Clinical recommendations on Cardiac-CT in 2015: a position paper of the Working Group on Cardiac-CT and Nuclear Cardiology of the Italian Society of Cardiology

Daniele Andreini[a,b], Eugenio Martuscelli[c], Andrea Igoren Guaricci[d,e], Nazario Carrabba[f], Marco Magnoni[g,h], Carlo Tedeschi[i], Antonio Pelliccia[l] and Gianluca Pontone[a], on behalf of the Working Group on Cardiac-CT and Nuclear Cardiology of the Italian Society of Cardiology

We worked out a position paper on cardiac-computed tomography (CCT) endorsed by the Working Group on CCT and Nuclear Cardiology of the Italian Society of Cardiology. The CCT clinical indications were discussed and formulated according to the following two modalities: a brief paragraph dedicated to each indication, with the description of clinical usefulness of different indications; and each indication was rated by the technical panel for appropriateness, using a score assessing whether the use of CCT for each indication is appropriate, uncertain, or inappropriate. All conventional CCT clinical indications, regarding coronary and noncoronary evaluation, were discussed and rated. Moreover, we wrote specific sections regarding the newest CCT applications, such as stress perfusion computed tomography, noninvasive evaluation of fractional flow reserve, and CCT use in athletes. The present study has the following two main objectives: because the diagnostic performance of coronary computed tomography angiography (CCTA) is strictly dependent on adequate technology and local expertise, we strove to provide clinical recommendations on CCTA that may help Italian physicians involved with this diagnostic tool; and to give an update on new indications of CCTA, such as its use for safely discharging patients with suspected acute coronary syndromes from the emergency department, and latest clinical results that have been made possible by the remarkable technology developments of the scanners.

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[a]Centro Cardiologico Monzino, IRCCS, [b]Department of Clinical Sciences and Community Health, Cardiovascular Section, University of Milan, Milan, [c]University of Rome Tor Vergata, Tor Vergata, Rome, [d]Cardiology Unit, Department of Emergency and Organ Transplantation, University Hospital Policlinico Consorziale of Bari, Bari, Italy, [e]Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [f]Division of Cardiology, Careggi Hospital, Florence, [g]University Vita-Salute, San Raffaele Scientific Institute, Milan, [h]Fondazione 'per il Tuo cuore'-Heart Care Foundation Onlus, Florence, [i]Carlo Tedeschi, Cardiology Unit, San Gennaro Hospital, ASL Napoli 1 Centro, Naples and [l]Antonio Pelliccia, Institute of Sport Medicine and Science, Rome, Italy

Correspondence to Daniele Andreini, MD, PhD, Centro Cardiologico Monzino, Via C. Parea 4, 20138 Milan, Italy
Tel: +39 02 58002577; fax: +39 02 58002287; e-mail: daniele.andreini@ccfm.it

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Introduction

Coronary computed tomography angiography (CCTA) is currently considered a reliable diagnostic method for the evaluation of patients with known or suspected coronary artery disease (CAD) with high diagnostic performance for detection of significant coronary stenoses.[1] From 2006, the European and American Society of Cardiology and Radiology has identified appropriate clinical scenarios for CCTA indication, including patients with chest pain and intermediate pretest probability of CAD, patients with suspected coronary anomalies, and patients with new-onset heart failure.[1-5] Noteworthy, there is a large scientific literature demonstrating a remarkable diagnostic value of CCTA in stable patients with chest pain. This led the European Society of Cardiology (ESC) to include CCTA in the ESC guidelines as the first-line imaging technique for the management of stable CAD patients with low-to-intermediate pretest CAD likelihood.[6] The need for a position paper on cardiac-computed tomography (CCT) by the Working Group on CCT and Nuclear Cardiology of the Italian Society of Cardiology stems from the following two main conditions: the fast progress of CCTA technology requires frequent updates on new clinical indications, including the newest possibility to assess the functional relevance of a stenosis by CT perfusion or fractional flow reserve computed tomography (FFR-CT); and the diagnostic performance of CCTA is strictly dependent on adequate technology and local expertise, substantiating the need of clinical recommendations for CCTA use that may help Italian physicians involved with this diagnostic tool.[7]

Methods

The CCT clinical indications were discussed and arranged according to the following two modalities: a brief paragraph dedicated to each indication, with the

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description of its clinical usefulness; and each indication was rated by the technical panel for appropriateness, using a score previously described.[1] In particular, the technical panel first rated indications independently. In rating these criteria, the technical panel was asked to assess whether use of the test for each indication is appropriate, uncertain, or inappropriate, as defined below. An appropriate imaging study is one in which the expected incremental information, combined with clinical judgment, exceeds the expected negative consequences by a sufficiently wide margin for a specific indication, so that the procedure is generally considered an acceptable care and a reasonable approach for the indication.

The technical panel scores each indication as follows:

(1) Scores 7–9: 'Appropriate' test for a specific indication (the test is generally acceptable and is a reasonable approach for the indication).
(2) Scores 4–6: Uncertain for a specific indication (the test may be generally acceptable and may be a reasonable approach for the indication). Uncertainty also implies that more research and/or patient information is needed to classify the indication definitively.
(3) Scores 1–3: Inappropriate test for a specific indication (the test is not generally acceptable and is not a reasonable approach for the indication).

Then, the panel members met *vis-à-vis* for discussing and agreeing on each indication. At this meeting, they provided their scores and received a blinded summary of their peers' scores. After a consensus meeting, they were asked to independently provide their final scores for each indication. The final score reported in Tables 1–4 is the arithmetic mean of the scores of each individual panelist.

Table 1 Cardiac-computed tomography appropriate use criteria

Indication	Appropriate use score
Calcium scoring and CCTA as screening in primary prevention in asymptomatic patients	
Calcium scoring	
Measurement of CAC for reclassification of patients at low-to-intermediate risk	A (8)
Measurement of CAC as gatekeeper of CCTA	U (5)
Use of CT angiogram	
Screening for CAD in asymptomatic patients at low-to-intermediate risk	U (4)
Screening for CAD in asymptomatic patients at high risk	U (6)
To exclude CAD in asymptomatic patients with prior positive functional tests	A (7)
The use of CT in the emergency department	
CCTA for safe discharge of patients with possible ACS and unknown CAD	
Acute chest pain, first troponin-negative, no ECG ST-segment elevation in ER in patients with low-intermediate pretest probability of CAD	A (8)
Acute chest pain, first troponin-negative, no ECG ST-segment elevation in ER in patients with high pretest probability of CAD	U (6)
Triple rule-out to exclude obstructive CAD, pulmonary embolism, and aortic dissection in acute setting	
Acute chest pain of uncertain cause (differential diagnosis includes pulmonary embolism, aortic dissection, and ACS)	A (8)
CCTA in stable patients symptomatic for chest pain	
Evaluation of chest pain syndrome in patients with low pretest likelihood of CAD and positive appropriate functional stress test	A (8)
Evaluation of chest pain syndrome in patients with high pretest likelihood of CAD and negative appropriate functional stress test if a scanner with a nominal spatial resolution of 0.23 mm is available	A (7)
Evaluation of chest pain syndrome in patients with intermediate pretest likelihood of CAD as first-line test	A (7)
Evaluation of chest pain syndrome in all patients regardless the pretest likelihood of CAD when appropriate functional stress test is equivocal or un-interpretable	A (7)
Evaluation of suspected coronary anomalies	
Assessment of anomalies of coronary arterial and other thoracic arteriovenous vessels in adult	A (8)
Assessment of anomalies of coronary arterial and other thoracic arteriovenous vessels in infant when CMR is contraindicated and low-dose CCTA is available	A (8)
Evaluation of coronary arteries in patients with new-onset heart failure to assess cause	
Evaluation of coronary arteries with CCTA in patients with new-onset heart failure to assess cause	A (8)

ACS, acute coronary syndrome; CAC, coronary artery calcium; CAD, coronary artery disease; CCTA, Coronary computed tomography angiography; CT, computed tomography; ER, emergency room. Coronary artery evaluation 1.

General topics

Patient preparation

The aim of patient preparation is to optimize his/her physiology conditions for achieving an image quality as high as possible and to limit contrast medium-induced acute kidney injury. One of the pivotal parameters to take into consideration is the heart rate (HR), which should be less than 65 beats per minute (b.p.m.) in order to have a longer diastolic time interval, hence motionless coronary arteries. The higher the HR,the fewer the segments available for a correct visualization owing to motion artifacts.[8] Premedication with intravenous beta-blockers or oral ivabradine is indicated in order to lower the HR prior to CCTA.[9–11] Recently, although the low and stable HR is still fundamental to reduce radiation exposure and improve coronary interpretability, the last scanner generations have demonstrated achieve ment of diagnostic image quality even in patients with a HR more than 65 b.p.m.[12,13] Brief apnea training is encouraged with the intent of avoiding artifacts related to breathing movements. The administration of sublingual nitrates is endorsed because the associated coronary vessel dilation increases intraluminal contrast density, thus improving image quality.[5] Intravenous administration of plentiful isotonic electrolyte solution, eventually associated with forced diuresis, is advisable for acute kidney injury prevention in patients at risk.[14]

Appropriateness of technical equipment and radiation dose

The CCTA standard equipment is composed of an X-ray source and a matrix detector that rotate simultaneously

Table 2 Cardiac-computed tomography appropriate use criteria

Indication	Appropriate use score
Use of CCTA for CAD evaluation before valve surgery and noncardiac surgery	
Use of CCTA for CAD evaluation before valve surgery in patients at low-to-intermediate risk	A (7)
Use of CCTA for CAD evaluation before valve surgery in patients at high risk	U (6)
Preoperative risk assessment in patients at intermediate-to-high risk before noncardiac surgery	U (5)
CCTA after heart transplantation	
CCTA in lieu of serial invasive coronary angiography following heart transplantation	A (7)
Coronary stents	
Symptomatic (ischemic equivalent)	
Prior coronary stent with stent diameter <3 mm or not known	U (4)
Prior coronary stent with stent diameter ≥3 mm	A (7)
Asymptomatic	
Prior left main coronary stent, time since PCI <2 years	A (7)
Stent diameter ≥3 mm, time since PCI <2 years	U (4)
Prior left main coronary stent, time since PCI >2 years	U (6)
Stent diameter ≥3 mm, time since PCI >2 years	U (5)
Coronary artery bypass grafts, including noninvasive coronary arterial mapping prior to repeat cardiac surgical revascularization	
Asymptomatic, time since CABG <5 years	I (3)
Asymptomatic, time since CABG >5 years	U (6)
Symptomatic with unclear signs or without signs of stress test ischemia	A (8)
Symptomatic with clear signs of stress test ischemia	U (6)
Localization of coronary bypass grafts and other retrosternal anatomy prior to reoperative chest or cardiac surgery	A (8)
Use of CCTA in the evaluation of complex lesions before PCI (i.e. chronic total occlusions, bifurcation lesions)	
Total, long, chronic occlusion	A (7)
Bifurcation lesions Medina 1,1,1	U (5)
Heavy calcifications	I (3)
Distal left main	A (7)

CABG, coronary artery bypass graft; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CT, computed tomography; PCI, percutaneous coronary intervention. Coronary artery evaluation 2.

Table 3 Cardiac-computed tomography appropriate use criteria

Indication	Appropriate use score
Assessment of valvular heart disease, including anatomical assessment before TAVI	
Anatomical assessment before TAVI	A (8)
Anatomical assessment, including arterial coronary circulation, before TAVI	A (8)
Characterization of native cardiac valves in patients with suspected clinically significant valvular dysfunction and inadequate images from other noninvasive methods	A (7)
Characterization of prosthetic cardiac valves in patients with suspected clinically significant valvular dysfunction	U (6)
Characterization of prosthetic cardiac valves in patients with suspected clinically significant valvular dysfunction and inadequate images from other noninvasive methods	A (7)
Assessment of complex congenital heart disease, including anatomical assessment before percutaneous device closure of ASD or VSD	
Assessment of complex adult congenital heart disease	A (8)
Anatomical assessment before percutaneous or surgical closure of ASD or VSD	A (7)
Assessment of myocardial viability, function and morphology	
Initial evaluation of left ventricular function following detrimental clinical conditions	I (3)
Initial evaluation of left ventricular function following detrimental clinical conditions when other imaging modalities are inadequate or contraindicated	A (7)
Assessment of right ventricular morphology and function in suspected arrhythmogenic right ventricular dysplasia	U (4)
Assessment of right ventricular morphology and function in suspected arrhythmogenic right ventricular dysplasia when other imaging modalities are inadequate or contraindicated	A (7)
Assessment of left ventricular systolic dysfunction and myocardial viability prior to myocardial revascularization	U (4)
Assessment of left ventricular systolic dysfunction and myocardial viability prior to myocardial revascularization when other imaging modalities are inadequate or contraindicated	U (6)
Evaluation of cardiac mass and pericardial conditions	
Evaluation of known or suspected cardiac mass (tumor or thrombus) with CCT in patients with technically limited images from echocardiogram, MRI or TEE	A (8)
Evaluation of pericardial conditions (pericardial mass, constrictive pericarditis, or complications from cardiac surgery) with CCTA in patients with technically limited images from echocardiogram, MRI, or TEE	A (8)
Evaluation of left atrium and pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation and noninvasive coronary vein mapping prior to placement of biventricular pacemaker	
Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation	A (8)
Use of Cardiac-CT for the rule-out of LA thrombosis in patients with atrial fibrillation when transesophageal echocardiography is unfeasible or contraindicated	A (7)
Noninvasive coronary vein mapping with CCTA prior to placement of biventricular pacemaker	A (8)

ASD, atrial septum defect; CCTA, coronary computed tomography angiography; LA, left atrium; LV, left ventricle; TAVI, transcatheter aortic valve implantation; TEE, transesophageal echocardiography; VSD, ventricular septum defect. Noncoronary artery evaluation.

around the patient while the table moves (helical scan modality) or while the table remains stationary (axial scan). The X-ray tube rotation time and the detector width are the major determinants of spatial and temporal resolution, respectively, and to improve both, the scanners need a minimum number of very thin slices (from 64 up to 350 slices with slice width <0.6 mm) and a minimum gantry with rotation time of 350 ms.[15] Unfortunately, to keep the image quality at the diagnostic level with such reduced slice width and high gantry rotation speed, high levels of tube current and voltage are required, resulting in an increased effective radiation dose. However, according to the principle of optimization, as pointed by the International Commission of Radiological Protection, the number of individuals exposed and the magnitude of their doses should all be kept as low as reasonably achievable (ALARA). Accordingly, several strategies for reducing radiation exposure have been developed. They can be summarized as follows: modification of X-ray output such as low tube voltage and tube current set-up[16,17]; tube current modulation-ECG triggered[16,17]; prospective ECG-triggering[18–20] and adaptive iterative reconstruction algorithm rather than filtered back projection algorithm[21–23]; reduction of the extent or duration of X-ray exposure such as optimization of scan length,[16] dual-source CT,[24,25] or high-pitch CT[12]; and reduction of z-overbeaming and/or z-overscanning such as large detector scanners (256 and 320-slices multidetector computed tomography).[13,26] It is noteworthy that with the recent combination of effective strategies for dose reduction, a submillisiviert CCTA is an attainable achievement.

Table 4 Cardiac-computed tomography appropriate use criteria

Indication	Appropriate use score
CCTA in patients with atherosclerosis in other vascular territories	
CTCA study in case of asymptomatic severe carotid or other large-vessel atherosclerosis	U (6)
CTCA study in case of TIA, stroke, or symptomatic peripheral arterial disease	U (6)
Fractional flow reserve CT and CT perfusion	
CT perfusion as alternative to SPECT or stress MRI in patients with evidence of obstructive CAD at rest CCTA	U (6)
Evaluation of fractional flow reserve by CCTA in case of intermediate coronary artery lesions detected by CCTA	U (6)
Evaluation of fractional flow reserve by CCTA to improve the specificity and positive predictive value in case of calcified coronary lesions at CCTA	U (5)
Left atrium thrombosis	
Use of cardiac-CT for the rule-out of LA thrombosis in patients with atrial fibrillation when transesophageal echocardiography is unfeasible or contraindicated	A (7)
Cardiac-CT and athletes	
History of family young sudden death	A (7)
After resuscitation	A (8)
After uncertain syncope	A (7)
Asymptomatic competitive athletes with positive ECG stress test, regardless of age and CV risk profile	A (8)
Equivocal symptoms for ischemic heart disease in competitive athletes with normal or near normal ECG stress test, regardless of age and CV risk profile	A (7)
ECG with rest anomalies in young athletes, after MRI excluded underlying structural cardiac disease	A (8)

CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CV, cardiovascular; LA, left atrium; SPECT, single-photon emission computed tomography. New proposed emerging applications.

Appropriateness of reader's expertise and reporting

Minimum requirements for competency in CCT have been defined for three levels of proficiency, in accordance with the American College of Cardiology (ACC)/American Heart Association (AHA) recommendations.[27] Briefly, for CCTA, level 1 defines a basic knowledge of CCT, which is sufficient for practice of general adult cardiology or general radiology, but not for independent interpretation of datasets. It requires 4 weeks of training, as well as hands-on study and interpretation of 50 cases of CCTA. Level 2 training defines the minimum recommended experience in order to independently perform and interpret CCTA. Level 2 training requires a cumulative duration of 8 weeks, mentored performance of 50 contrast-enhanced and 50 noncontrast scans, and hands-on study and interpretation of 150 contrast-enhanced CCT datasets. Level 3 training would qualify an individual to direct an independent CCT program. It requires 6 months of training, 100 cases performed, and 300 cases interpreted, and also 40 h of continuing medical education.

Coronary artery evaluation

Calcium scoring and coronary computed tomography angiography as a screening tool in asymptomatic patients

Noncontrast CCT for the assessment of coronary artery calcification (CAC) provides a noninvasive direct measure of coronary atherosclerosis. CAC scoring has a prognostic impact and has been shown to be an independent predictor of CAD, and to enhance traditional risk factor-based prediction models.[28] The AHA/ACC and the ESC guidelines recommend CAC use in asymptomatic adults at intermediate risk (class IIa) or with diabetes who are at least 40 years old and at low-intermediate risk (class IIb) to improve the assessment of patients with uncertain risk.[29,30] Although the acknowledged limitation of CAC scoring to rule out noncalcified plaque (NCP), among individuals with CAC 0, the prevalence of NCP is low and the prognostic impact is minimal because of the low event incidence occurring in patients with CAC 0 and the risk classes for whom CAC is recommended (low-to-intermediate risk score).[31] Summarizing, an extensive scientific literature demonstrated that CAC is an independent risk factor for cardiac events. Contrast CCTA is reliable for ruling out significant CAD in symptomatic low-to-moderate risk patients.[32] However, despite the reduction of the radiation dose, the risk of allergic reactions and kidney injury due to contrast agents is still a matter of some concern. Moreover, the negligible net reclassification improvement resulting from the addition of CCTA to a model based on standard risk factors and CAC in asymptomatic patients, as demonstrated by the COronary CT Angiography EvaluatioN For Clinical Outcomes (CONFIRM) registry,[33] may discourage the screening use of CCTA in this patient population.

Stenosis quantification, coronary plaque characterization, and correlation with atherosclerosis in other vascular territories

Coronary computed tomography angiography is able to provide a detailed assessment of the degree of coronary stenosis, with good correlation versus invasive coronary angiography (ICA) results, and atherosclerotic plaque features.[34] Although the available tools do not allow the exact measurement of stenosis degree, technology developments made some important steps forward.[35] The recommended stenosis grading endorsed by the Society of Cardiovascular Computed Tomography[36] and by this 'Working Group' is reported as follows:

(1) 0: absence of plaque and no luminal stenosis
(2) 1: (minimal) – plaque with less than 25% stenosis
(3) 2: (mild) – 25–49% stenosis
(4) 3: (moderate) – 50–69% stenosis
(5) 4: (severe) – 70–99% stenosis
(6) 5: (occluded) – 100% stenosis

Coronary computed tomography angiography provides an adequate description, at least with regard to the larger mid-proximal coronary segments of the atherosclerotic plaque, including presence and amount of calcium, plaque/vessel outward remodeling, and eccentricity and plaque volume.[37,38] Correlation studies between CAD and the atherosclerotic process affecting other vascular beds, performed by ICA[39] and more recently by CCTA,[40,41] showed that the presence of coexistent peripheral artery disease is associated with higher risk of recurrent cardiac symptoms and events. The reference literature suggests that 25–60% of patients with carotid artery disease have severe CAD markers, and one-third of peripheral artery disease patients have significant CAD.[42,43] On this basis, a low-dose CCTA study may be advised when the work-up reveals carotid or other large-vessel atherosclerosis.

The use of computed tomography in the emergency department

Computed tomography scan for safe discharge of patients with possible acute coronary syndrome

Scientific evidence for the use of CCTA in the emergency department (ED) has been substantiated further by two large trials: Randomized Controlled Study of a Rapid ''Rule Out'' Strategy Using CT Coronary Angiogram Versus Traditional Care for Low-Risk ED Patients with Potential Acute Coronary Syndromes (ACRIN-PA) [44] and Rule Out Myocardial Infarction using Computer Assisted Tomography.[45] Overall, the studies enrolled 2370 low-to-intermediate risk patients presenting with possible acute coronary syndrome (ACS) to the ED in the United States, and compared traditional care with a protocol including an early CCTA. The results show a significant reduction in length of stay and increased rate of discharge from the ED in the CCTA group without any adverse clinical event. However, incorporation of CCTA resulted in an increase in downstream testing and radiation exposure, with no decrease in overall costs of care. In a meta-analysis of four randomized controlled trials,[46] the use of CCTA in the ED was associated with decreased ED cost and length of stay. On the basis of these results and according to the current European guidelines, CCTA use in the ED should be considered as an alternative to ICA (as IIa, B) to exclude ACS when there is a low-to-intermediate likelihood of CAD, and when troponin and ECG results are inconclusive.[47]

'Triple rule-out' to exclude obstructive coronary artery disease, pulmonary embolism, and aortic dissection in the acute setting

The term 'triple rule-out' indicates an ECG-gated CT study for the evaluation of patients with acute chest pain in the ED to rule out three potential causes of symptoms: aortic dissection, pulmonary embolism, and CAD. The inherent advantage of CT is the rapid diagnosis with high negative predictive value (NPV) of these life-threatening conditions.[48] Of note, triple rule-out CT should be used in the ED, taking in account local expertise and availability of low-dose CT. However, according to the current guidelines, its role remains uncertain.[49]

Coronary computed tomography angiography in stable patients symptomatic for chest pain

Several noninvasive tests (exercise stress testing, stress echocardiography, myocardial perfusion imaging by Single Photon Emission Computed Tomography, or cardiac magnetic resonance) are commonly used as gatekeepers to ICA in stable symptomatic chest pain patients. Unfortunately, despite routine use of these tests, a little more than only one-third of the patients without known CAD who undergo elective ICA have obstructive CAD.[50] Moreover, the likelihood of obstructive CAD in patients with positive results of only noninvasive tests is moderately higher than in those who did not undergo any testing.[50] One potential explanation of the low diagnostic yield of elective ICA is the limited accuracy of noninvasive functional stress tests. The diagnostic accuracy of CCTA is highly influenced by different pretest likelihood of disease. Indeed, this imaging modality is associated with the higher diagnostic accuracy, mainly in patients with low-to-intermediate CAD risk,[51-53] whereas a moderate specificity and positive predictive value (PPV) has been found in high-risk patients.[53] In the latter patient group, coronary calcification was identified as the underlying reason for overestimation of coronary lumen obstruction.[54] However, it should be added that the recent introduction of high spatial resolution CCTA has partially improved the PPV.[37] As compared with exercise ECG, CCTA shows higher sensitivity and specificity,[55,56] and incremental prognostic value for adverse event prediction.[57,58] Therefore, in low-to-intermediate risk patients, coronary anatomy evaluation with CCTA may be the first-line diagnostic tool, followed by functional stress tests in the subset of patients with CAD above 50% only. This may allow the stratification of patients into the following three groups: patients with normal coronary anatomy in whom short/mid-term follow-up is not required; patients without flow-limiting coronary atherosclerosis in whom aggressive risk factor modification and mid-term follow-up are needed; and patients with flow-limiting stenoses in whom the need of revascularization could be highly advisable.

Evaluation of suspected coronary anomalies

Although coronary anomalies are relatively rare, some of them have the potential for causing ischemia, myocardial infarction, and sudden death.[59] In young athletes, coronary artery anomalies are the second most common cause of sudden death.[60] ICA is not always the best modality for identifying the origin and course of aberrant coronary arteries. By virtue of the three-dimensional nature of the dataset, CCTA is very well suited to detect and define the anatomic course of anomalous coronary arteries and their relationship to other cardiac and noncardiac structures. Reliability and accuracy of coronary anatomy assessment by CCTA in these patients are close to 100% and this has been shown in several studies.[61–63]

Evaluation of coronary arteries in patients with new-onset heart failure to assess cause

In two-thirds of heart failure cases, CAD is the underlying cause. Currently, clinical guidelines recommend ICA for patients with heart failure and angina (class I, level B), and for patients with heart failure and chest pain or suspected CAD (class IIa, level C).[64] However, ICA is inconvenient for patients and expensive for the community, associated with a non-negligible risk of complications (stroke, myocardial infarction, aortic dissection) and mortality, and requires technical skills and routine follow-up care.[65,66] Thus, patients with dilated cardiomyopathy (DCM) and a low-to-intermediate likelihood of CAD may benefit from a reliable noninvasive coronary imaging technique, whereas ICA may be reserved for those with proven CAD and in whom coronary revascularization may be indicated. Two studies have demonstrated that CCTA allows an accurate differentiation between idiopathic DCM and DCM caused by severe CAD – the so-called 'ischemic DCM'[2,67] that is commonly associated with at least significant two-vessel disease or significant lesions of the left main or proximal left anterior descending coronary arteries.[68] The excellent CCTA diagnostic accuracy may be explained by cardiac and coronary motion reduction due to the severe systolic dysfunction that probably plays a positive role in image quality.[2,67]

The first part of indications for coronary artery evaluation is reported in Table 1.

Use of coronary computed tomography angiography for coronary artery disease evaluation before valve surgery and noncardiac surgery

The current guidelines recommend ICA in all patients with valvular heart disease requiring valve surgery, apart from young patients (men <40 years and premenopausal women) without risk factors for CAD or when the risks of ICA outweigh the benefits (e.g. aortic dissection, aortic leaflet vegetations close to the coronary ostia, or occlusive prosthetic thrombosis leading to unstable hemodynamic condition).[69] CCTA is useful for excluding CAD in patients who are at low and intermediate risk of atherosclerosis. At present, limited data are available in the setting of preoperative risk stratification.[70] In a stepwise approach to preoperative cardiac assessment, CCTA may be considered when functional and imaging tests are inclusive or as an alternative to ICA in patients at low or intermediate risk.[70]

Assessment of the functional relevance of stenosis

The evaluation of the functional relevance of CAD can be done with stress perfusion computed tomography (CTP) or more recently with noninvasive evaluation of FFR-CT. Investigation in the field of CTP started two decades ago, but clinical use of the technique was limited by technical issues such as limited temporal, spatial and contrast resolution, and z-axis coverage. However, last generation scanners have partially overcome these limitations. Two main types of CTPs can be performed: static CTP, usually preferred for scanners with low temporal resolution and long scan time; and dynamic CTP, usually performed with scanners providing high temporal resolution and multiple samples of myocardial attenuation at sequential time points after contrast injection. For both approaches, intravenous (i.v.) adenosine infusion is usually used as a stressor. Until now, a few single-center studies only assessed the diagnostic accuracy of CTP and showed sensitivity and specificity ranging between 86–96% and 64–100%, respectively, with a mean radiation dose of about 11 mSv – a value comparable with that usually associated with nuclear stress test.[71,72] Recently, in the 'era' of Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trial, an emerging interest has increased regarding the possibility of measuring the FFR in a noninvasive setting.[73] Results from three prospective multicenter trials have suggested a good diagnostic accuracy of FFR-CT as compared with invasive FFR.[74–76] Nowadays, the ongoing Prospective LongitudinAl Trial of FFRCT: Outcome and Resource IMpacts study trial is evaluating if this technique, offering coronary anatomy and functional relevance of CAD in 'one-stop shop' without use of stressor, will be sustainable in terms of cost-effectiveness in intermediate-risk patients.

Coronary computed tomography angiography in lieu of serial invasive coronary angiography following heart transplantation

Cardiac-CT scan can evaluate wall thickening, as well as intimal hyperplasia, and might therefore be a useful mode of transplant CAD evaluation, grading, and monitoring.[77] Studies directly comparing CCTA with ICA for detecting cardiac allograft vasculopathy have demonstrated sensitivities of 70–86%, specificities of 92–99%, PPVs of 81–89%, and NPVs of 77–99%.[78]

Coronary stents

Use of CCTA has very high NPV in the range of 78–100% for ruling out in-stent restenosis (ISR), whereas the PPV is markedly worse (25–100%). The CCTA performance was further improved with recent scanner generation, including DSCT, that allowed reducing the number of stented segments excluded from analysis. There are four meta-analyses on the reliability and usefulness of CCTA for coronary stent assessment.[79–82] In the meta-analysis by Kumbhani *et al.*,[80] the overall sensitivity, specificity, PPV, and NPV for assessable stents were 91, 91, 68, and 98%, respectively. The meta-analyses by Sun and Almutairi[81] were based on the same clinical studies, but reached different conclusions. Indeed, these authors consider CCTA a reliable alternative to ICA, whereas Kumbhani *et al.*[80] concluded that stress imaging remains the most reliable noninvasive technique for diagnosing ISR. In addition to blooming effect and motion artifacts, stent-related factors such as stent diameter, strut thickness, stent design, and stent deployment technique may influence the visibility of stent lumen. There is consensus that stents with a diameter less than 3 mm are less likely to be accessible than stents with a diameter of at least 3 mm.[83–85] Moreover, the visibility of stent lumen may be also affected by previous complex procedures such as bifurcation or overlapping stenting. The impact on visibility of the stent design (open and closed cell) remains unclear.[84] Recently, the use of the new generation of scanner with a nominal spatial resolution of 0.23 mm has been demonstrated to allow a more accurate detection and quantification of coronary ISR – thanks to the improved spatial resolution.[86]

Coronary artery bypass grafts, including noninvasive coronary arterial mapping prior to repeat cardiac surgical revascularization

In coronary artery bypass graft (CABG) patients, CCTA showed excellent diagnostic results for the evaluation of venous and arterial grafts, whereas assessment of native vessels resulted limited mostly because of the severe calcifications often present in these patients, with about 10% of coronary segments being judged as nondiagnostic.[87–92] In the past 2 years, evolution of scanners markedly reduced radiation dose (<2 mSv), total amount of contrast media (<90 ml), acquisition time (few seconds), and global risk that is now close to zero.[93] Such technical improvements have the potential to significantly reduce the need for ICA in these patients.

Use of coronary computed tomography angiography in the evaluation of complex lesions before percutaneous coronary intervention (i.e. chronic total occlusions)

The endless development of new interventional devices expanded percutaneous coronary intervention (PCI) indications to ever-increasing coronary lesion complexity such as true bifurcation lesions (Medina1,1,1 chronic total occlusions, heavily calcified lesions, and left main trunk stenoses.[94–98] Multimodality and integrated imaging (ICA, CCTA, Intravascular ultrasound, optical computed tomography) have the potential to improve indication, intervention planning, and revascularization technique.[99]

The second part of coronary artery CCTA indications is reported in Table 2.

Noncoronary evaluation

Assessment of valvular heart disease, including anatomical assessment before transcatheter aortic valve implantation

Cardiac-computed tomography is a valuable complementary imaging method to assess valvular morphology and function.[100,101] Nowadays, its diagnostic role is particularly relevant in patients with inadequate images from other noninvasive imaging modalities (or with contraindications), as established by the latest criteria by Amaerican College of Cardiology Foundation, Society of Cardiovascular Computed Tomography (SCCT), American Heart Association on CCT appropriate use.[1] Indeed, CCT is emerging as a useful imaging technique in some patient subsets. To give an example, patients with severe aortic stenosis and discordant mean aortic gradient may pose a clinical dilemma. In these cases, assessment of CT-derived calcification load demonstrated to be able to confirm the severity of aortic stenosis. Other emerging indications are simultaneous aortic valve, thoracic aorta and coronary artery evaluation, and assessment of valve surgery complications.[102,103] Moreover, recent scientific literature shows a rising role for CCT in the field of prosthetic valve dysfunction, particularly in differential diagnosis between pannus and thrombus, based on the attenuation values.[104–106] Finally, CCT plays a critical role in patients scheduled for transcatheter aortic valve implantation (TAVI), providing detailed anatomic assessment of aorta and iliofemoral vessels, and of the aortic root and valve annulus, including annulus diameters and area, valve leaflet length, degree of leaflet calcifications, and distance between aortic annulus and coronary ostia.[107,108] Finally, recent data demonstrated that CCTA is also able to correctly rule out significant coronary stenoses in TAVI patients.[109]

Assessment of complex congenital heart disease, including anatomical assessment before percutaneous device closure of atrial septum defect or ventricular septum defect

Use of CCT for congenital heart disease (CHD) evaluation reaches different appropriateness levels depending on both the patients' clinical conditions and the kind of disease. It is particularly suitable for patients in the ICU who needs a fast diagnostic technique, allowing comprehensive evaluation of cardiac anatomy. Due to higher spatial resolution, CCT may be a preferable alternative to other imaging modalities for presurgical and postsurgical studies, particularly when an advanced morphology evaluation is requested.[110] However, some concerns regarding ionizing radiation may arise, especially in the younger patient population. Of note, in case of nondiagnostic echocardiography, CCT can define the anatomy of unusually located ventricular septum defects (VSDs) and characterize presence, size, and location of atrial septum defects (ASDs).[111] In summary, CCT may be recommended in specific clinical situations, particularly when cardiac magnetic resonance (CMR) is unfeasible, even considering that it provides limited functional information.[112,113]

Assessment of myocardial viability, function, and morphology

The ongoing advancements of CT technology allow improve ment in the visualization of myocardial tissue and iodine contrast distribution. Preliminary studies showed that CCT can be employed in the context of both acute and chronic myocardial infarction in order to evaluate early perfusion defects and delayed enhancement images.[114] Clinical studies indicated that CT may be able to provide similar information as CMR and PET in terms of myocardial viability using contrast enhancement technique.[115–118] The combination of coronary angiography phase-derived information with myocardial viability evaluation and regional function offers the possibility to readily infer an underlying ischemic cause. Despite the fact that CMR represents the most powerful tool to identify viable myocardium and nuclear imaging the most standardized technique, CT clinical trials show promising results in terms of both accuracy and prognosis.[119,120] Due to high spatial and temporal resolution, CCT has been validated for measurements of functional parameters such as left and right ventricular volumes and ejection fractions in addition to morphology visualization of cardiac chambers.[121,122]

Evaluation of cardiac masses and pericardial conditions

Echocardiography and CMR are the most frequently used and recommended imaging techniques to evaluate cardiac masses.[123] However, CTA appears a good alternative to CMR because of the ability of describing cardiac structures, the intrinsic advantage of defining the cardiovascular extent of the mass, and the capability of excluding CAD prior to surgical intervention.[1,124] Through multiplanar reconstruction and wide field of view, CTA allows detailed evaluation of cardiac and paracardiac masses and adjacent structures, including the lungs, enabling the planning surgery or interventional treatment strategies. Furthermore, CTA may also be useful in tumor staging by identifying metastases. Integration of CTA with 2-[18F] fluoro-2-deoxy-D-glucose (18F-FDG) PET may help to distinguish benign from malignant lesions, to more accurately stage malignancies, and to assess therapy response.[125]

Evaluation of left atrium and pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation and noninvasive coronary vein mapping prior to cardiac resynchronization therapy

Because of the technical complexity of radiofrequency catheter ablation (RFCA) of the pulmonary veins, the pivotal role of CCT has been proven in terms of reduced fluoroscopy time, arrhythmia recurrence, and the need for repeat procedure.[126] Moreover, an absolute increase in the single-procedure success rate ranging between 8.9[127] and 19%[128] has been demonstrated by three-dimensional (3D)-mapping with CCT. These data were further confirmed by the Italian multicenter registry[129] that showed higher recurrence rate of atrial fibrillation in patients with fluoroscopy-guided RFCA (44.6%) versus anatomy and electroanatomy LA mapping merging (22.6%). An additional electrophysiology indication for CCT is the evaluation of cardiac vein anatomy in patients referred to cardiac resynchronization therapy (CRT), in whom lead position in the latest segment of mechanical activation was shown to be a prerequisite for achieving better remodeling and improvement in outcome versus patients in whom lead position was not adequate.[130] Failing to position the left ventricular catheter in the target area is considered the main cause of inefficacy of CRT.[131] Accordingly, evaluation of cardiac vein anatomy by CCT[132] prior to CRT has been demonstrated to better guide the procedure in terms of lowering mean procedure and total fluoroscopic times, and improving the clinical outcome at follow-up.[133]

Noncoronary indications of CCTA are reported in Table 3.

Final topics

Prognostic role of coronary computed tomography angiography

Recently, CCTA was demonstrated to have robust prognostic value in patients with suspected but unknown CAD and in those with known CAD, including patients after CABG. Particularly, the results of the CONFIRM registry – a large, international, multicenter study – confirmed that CCTA has a leading role in mid-term prediction of all-cause mortality among more than 23 000 individuals without known CAD. Indeed, nonobstructive and obstructive CAD diagnosed by CCTA was associated with higher rates of mortality, with risk profiles differing for age and sex. It is noteworthy that absence of CAD was associated with a very favorable prognosis at mid-term (2.3 years) follow-up.[134] Subsequently, several studies derived from the CONFIRM registry strengthened the relevant mid-term prognostic value of CCTA in many ways: in symptomatic patients without known CAD and CAC score of 0, CCTA allows obstructive CAD diagnosis, which is associated with an increased event rate[135]; coronary revascularization in patients undergoing CCTA is associated with a survival benefit versus medical therapy when only high-risk CAD features are present[136]; the analysis of post-CCTA patterns of ICA and revascularization of intermediate-likelihood patients supported CCTA as an effective gatekeeper to ICA.[137] More recently, a few single-center studies demonstrated that CCTA maintains an important prognostic value at long-term follow-up (5 years), predicting a high rate of hard cardiac events in patients with obstructive CAD and demonstrating excellent prognosis in patients (including diabetic patients) without evidence of CAD.[138,139] Finally, a recent study showed CCTA is able to provide long-term prognostic information in CABG patients.[140]

Cardiac-computed tomography and athletes

Screening of structural cardiac disease, anomalies in origin-course-connection of the coronary arteries, and proarrhythmic conditions, namely arrhythmogenic cardiomyopathies, play a pivotal role in the prevention of sudden death in young elite athletes.[58] In adult competitive athletes (>45–50 years), timely detection of atherosclerotic significant lesions by CCTA has been proved to be superior to traditional noninvasive techniques.[141] For example, Kim *et al.*[142] reported that 2 in every 100 000 marathon runners (mean age 52 years) incurred sudden cardiac arrest/death (SCD). Among the eight survivors of cardiac arrest, nonobstructive CAD was the underlying cause in five athletes, none of whom had angiographic evidence of ruptured plaque. This observation suggests that even stable CAD may constitute a risk for SCD among the milieu of hemodynamic, catecholaminergic, and electrolyte imbalance associated with prolonged and intense exercise. Submitting athletes to CCTA is still an undefined indication due to the lack of prospective studies in large athlete populations. Other issues are the financial burden of screening low-risk patients and the potential to cause harm due to contrast agent allergies and radiation exposure.

Having these considerations in mind, the new proposed indications are reported in Table 4.

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