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Non-invasive Coronary Angiography: the Present and Future of Multi-slice Computed Tomography Coronary Angiography

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INTRODUCTION

During the last five years, since the advent of 64-slice multi-slice computed tomography (MSCT) and thanks to the continuous technological improvements of this technique, the non-invasing imaging of the coronar y arteries has become much more reliable. Nowadays, MSCT coronary angiography (CTCA) enables visualization of not only the coronary artery stenoses and occlusions, but also of the atherosclerotic changes and plaques that are confined to the coronary vessel wall without causing significant stenoses.

Conventional selective X-ray coronary angiography (SCA) remains the undisputed standard of reference for the assessment of the lumen of coronary arteries. However, this is an invasive procedure with a small but not negligible health risk that needs even short hospitalization and causes patient discomfort. Among the more than 2.5 million examinations of SCA performed annually in U.S.A. and Europe, approximately 25% do not reveal essential findings and more than 40% are not followed by any kind of interventional or surgical procedure.[1] On the other hand, SCA does not provide any information concerning the coronary wall, while almost 80% of deadly myocardial infarctions are attributed to vulnerable plaques which did not cause hemodynamically severe stenoses.[2] Myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) is a well-established and clinically useful technique for the detection of coronary artery disease (CAD), but its results can be normal in cases of non-significant (<50%) coronary artery stenoses and even in cases of high-risk CAD (left main and balanced 3-vessel CAD).

MSCT: TECHNICAL ISSUES

MSCT coronary angiography is performed during a single breath-hold and the coronary lumen is opacified by a very fast (bolus) intravenous injection of an iodinated contrast medium (80-100 ml are generally sufficient with the latest technology scanners), followed by a flush bolus of 100 ml of normal saline. ECG is simultaneously recorded during data acquisition, allowing retrospective gating and slice reconstruction at the most appropriate position within the cardiac cycle; this is, typically, the mid-to-end diastolic period, in order to minimize motion artifacts, but it may vary for each coronary branch (particularly at faster heart rates).[4] MSCT scanners have an inherently limited temporal resolution (the time needed for data collection per cardiac cycle), which cannot be better than 165 ms with the 64-slice technology and, in general,

with any scanner that uses a single X-ray tube. At high heart rates, motion artifacts are often observed and degrade the image quality. This problem can be managed by the use of oral or intravenous (IV) β-receptor blocking agents. A heart rate between 50 and 60 beats per minute (bpm) is considered to be ideal and, if it remains during the data acquisition, significantly increases the number of assessable coronary segments. Also, sublingual administration of nitrates, just a few minutes before the CT coronary angiography (CTCA), was found to result in significantly larger proximal coronary diameters and is now widely recommended for routine examinations.

The evolution from 4-slice to 64-slice technology permitted significant decrease of the breath-hold duration (from 35-40 sec to 5-12 sec) and of the amount of iodinated contrast medium needed (from 180 to 80-100 ml). Also, the spatial resolution improved. The direct benefit was the significant improvement of the proportion of the evaluable coronary segments (approximately from 70% to 95%). Additionally, a significant improvement of all the parameters of diagnostic performance of CTCA, both at patient and coronary segment level, was validated.[4-10]

CTCA: DIAGNOSTIC PERFORMANCE

There are cumulative data from the literature, providing validation of CTCA in comparison to SCA, for detecting significant coronary artery stenoses. All the studies reported a very high negative predictive value (NPV) as a major strength of this modality. Many studies, comparing 64-slice CTCA with SCA in patients with suspected CAD, showed, at coronary segment level, sensitivity of 88-97% (average 93%), specificity of 96-97% (average 96%), positive predictive value (PPV) of 66-87% and an excellent NPV of 99% for detecting stenoses >50% at coronary segments with a lumen diameter >1.5 mm. About 85-100% of all coronary segments could be evaluated with CTCA, depending on the selection criteria of the population of each study. At patient-based detection, sensitivity and specificity were up to100%. However, high-performance results achieved at academic sites with high expertise are probably not reproducible at a wider practice of CTCA. Additionally, the results are influenced by the patient selection criteria.[9-16]

The technology of dual-source 64-slice MSCT is already widely available and established new milestones in non-invasive coronary imaging. By using two coupled X-ray tubes, it became possible to achieve a true temporal resolution of 83 ms, thus permitting reliable visualization of the distal coronary arteries even with high heart rate and, in most cases, obviating the need for β-blockers. Examinations of good to excellent quality, even in cases of arrhythmia or atrial fibrillation, are now routinely acquired with that new technology. Additionally, a significant decrease of the mean radiation dose seems to be achievable.[17,18]

CTCA: INDICATIONS (TABLE 1)

Evolving and proposed indications for the clinical use of CTCA include:[19,20]

a. detection of congenital anomalies of the coronary arteries; however, this goal can be reliably accomplished with MRI, obviating the need for iodinated contrast medium and without exposure to ionizing radiation.
b. exclusion of coronary artery disease (CAD) in individuals with low-to-moderate pretest probability: asymptomatic high-risk, patients with atypical chest pain and/or equivocal stress-test results. According to the recent guidelines of the American Heart Association (AHA) and European Society of Cardiology (ESC), the potential benefit from the use of CTCA is greater in symptomatic patients with intermediate clinical risk for CAD (category IIa-B test, according to AHA guidelines).[21,22] Some recently published studies concluded to similar recommendations.[23-25]
c. patients with a SCA that was incomplete or failed to visualize a major coronary branch or posed the suspicion of left main coronary artery stenosis.
d. evaluation of by-pass grafts: CTCA is highly accurate in confirming patency or occlusion, but its accuracy for evaluating the degree of graft stenosis has not been well established yet. Since the advent of 64-slice scanners, it seems reliable to assess graft stenosis, patency of the anastomosis with the indigenous artery and visualization

TABLE 1. Indications for the clinical use of computed tomography coronary angiography

- detection of congenital anomalies of the coronary arteries (however, this can be reliably accomplished with MRI, obviating the need for contrast medium and exposure to ionizing radiation)
- exclusion of coronary artery disease in individuals with low-to-moderate pretest probability
- incomplete or failed visualization by SCA of a major coronary branch or suspicion posed by SCA of left main coronary artery stenosis
- evaluation of coronary by-pass grafts
- evaluation of coronary arteries in patients scheduled to undergo non-coronary cardiovascular surgery, such as valve replacement and aortic aneurysm repair
- patients with atrial fibrillation, prior to administration of anti-arrhythmic drugs and catheter ablation
- to assess (with a single examination) for coronary artery disease, aortic dissection or rupture, and pulmonary embolism ("triple rule-out") in patients presenting with acute chest pain in the emergency department, without specific ECG-changes and normal cardiac enzymes

of the lumen of the more distal coronary segments.[26]

e. evaluation of the coronary arteries in patients scheduled to undergo non-coronary cardiovascular surgery, such as valve replacement and aortic aneurysm repair.[27]
f. patients with atrial fibrillation, prior to administration of anti-arrhythmic drugs and catheter ablation.
h. patients presenting with acute chest pain in the emergency department, without specific ECG-changes and normal counts of cardiac enzymes: CTCA can be used effectively for detecting or excluding (with a single examination) CAD, aortic dissection or rupture and pulmonary embolism ("triple rule-out").[28-30]

The diagnostic accuracy and subsequent clinical usefulness of CTCA are dependent on the risk profile for CAD of the patient population. It should be noted that CTCA has not yet proven to be suitable for evaluating patients with already known or very probable CAD, since its accuracy for grading the degree of lumen stenosis -especially from heavily calcified plaques- is not yet established.[31]

CTCA: LIMITATIONS

CTCA may be impaired from artifacts caused by dense calcifications and other hyperdense structures, such as surgical clips, sternal sutures and stents. Practically, patients with a high calcium score cannot be reliably evaluated by CTCA. Heavily calcified plaques, especially those with a concentric pattern, are accompanied by the "blooming artifact" which often precludes accurate evaluation of the degree of lumen stenosis, usually leading to overestimation.[12,32] Obese patients can now be examined more reliably, by using the 64-slice or newer technology, even accepting the lower image quality and at the expense of higher radiation dose. The lumen within coronary stents cannot be routinely well visualized, but patency of the stented segment can usually be assessed. The assessability of a stent depends on its particular structure and size and varies significantly among the different stent types. Some recent studies using the 64-slice or newer technology showed very promising results for assessing in-stent restenosis, but broader studies are needed to validate this reported high diagnostic performance.[33,34]

The need for intravenous injection of a significant quantity of iodinated contrast medium and the exposure to radiation are the main disadvantages of CT, compared to magnetic resonance imaging (MRI), and preclude its use in patients with renal insufficiency or allergy to iodine and in pregnant women. However, the image quality of a non-invasive coronary angiography (in terms of spatial resolution and contrast-to-noise ratio) using CT, is by far better compared to MRI.

The issue of *radiation exposure* has to be seriously considered, especially when the possible role of CTCA as a screening tool in high-risk asymptomatic patients is discussed. Using state-of-the-art 64-slice scanners, the effective radiation dose during CTCA was measured equal to 10-15 mSv in men and 14-21.4 mSv in women.[9-13] This is higher of the average dose of diagnostic SCA (up to 11.4 mSv) and comparable to that of thallium or technetium myocardial scintigraphy (8-18 mSv). However, recent data and our initial personal experience by using dual-source 64-slice CTCA with ECG-tube modulation (which reduces the X-ray tube current and, consequently, the radiation exposure during the part of the cardiac cycle where data are not selected) show a significant decrease of the average radiation dose.[35] In any case, CTCA should be avoided in young patients and, especially, young women.

CTCA: EVALUATION OF CORONARY WALL AND PLAQUE STRUCTURE

Besides of evaluating the coronary lumen, CTCA is currently the only available tool for non-invasive assessment of the coronary vessel wall. By using 64-slice and newer technology, the coronary plaques can now be reliably detected and classified, according to their density, into calcified, non-calcified (soft) and mixed. Exact localization and estimation of the total atherosclerotic plaque burden (plaque volumetry) and, also, detection of the positive or negative remodeling of the coronary vessel wall, are now feasible. Several studies have shown moderately good correlation of MSCT findings with those of intravascular ultrasound. The capability of accurate and reproducible plaque volumetry could be used in monitoring the therapeutic result of lipid lowering therapy. However, current resolution of CTCA does not allow detection of certain characteristics of the vulnerable plaque, such as a thin fibrous cap, a lipid core or inflammation.[36-38]

CTCA: PROGNOSTIC VALUE

During the last 3 years, cumulative data from several studies confirm the independent prognostic information, over conventional clinical risk factors, that multislice CTCA can provide in patients with known or suspected CAD. An excellent prognosis was noted in patients with a normal CTCA, a result that underscores the excellent NPV of this test for excluding the presence of CAD. Additionally, an elevated rate of "coronary events" -like nonfatal myocardial infarct, unstable angina requiring hospitalization, revascularization or even death due to acute myocardial infarct- was reported in patients with nonobstructive or non significant CAD (lumen stenosis between 25-75%), even in medium-term follow-up periods of 16 to 72 months. Other studies showed that CTCA is an independent predictor of coronary events and provides incremental prognostic value to myocardial perfusion imaging with SPECT.[39-44]

MSCT: OTHER INFORMATION

Beyond the visualization of coronary arteries, the same data set that is acquired during CTCA, also contains valuable information that can be used for assessment of the morphology and function of cardiac ventricles, with accuracy similar

to that of MRI, morphological and functional evaluation of cardiac valves, with results comparable to echocardiography, and estimation of myocardial viability, with an accuracy comparable to that of MRI.[45-49]

MSCT: FUTURE PERSPECTIVE

Awaiting for the results of large studies using the dual-source 64-slice technology, the first 256, 320 and even 420-slices single-source scanners, allowing examination of the entire heart during one heartbeat, are already available in a few, mostly academic, sites. However, as single source scanners, they are still hampered by suboptimal temporal resolution (>120 ms). In parallel, recent technological advances made the dual-source technology even more robust and efficient. At the same time, the intense effort of all MSCT system vendors for reducing the radiation dose, has reached a point where examination doses as low as 1 mSv seem to be feasible.

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