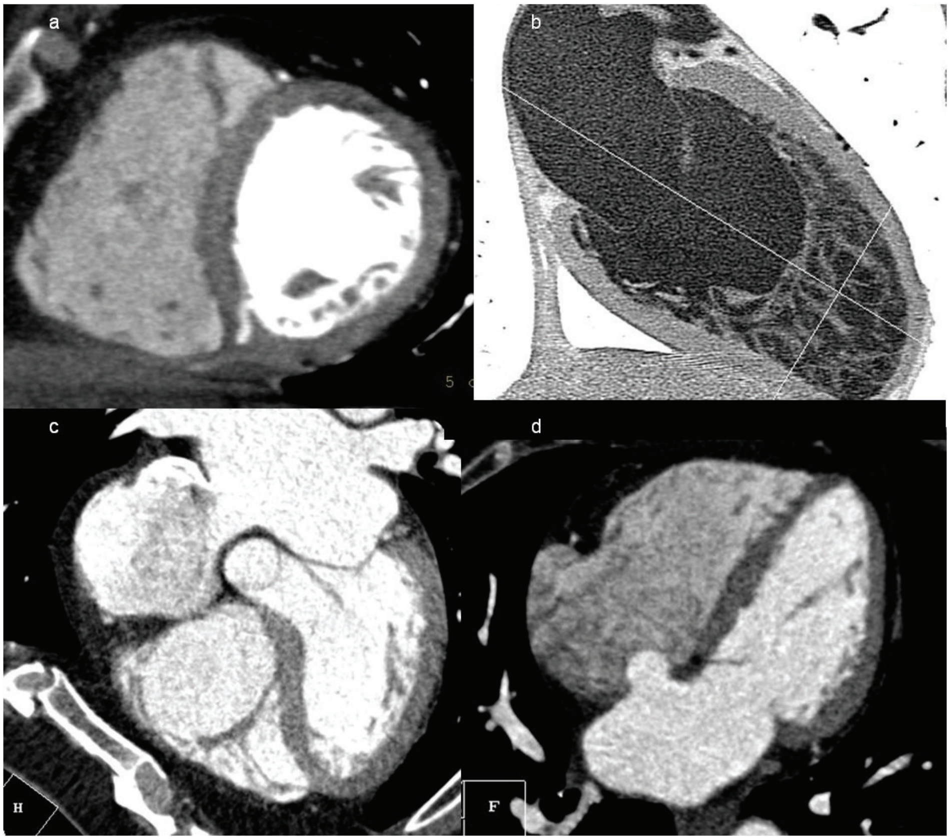

Fig. 7. Ventricular diverticulum (**a**), non-compacted myocardium (**b**), ostium secundum type atrial septal defect (**c**), and atrial septal aneurysm (**d**).

addition to coronary anomalies and coarctation of the aorta, MDCT can accurately assess interatrial and interventricular septal defects, anomalous pulmonary connections, and complex heart diseases (Figure 7).69,70 A recent study even showed a sensitivity and specificity of MDCT to detect patent foramen ovale of 77% and 86%, respectively, using TEE as reference standard.71 Finally, the value of MDCT to assess cardiac masses and pericardiopathies should also be considered. In particular, the atrial appendage thrombus, as well as the thrombus in the apex, can be accurately detected (Figure 4 a).62-64, 72-73

Conclusions and future perspectives

Coronary artery MDCT is a rapidly emerging strategy that can accurately detect the presence of coronary artery stenosis. During the course of these studies, clinically relevant noncoronary cardiovascular disease is identified in approximately 1% of the patients.74

As discussed in the text, there are several noncoronary applications of the cardiac MDCT; most of them can be evaluated during the study of coronary arteries without requiring additional radiation or contrast agents. The ability of the method for simultaneous evaluation of morphology and function allows a comprehensive approach to a broad spectrum of conditions within the same study. The acquisition of studies through prospective ECG-gating techniques can significantly reduce the effective radiation dose to ~3 mSv.75 However, being an axial end-diastolic acquisition, it does not provide for the functional assessment of the left ventricle. Instead, since radiation of the tube current modulation is reduced by 80% throughout the cardiac cycle (except for an optimal image quality in a diastolic 'window') in retrospective gating acquisition, it significantly reduces the effective radiation dose, even to conventional coronary angiography levels (5.4-9.4 mSv), and simultaneously evaluates the left ventricular function (see Table 1).11,76 The increasing development of dedicated softwares that display cardiac MDCT images in the cath lab allows for the fusion of images with electroanatomic mapping during radiofrequency ablation procedures, or even the identification of optimal projections prior to coronary and noncoronary procedures; this leads to better selection of material, shorter procedure time and reduced effective radiation dose and contrast volume.77,78

RESUMEN

Aplicaciones no coronarias de la tomografía computada cardíaca

El gran valor predictivo negativo de la angiografía coronaria por tomografía computada multidetector (ACTCMD), ha llevado a la creciente incorporación del método en el algoritmo diagnóstico para pacientes con sospecha de enfermedad coronaria. Además, gracias a una adquisición volumétrica del área cardíaca y al gatillado electrocardiográfico, la ACTCMD permite simultáneamente, realizar reconstrucciones submilimétricas en todos los ángulos posibles y en distintos tiempos del ciclo cardíaco. Esto genera un escenario propicio para la evaluación morfológica y funcional, y abre un amplio abanico de aplicaciones no coronarias posibles; la mayoría

de ellas evaluables durante el mismo estudio de las arterias coronarias, y sin requerimiento de contraste ni radiación adicional. La capacidad de evaluar simultáneamente morfología y función, permite una aproximación comprensiva de un amplio espectro de patologías mediante un mismo estudio.

Palabras clave > Diagnóstico por imágenes - Perfusión - Viabilidad - Tomografía - Función ventricular

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