During the last decade, non-invasive cardiac imaging using computed tomography (CT) has achieved unprecedented level influencing our routine clinical practice. Technical advances in improving image quality and dedicated post-processing tools sustain this development. The early enthusiasm was rapidly tempered by radiation exposure resulting from cardiac CT (CCT). On the other hand, the advancement was so rapid that it was very difficult to clear the role of CCT and its adding value in patient management and decision therapeutic making in cardiovascular medicine. The last years had, however, considerably improved both issues and the utility of CCT; they can be broadened to resolve multiple questions in a wide spectrum of clinical situations. The main indications are certainly to answer multitude of questions within ischemic cardiomyopathy from risk assessment to postoperative assessment.

The objective of this review is to outline current routine indications (established indications) of CCT and report and discuss emerging applications. The reported indications are mainly based on
the intersociety 2010 report regarding the appropriate use criteria for CCT [1], the intersociety 2010 Expert consensus document on coronary CT angiography [2], and the ACCF/AHA clinical expert consensus document on coronary artery calcium scoring computed tomography in global cardiovascular risk assessment [3]. Recommended indications assume that the CCT is performed in accordance with the best practice guidelines by a trained team, an on dedicated and optimal equipment including possibilities for optimization of the scan protocol to the clinical indications, particularly to limit radiation dose. This assumes also that patients are correctly selected and prepared for CCT including ability to follow breath-hold instructions, regular heart rate, ability to receive beta blockers and at adequate body mass index (< 40 kg/m²). Table I summarizes exclusion criteria for optimal CCT angiography.

Ischemic heart cardiomyopathy

The main area for using CCT in routine practice is ischemic heart disease. While non-contrast enhanced CCT is used for global risk stratification, CCT angiography should be used in several clinical situations in symptomatic and asymptomatic patients with or without known CAD. Appropriate use of CCT supposes a clear understanding of the clinical situations. Particularly, the pretest clinical probabilities used to evaluate patient with suspected CAD or a cardiovascular risk is part of the knowledge precluding this appropriate use. Practically, there are two pretest probabilities, the first one is applied to asymptomatic patients and the second applied to symptomatic patients with non-acute symptoms, and a score applied to patient with acute chest pain. Different systems and algorithms have reported and evaluated in the literature [4–6].

Despite the absence of absolute consensus for using one homogenous and standardized method, the concept is still similar:

- pretest risk assessment in asymptomatic patients: the absolute risk is defined as the probability of developing hard cardiac (or cardiovascular) events in the next 10 years:
  - low risk, defined by age-specific risk less than 10%,
  - intermediate risk, defined by age-specific risk between 10 and 20%,
  - high risk, defined as the presence of diabetes mellitus in patient greater or equal to 40-year-old, peripheral arterial diseases or the 10-year greater than 20%;

- pretest probability of obstructive/significant CAD for symptomatic patients: the probability might be subject of variation by age and sex [1,7]:
  - low probability, less than 10% to have CAD,
  - intermediate probability, 10 to 90% to have CAD,
  - high probability, greater than 90% to have CAD;

- Thrombolysis in Myocardial Infarction (TIMI) score for patients with acute chest pain: the TIMI-risk score, which was initially developed for use in patients with unstable angina or non-ST-segment elevation myocardial infarction [8] is the most used and the most evaluated score for determining risk of having ACS:
  - low risk, defined as score of 0 or 1 and less than 5% likelihood to require intervention,
  - intermediate risk, defined as score between 2 and 5,
  - high risk, defined as score of 6 or 7 and 40% likelihood to require intervention.

Table II reports predictor variables used to calculate the TIMI score.

Detection of coronary artery stenosis

The main advantage of CCT is to provide high-resolution 3D angiogram of coronary arteries. Thus, the leading indication is to identify a significant coronary artery stenosis (CAS) (≥ 50%).

The proof of concept of CCT, using the latest generations of CT technologies (64-slices and higher), has been achieved in identifying significant CAS in patients with [2]. CCT was reported to have sensitivity and specificity, on per-patient basis, of 87 and 96%, respectively in the meta-analysis of Hamon et al. [9]. In a more recent review published in 2008 by Stein et al. [10], the mean positive predictive value was 93% and the mean negative predictive value was 96%. However, the mean prevalence of obstructive CAD in the population was 61%.

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**Table I**

Exclusion criteria for optimal cardiac CT

<table>
<thead>
<tr>
<th>Inability to breath-hold</th>
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<td>Arrhythmia, frequent ectopic beats</td>
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<td>Tachycardia</td>
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<td>Pacing wires</td>
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<td>Body mass index &gt; 40 kg/m²</td>
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**Table II**

Predictor variables for TIMI score determination (sum of factors: 0 to 7)

- Age > 65 years
- At least 3 risk factors for atherosclerosis
- Known coronary artery disease
- Two or more episodes of anginal chest pain in the preceding 24 hours
- Acetylsalicylic acid use in the seven days before hospitalization
- ST-segment deviation of 0.05 mV or more
- Elevated cardiac markers
multicenter CORE 64 trial [11] using the same 64-slices CT scan, with a prevalence of obstructive CAD of 56%, found a PPV of 91% and a NPV of 83%. Observed differences between single center and multicenter studies reflect also potential differences in the performance of expert CCT readers and community-based readers. Interpretation of CCT necessitates specific knowledge and dedicated training.

In patients with acute setting, CCT could be a reliable for rapid triage of patients presenting to emergency centers with chest pain, and for evaluation of patients with equivocal stress test results who might otherwise require invasive angiography. Beside its clinical value, the CCT is considered the most cost-effective strategy for the initial evaluation of patients who have chest pain with an intermediate prevalence of obstructive CAD, followed by invasive coronary angiography for severe CAD or equivocal test results [12]. The application of CAS detection in clinical practice using CCT is of interest in multiple clinical situations.

CCT is indicated as primary investigation modality or in case of failed or equivocal previous tests. In non-acute circumstances, there are two different target populations that have benefit from CCT as primary investigation to detect CAS:

- non-acute symptomatic patients without known CAD:
  - symptomatic patients AND with low or intermediate pretest probability of having CAD,
  - symptomatic patients with coronary graft to evaluate graft patency;
- asymptomatic patients:
  - asymptomatic patients with prior percutaneous coronary intervention to evaluate a left main coronary stent with a diameter of 3 mm or greater,
  - asymptomatic patient at intermediate pretest probability of CAD AND candidate for non-coronary cardiac surgery.

The CCT angiography is indicated in specific clinical situations as an additional test after [1]:

- ECG exercise test:
- in patient with continued symptoms AND normal ECG exercise test,
- in patient with Duke Treadmill Score-Intermediate risk findings;
- stress perfusion imaging:
  - in patient with discordant ECG exercise test and stress perfusion study findings,
  - in patient with equivocal result of stress perfusion imaging,
- in patient with new onset or worsening symptoms in the setting of normal past stress perfusion imaging.

In patients with acute chest pain, the CCT is recently added to the care work-up for reliable triage of patients in emergency units. The role of CCT angiography is regarded as an additional tool to exclude acute coronary syndrome (ACS) in patients with low and intermediate risk of ACS. The pooled data demonstrates that the predictive negative value of CCT angiography in this group of patient is very high, about 99% [13–15]. This is supported by the very low major cardiac events, characterized by death, cardiac death, or myocardial infarction at 30 days, 6 months, or at 1 year in patients who were discharged with no or mild non-obstructive diseases on the CCT angiography [15].

In the trial Coronary Computed Tomography for Systematic Triage of Acute Chest Pain (CT-STAT) CCT angiography reduced the time to diagnosis as compared to the standard of care in more than 50%, reduced costs by approximately 40%, and lowered the radiation dose by approximately 30% [16]. CCT is considered as appropriate indication [1] in:
- patient with chest pain AND with low or intermediate risk of having ACS.

Implementation of the CCT for chest pain work-up needs however several prerequisites as building a coordinated multidisciplinary team with emergency physicians, radiologists, cardiologists, evolving well-trained technicians and nurses and having administration support. Availability for 7 days a week and 12 at least 12 hours a day is a key of success of such process.

**Evaluation of cardiac function**

In case of complete acquisition of data during the whole cardiac cycle (acquisition with retrospective synchronized reconstructions to the ECG), global and regional wall motion anomalies can be detected and quantified from cine CCT. Calculated systolic and diastolic volumes allow stroke volume measurement and ejection fraction determination. These values are comparable to those obtained by other techniques as previously reported in comparative studies [17–19].

Evaluation of the left ventricle function is considered appropriate in patients following myocardial infarction or in patient in heart failure AND inadequate assessment from other non-invasive methods.

Evaluation of the right ventricle is considered appropriate in patients suspected for arrhythmogenic right ventricular cardiomyopathy or for quantitative evaluation of the right ventricle function [1].

Since assessment of cardiac function necessitates data from the whole cardiac cycle, which needs dedicated protocols with significantly higher radiation exposure, assessment of the left ventricle and ejection fraction estimation could not be recommended as a part of all routine CCT, especially for CAD indications.

**Global cardiovascular risk stratification**

After more than a decade of debate and controversies, the role of CCT as a tool for assessment of the global cardiovascular risk was clearly recognized just 5 years ago [1,3,20]. However, the role seems to be largely underused, especially in Europe. Basically, the historic coronary calcium score (CCS) described by Agatston et al. [20] is still the reference despite reported convincing improvements both in the detection and in the quantification processes [21,22]. The use of the CCS is mainly justified by the extensive literature and evaluation of the method during the last decades.

Indication of the CCS is considered appropriate in two clinical situations:
- patient without a known CAD and at intermediate risk for cardiovascular events;
- patient with family history of premature CAD at a low risk for cardiovascular events.

Technically, the CCT for the CCS determination requires no contrast media and is a low dose CT.

**Non-ischemic cardiomyopathies**

Additionally to the evaluation of coronary arteries to determine the etiology of cardiomyopathy (ischemic versus non-ischemic), CCT might have a role to assess the myocardium and cardiac function in non-ischemic cardiomyopathies as in hypertrophic cardiomyopathy, non-compaction or restrictive cardiomyopathies [23] as well as in the arrhythmogenic right ventricular cardiomyopathy [18]. However, indication of CCT is limited to clinical situations where other non-invasive techniques are not completely diagnostic or contraindicated.

**Congenital heart disease**

CCT could reasonably be added to the armamentarium for imaging adult congenital heart diseases as an alternative method to cardiac MR and echocardiography [19,24]. Coronary anomaly, aneurysm or fistula should be regarded with a specific interest. Evidence supports the use of CCT for detection and preoperative mapping of anomalous coronary arteries [25,26] (figures 2–4).

Indications for CCT are considered appropriate for [1]:
- assessment of anomalies of coronary arteries and other thoracic arteriovenous vessels;
- assessment of complex adult congenital heart disease.
Cardiac valves

Based on morphologic and functional possibilities offered by 3D isotropic imaging of the leaflets of aortic and mitral valves, CCT has been used to assess these valves in several clinical settings (figure 5). Detection and quantification of calcifications of the aortic and mitral valve can be easily obtained [27]. The calcification severity correlates significantly to aortic stenosis [28]. The residual valve area that could be derived from CCT data is significantly correlated with the valve area obtained by echocardiography for aortic valve as well as for mitral valve [29].

Induced changes by valve diseases in the cardiac morphology and function could be accurately assessed by the CCT. However, the role of CCT in routine practice for these indications is limited as echocardiography and cardiac MR are the mainstays of identifying and characterizing valve stenosis and/or insufficiency. Indication for CCT is considered appropriate for patient with clinically suspected significant native or prosthetic valve dysfunction and inadequate images from other non-invasive methods [1].

In contrast, the recent advances in transcatheter therapies applied to the cardiac valve open new applications for CCT.

Figure 2
Patient with recent chest pain and myocardial ischemic pattern in myocardial perfusion study in the left ventricle inferior wall
The patient had multiple coronary artery by-pass grafts (CABG) performed 15 years and 20 years ago. Cardiac CT angiography: A, B: axial transverse images show a large aneurysm of the right CABG. C: 3D volume rendering reconstruction shows the extent of the aneurysm. The CABG is still patent.

Figure 3
Chest pain with equivocal ECG exercise in a 38-year-old patient
Cardiac CT angiography: A: centerline based reconstruction of the left anterior descending artery. A significant stenosis in the proximal segment related to non-calcified plaque. B: centerline based reconstruction (long axis) of the right coronary artery. Notice the anomalous of the origin from the left antro-lateral cusp with an inter-vascular course of the proximal segment. C: 3D volume rendering reconstruction.
The transcatheter aortic valve implantation could be done either by a retrograde transfemoral or an antegrade transapical approach [30]. Both approaches require morphologic evaluation of the ascending aorta, coronary arteries, aortic annulus and left ventricle out-flow tract [27,31] (figure 6). In more sophisticated approach, angulations of the aortic valve plane could be given to optimize the view for the valve implantation [30,32]. For the transfemoral access, CCT should be combined to CT angiography of the abdominal aorta and pelvic arteries to complete information needed for using pelvic (minimal diameter of arteries, angulations and degree of calcifications).

**Pulmonary veins and left atrium**

Patients with refractory atrial fibrillation have benefit from electrical isolation of the pulmonary vein antrum. The technique, based on radiofrequency ablation catheter, requires delineation of pulmonary vein and characterization of the left atrial anatomy including the left appendage [33]. CCT is the most reliable method to provide vital information for optimal procedure compared to echocardiography, trans-oesophageal echocardiography or retrograde invasive venography [34] (figure 7).

There are two objectives of CCT in the atrial fibrillation management:

- preoperative evaluation of the pulmonary vein and the left atrium;
- postoperative evaluation of pulmonary vein. Pulmonary vein stenosis is a rare but the most important induced complication of the electrical ablation. Serial CCT a 3 and 6 months after the procedure are usually recommended.
Indication of CCT for evaluation of pulmonary vein anatomy is considered as appropriate prior to radiofrequency ablation for atrial fibrillation [1].
From the technical point of view, a low dose CCT is recommended for pulmonary vein assessment [35]. In addition, the CCT with high-resolution isotropic images offers the best digital imaging platform that could be integrated to electroanatomical mapping to improve localization of pulmonary veins and reduce fluoroscopy time of ablation procedure [36].

**Coronary veins**
The objective of cardiac resynchronization therapies is achieved by endocardial implantation of a left ventricular pacing lead into the lateral cardiac veins through the coronary sinus. Due to the large anatomic variations, the CCT might have a significant adding value in the procedure plan to facilitate catheterization procedure and optimize the resynchronization [37] (figure 8).
Indication of CCT for non-invasive coronary vein mapping is considered as appropriate prior to placement of biventricular pacemaker [1].

**Figure 6**
Pretherapy assessment prior to transapical aortic valve implantation with CCT
2D multiplanar reconstructions evaluated the aortic valve (A, C), the coronary arteries position and the annulus (B) and the left ventricle apical wall.

**Figure 7**
Cardiac CT of the pulmonary veins
A: axial transverse image. B: 2D reconstruction along the inferior right pulmonary vein. C: 3D volume rendering reconstruction.
Cardiac masses

While echocardiography and cardiac MR are the mainstays for cardiac mass characterization, CCT could be useful to detect calcifications or fatty component. It can be used for further evaluation of intracardiac thrombus following inconclusive or abnormal echocardiography, or when echocardiography is not feasible, particularly to assess the left atrium and the left appendage (figures 9–11).

**Figure 8**
Cardiac CT to assess coronary veins after failure of lead implantation to resynchronization in a patient with ischemic heart failure
A: axial transverse image showing enlarged left ventricle with of a myocardial scar. B and C: 3D volume rendering reconstructions with variable transparency of the coronary venous drainage

**Figure 9**
Axial transverse CT scan
Thrombus visible in the apex of the left ventricle of patient with recent history of myocardial infarct

**Figure 10**
Axial transverse CT scan
Thrombus in the left atrium missed in echocardiography
Indication of CCT is appropriate for evaluation of cardiac mass (suspected tumor or thrombus) and inadequate images from other non-invasive modalities [1].

**Pericardial diseases**

Delineation of the pericardial anatomy and detection of pericardial calcification are the most important advantages of CCT over other imaging modalities. Indication of CCT to evaluate pericardial anatomy is considered appropriate [1].

**Emerging indications**

**Plaque imaging**

The plaque imaging is probably the most challenging area for the future of CCT. Despite the initial enthusiasm about the potential of CCT to characterize different components in the plaque, offering a virtual histology of atherosclerotic plaque [38,39], the place of CCT in routine practice is still uncertain [2]. Given the ability of CCT to identify calcified and non-calcified components of the plaque and given its potential to differentiate certain non-calcified components, the CCT is expected to play a role in detecting vulnerable plaque, vulnerable patient and monitor the progression or regression of the disease over time. Multiple factors limit the current enthusiasm. This includes non-standardized definitions and protocols, high variability [40], radiation exposure issue and the few data that the literature provides in limited selected populations. In addition, contrast media might change the attenuation value of the plaque components [41] and therefore a CT attenuation value-based subclassification of the non-calcified component becomes more complex than expected.

Several reports have recently outlined the feasibility and the potential of perfusion CCT (rest CCT and pharmacologic stress CCT) in the detection of ischemic myocardium [42–45] with accuracy. Even if theoretical incremental value of ischemia detection in the same examination than coronary assessment is of interest, the place of such procedure requires further evaluations. Furthermore, the exposure issue should be also integrated in building pathways in patients with suspected CAD.

**Myocardial viability**

CCT is comparable to cardiac MR in detection and quantifying acute and chronic myocardial infarct [46–49]. Furthermore, CCT predicts left ventricle function recovery after revascularization [50]. Thus the CCT is an alternative method to cardiac MR for viability assessment. However, viability CCT requires additional radiation dose and needs larger volume of contrast media than routine CCT for coronary assessment. The role in clinical practice has to be defined [50].

**Conclusion**

Major advances in CT technology have been achieved over the last years, particularly in cardiac applications. Major efforts have been made to optimize image quality, standardize protocols regarding clinical indications and limit the radiation exposure. In a few years many clinical studies have been conducted with a high level of consistency to provide a solid background for defining the role of CCT in clinical practice. The primary role is probably the adding value if CCT in patients with suspected CAD. The CCT is now ready to be a part of routine practice in evaluating symptomatic patients as well as a
valuable tool in the risk stratification. However, even if research and evaluation should continue to refine the role of CCT for future, appropriate use of CCT is recommended. Optimal preparation of the patient, training of physicians, and the multidisciplinary interaction between actors are the key of successful implementation of CCT in daily practice.

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References


Cardiac CT: Practical approach to integrate appropriate indications in daily practice


