Appropriateness criteria for the use of cardiac computed tomography, SIC-SIRM part 2: acute chest pain evaluation; stent and coronary artery by-pass graft patency evaluation; planning of coronary revascularization and transcatheter valve procedures; cardiomyopathies, electrophysiological applications, cardiac masses, cardio-oncology and pericardial diseases evaluation

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In the past 20 years, cardiac computed tomography (CCT) has become a pivotal technique for the noninvasive diagnostic work-up of coronary and cardiac diseases. Continuous technical and methodological improvements, combined with fast growing scientific evidence, have progressively expanded the clinical role of CCT. Randomized clinical trials documented the value of CCT in increasing the cost-effectiveness of the management of patients with acute chest pain presenting in the emergency department, also during the pandemic. Beyond the evaluation of stents and surgical graft patency, the anatomical and functional coronary imaging have the potential to guide treatment decision-making and planning for complex left main and three-vessel coronary disease. Furthermore, there has been an increasing demand to use CTT for preinterventional planning in minimally invasive procedures, such as transcatheter valve implantation and mitral valve repair. Yet, the use of CCT as a roadmap for tailored electrophysiological procedures has gained increasing importance to assure maximum success. In the meantime, innovations and advanced postprocessing tools have generated new potential applications of CCT from the simple coronary anatomy to the complete assessment of structural, functional and pathophysiological biomarkers of cardiac disease. In this complex and revolutionary scenario, it is urgently needed to provide an updated guide for the appropriate use of CCT in different clinical settings. This manuscript, endorsed by the Italian Society of Cardiology (SIC) and the Italian Society of Medical and Interventional Radiology (SIRM), represents the second of two consensus documents collecting the expert opinion of cardiologists and radiologists about current appropriate use of CCT.

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Introduction

At the dawn of the new millennium, cardiac computed tomography (CCT) aroused a stunning breakthrough in the noninvasive diagnostic work-up of coronary and heart disease.[1] The very high negative-predictive value (NPV) of CCT to identify obstructive coronary artery disease (CAD) is well known,[2] whereas the results of large multicenter randomized trials, designed to assess the prognostic value of CCT, have become available only very recently,[3,4] changing the perception of CCT in the clinical arena. As a result, the scientific community recognized the CCT as the first line diagnostic test for most of patients with suspected chronic coronary syndromes, including patients with no known CAD and stable typical or atypical chest pain, or angina equivalent.[5] Moreover, because of a continuous improvement of spatial and temporal resolution of last generation CT scanners, along with progressive radiation exposure lowering, the traditional role of CCT moves from the rule-out to the rule-in of CAD, proposing the CCT as a test to implement prevention strategies in some specific settings.[6] At the same time, different strategies were developed to integrate the outstanding CCT anatomical data, with functional assessment of stenosis (i.e. fractional flow reserve and myocardial perfusion imaging),[7] as well as plaque,[8] myocardial[9] and pericardial fat[10] characterization. Furthermore, evolving data define the role of CCT in the setting of acute chest pain,[11] in the setting of congenital diseases[12] and for planning trans-catheter valve implantation.[13] Finally, the European Society of Cardiology (ESC) has provided guidance regarding testing during the pandemic, where using CCT is the preferred test to noninvasive functional testing in patient with atypical ST-elevation myocardial infarction presentation.

In this complex and revolutionary scenario, there is a clear need of updating previously published documents on the appropriateness and the clinical/practical use of CCT.[14–17] Taking into account the existing guidelines and all the available evidence, the Italian Society of Cardiology (SIC) and the Italian Society of Medical and Interventional Radiology (SIRM) endorsed a working group of expert cardiologists and radiologists to conceive a shared position paper on appropriate use CCT, providing a practical approach and novel applications in daily clinical practice.

Definition of appropriateness and applied methodology

The writing committee discussed the table of content and assigned referrals for each chapter.

Each referral conducted literature searches and drafted the assigned section highlighting indications and rating them according to the following score:

(1) Strong recommendation: there is evidence, general agreement, or both, that the test is useful (benefit >>> risk).
(2) Moderate recommendation: there is conflicting evidence or opinion about the usefulness of the test; the weight of evidence/opinion; however, is strongly in favour of the test's usefulness (benefit >> risk).
(3) Weak recommendation: the test's usefulness is less well established; there is a small net benefit (benefit ≥ risk).
(4) No recommendation: there is evidence or general agreement that the risk/harm outweighs benefits (benefit < risk).
(5) Expert opinion: there is insufficient evidence or evidence is unclear or conflicting, and further research is recommended in this area. No clinical use. The use of this technology would have to be confined within accredited research centers.

Assigned scores were discussed in consensus by all authors and unanimously approved.[18]

Cardiac computed tomography in acute chest pain syndromes

Acute chest pain is one of the most frequent causes of access to the emergency department.[19] A prompt diagnosis of an acute coronary syndrome (ACS) is as undiagnosed ACS leads to increased risk of death and unstable angina.[20] Conversely, incorrect diagnosis of ACS leads to potential unnecessary hospital admissions, excess downstream testing and increased costs.

Evidence supporting the role of CTT in the emergency department

Several randomized controlled trials (RCT) and observational studies support the use of CCT in the emergency department. In the ROMICAT study, patients with low-to-intermediate likelihood of ACS and inconclusive triage, underwent CCT to detect CAD with more than 50% stenosis. Fifty percentage of patients were free of CAD by CCT and had no ACS.[21] A meta-analysis of observational studies confirmed a 99.3% NPV of CCT in excluding major adverse events in acute chest pain patients.[22] In the randomized CT-STAT trial, CCT strategy provided a more rapid and cost-efficient diagnosis than rest–stress myocardial perfusion imaging (MPI), without undiagnosed ACS. In the ROMICAT II trial, CCT strategy increased the rate of direct discharges and reduced the median length of stay and time to diagnosis in comparison to the standard of care (SOC).[11] In the ACRIN-PA trial, CCT strategy allowed a well tolerated and expedited discharge from the emergency department in comparison to SOC, without missed ACS.[23] These findings were also confirmed in a meta-analysis of the randomized trials.[24] Finally, in the CT-COMPARE study, CCT had better diagnostic performance compared with exercise stress ECG,[25] whereas in the PROSPECT study, CCT and MPI showed a similar performance.[26] However, around 10% of patients with ACS have angiographically normal coronary arteries. In this setting, the role of CCT for the evaluation of coronary dynamic obstruction, vasospasm, micro-circulatory dysfunction, or spontaneous coronary dissection remains to be established. In theory, coronary CCT has appeal for the diagnosis of suspected spontaneous coronary dissection, as it is noninvasive and provides visualization of the arterial wall as well as the lumen. However, it suffers from lower spatial and temporal resolution than conventional angiography, leading to lower sensitivity and risk of false-negative results.[27] Current guidelines do not recommend CCT as a first-line investigation for acute spontaneous coronary dissection, although there is emerging evidence of its utility in follow-up where it can help reassure clinicians and patients of healing and recanalization particularly in larger caliber arteries.[27] Further evaluation is now needed to determine if CCT should be used routinely for this purpose in clinical practice. One should realize 10% of nondiagnostic ACS is a relatively important limitation. However, normal coronary anatomy detected by CCT clearly does not need immediate percutaneous or surgical intervention, improving the yield of catheterization procedures. Obviously, the role of CCT for guiding further noninvasive evaluation in this 10% of patients with normal coronary arteries remains to be evaluated.

Value of so-called ‘high-risk plaque features’ in acute coronary syndromes

According the ROMICAT-II study,[28] CCT parameters indicating the ‘high risk plaque features’ include a ‘spotty’ pattern of calcification, low attenuation plaques (<30 HU), napkin-ring sign and large degree of positive remodeling. This trial has demonstrated that the high-risk plaques features assessed by a qualitative read of CT images were independent and incremental to significant stenosis and clinical risk assessment (age, gender, number of cardiovascular risk factors) for predicting ACS during the index hospitalization, with nine-fold increase in the likelihood of ACS. Importantly, the results of this study suggested that patients with mild stenosis and plaque features with increased probability to develop an ACS cannot be safely discharged from the emergency department, and the evaluation of hs-troponin will be necessary to exclude an ACS. Finally, take into account the results of the recent PROSPECT-II study, the management of these plaques, prone to rapid progression and rupture, remains matter of debate as further randomized trials are needed to determine whether medical therapy and/or interventions based on CTA characterization of these plaques improves clinical outcome in patients with ACS.[29]

’Triple rule out’ in the emergency department

It is well known that aortic dissection and massive pulmonary embolism may present with acute chest pain and may mimic or even overlap with ACS. The timely diagnosis of these two syndromes are of utmost importance for patient management.[30] Specialized ‘triple rule-out’ (TRO) protocols are currently used,[31,32] with a higher amount of contrast.[33] Regardless, the optimal scan settings are different between the region of interest, and in case of an aortic syndrome, visualization of the complete aorta and the iliac bifurcation may be warranted. Although some reports suggest a slightly higher yield of pulmonary embolism and aortic dissection in the emergency department, this benefit comes with higher nondiagnostic image quality, radiation and contrast dose.[34] However, the proximal ascending aorta is always evaluable in a coronary CCT study, while the opacification of the pulmonary artery is often compromised.[35] In clinical practice, the fundamental question is which population benefit most from TRO CCT. It is well known that coronary CTA and TRO CTA are similar with respect to diagnosis of CAD in patients with low–intermediate risk but there is not enough evidence to determine whether TRO compares favorably or unfavorably with dedicated angiography of the pulmonary arteries or the aorta.[36] However, as the coronary arteries are in the field of view of every contrast chest CTA, they may be evaluated by EKG gating a single-phase prospective acquisition. The most appropriate clinical scenario for TRO CTA use may be aortic dissection and pulmonary embolus (in men >45 years and women >55 years) as the CTAs are infrequently positive (<15%) and do not provide an explanation for the presenting symptoms for which, because of its prevalence, CAD may be the culprit.[37] Thus, other than the availability of adequate scanner technology, to avoid an increase in contrast volume and radiation dose, and the operator expertise in emergency department, it may be appropriate to use EKG gating for CTA performed for aortic dissection as well as pulmonary embolus studies in men older than 45 years and women older than 55 years, analyzing and reporting coronary arteries.

Cardiac computed tomography potentialities in detecting other cardiac causes of acute chest pain: acute myocarditis and cardiomyopathies

Other cardiac causes of acute chest pain may mimic an ACS, such as ischemic events without obstructive CAD, tako-tsubo cardiomyopathy, cardiac infective, inflammatory diseases (myocarditis, pericarditis), storage diseases and cardiomyopathies of unknown origin. In this clinical scenario, CCT has demonstrated a good correlation with cardiac magnetic resonance (CMR) in the assessment of regional ventricular function,[38,39] with a 10% increase in sensitivity for ACS detection,[40] and, yet, lead us the possibility to analyze myocardial strain in chronic infarcted patients.[41] Recently, CCT-based late iodine enhancement (LIE) demonstrated a good capability to detect and quantify focal scarring in different settings, such as heart failure,[42] myocardial infarction[43] and structural arrhythmogenic cardiac diseases.[44] In addition, using precontrast and postcontrast scan, CCT offers the possibility of quantifying myocardial extracellular volume fraction (ECV), increased in myocardial fibrosis, with results validated both against CMR and histological picture.[45] The combination of CAD assessment, functional evaluation, focal scar and interstitial fibrosis detection, proposes CCT as an attractive imaging modality in emergency department when CT scan is already clinically indicated, or CMR is contraindicated or not available. However, only very few reports support these potential application of CT scan: for detecting acute myocarditis,[46] for differentiating ACS from acute myocarditis or cardiac amyloidosis[47] and for detecting takotsubo cardiomyopathy.[48] Large and dedicated studies should be performed before the implementation of these new CT application in clinical practice.

Cardiac computed tomography during the pandemic for 'quadruple-rule-out' protocol

COVID-19 has disrupted traditional cardiovascular care pathways, leading to significant challenges. Historically, CCT has been used for TRO of acute chest pain. However, during the pandemic, COVID-19 pneumonia, acute viral peri-myocarditis and pulmonary embolism were common findings,[49] and CCT may be a front-line test for the evaluation of chest pain, considering the testing logistical problems, leading to the creation of a 'quadruple-rule-out' protocol.[50] A recent study showed that the short times required for a CCT, with limited human contacts, are particularly suitable for a COVID-19 setting.[51] In this study, the clinical role of TRO remains modest. Moreover, the LIE-CT protocol, as an alternative to CMR, may be helpful in the diagnosis of COVID-19 myocarditis, especially considering fulminant associated myocarditis presenting as ST-elevation myocardial infarction. Furthermore, in COVID-19 setting, studies have shown that CCT can provide imaging biomarkers, such as total thoracic calcium volume and pulmonary artery diameter, capable of predicting the prognosis of the patients, potentially allowing better allocation of scares resources.[52,53] The use of CCT in advance of ICA, might be particularly helpful whereby the findings of ST-elevation and echocardiography are divergent. The ESC has provided guidance, in which CCT is the preferred noninvasive functional test during the pandemic,[54] also for the evaluation of the left atrial appendage (LAA) thrombosis. Even in the American Society of Echocardiography (ASE) imaging guidelines under COVID-19, CCT is suggested as an alternative to echo imaging, because of the amount of increased viral shed exposure from aerosolization.[55]

Cardiac computed tomography for stent patency evaluation

Over the last decade, the evolution of coronary CT scanner for evaluation of stent patency has paralleled the evolution of stent design and construction. Specifically, the application of 64-slice coronary CT scan has a very high NPV, in the range of 78–100%, for exclusion of in-stent restenosis (ISR), whereas its positive-predictive value (PPV) is markedly worse (25–100%). Moreover, the number of unassessable stents progressively decreased from an average of 14% in 16-slice CT[56–58] to 8% with state-of-the-art 64-slice, and to 4.2% with last high definition CT scanner. There are currently three meta-analyses on the value of 64-slice CT imaging in coronary artery stents.[59,60] The overall sensitivity, specificity, PPV and NPV for assessable stents as reported by Kumbhani *et al.* were 91, 91, 68 and 98%, respectively. If all stents were included in the analysis, the overall sensitivity, specificity, PPV and NPV would have decreased to 87, 84, 53 and 97%, respectively.[59] Two of the meta-analyses on 64-slice CT are based on the identical set of clinical studies yet come to different conclusions. Although Sun and Almutairi[60] consider 64-slice CT as a reliable alternative to conventional coronary angiography, Kumbhani *et al.*[59] conclude that stress imaging remains the most acceptable noninvasive technique for diagnosing ISR. Using 64-slice CT, aside from blooming and motion artifacts, stent-related factors, such as diameter, thickness, design and type of placement (e.g. overlapping stenting) may influence the visibility of stent lumen. After at least 2 years from revascularization, there is a consensus that stents with a diameter below 3 mm are less likely to be accessible than stents with a diameter of at least 3 mm.[61–63] In addition, more complex procedures with bifurcation or overlapping stenting, where there are multiple layers of metal cause more blooming, thereby further limiting the visibility of the stent lumen. The effect of the stent design remains unclear, as no differences were found between open and closed cell design.[61] With the advent of bioresorbable vascular scaffolds (BVS), the ABSORB II trial showed that CTA in comparison to intravascular ultrasound have similar diagnostic accuracy to identify ISR.[64] However, the ABSORB III trial did not demonstrate a 3-year advantage of BVS in comparison to everolimus eluting stent, rising strong uncertainty on their safety and efficacy in clinical practice.[65] Thus, whether on one hand, the evolution of stent design and construction failed to achieve the goal of better stent patency, on the other hand the tremendous technical evolution of modern CT scanner demonstrated that the prospectively ECG-triggered single heart-beat, high-pitch spiral acquisition dual source CT is able to maintain diagnostic accuracy for the assessment of ISR, reducing radiation doses[66] Additionally, iterative reconstruction techniques are replacing filtered back projection (FBP), reducing image noise without affecting spatial resolution, and with low radiation doses.[67,68] Using a whole organ high-definition CT scanner Andreini *et al.*[69] showed that coronary CCT can evaluate ISR with high diagnostic accuracy and, moreover, the use of CCT stress perfusion[70] may improve the ISR diagnostic rate and accuracy of coronary CTT alone, compared with gold standard ICA and invasive FFR but its availability is still very limited in clinical practice.

Cardac computed tomography for coronary artery by-pass graft patency evaluation

In coronary artery by-pass graft (CABG) patients, CCT angiography, compared with ICA, is faster, less expensive and invasive, can be performed in an outpatient setting, and has a fair patient acceptability. CCT may be more accurate for graft than for native coronary arteries evaluation because of less movement through cardiac cycle, wider luminal diameter and lower rate of calcifications. The efficacy of CCT in the evaluation of CABG patients has been demonstrated in several studies. Hamon *et al.*[71] analyzed 15 pooled studies conducted with 16-slice and 64-slice CT. CCT demonstrated high diagnostic accuracy (90 and 96% for 16-slice and 64-slice CT, respectively), sensitivity (97.6%) and specificity (96.7%) using ICA as gold standard. However, 7.6% of grafts were not assessable. Older generation CT scanner limitations in the evaluation of CABG, namely radiation exposure, insufficient spatial and temporal resolution, beam-hardening artifacts (because of calcifications and surgical clips) and blooming artifacts, have been overcome by novel CT scanners.[72,73] In a recent meta-analysis by Chan *et al.*,[74] including 31 studies (1975 patients with 5364 graft) conducted with 64-slice CT, CCT demonstrated a sensitivity of 96.1%, specificity of 96.3%, PPV of 94.3% and NPV of 99% versus ICA for both graft stenosis or occlusion assessment. In addition, assessment of venous grafts showed superior sensitivity compared with arterial ones (97.6 vs. 89.2%, $P = 0.004$), without differences in specificity. Overall, CCT has a high sensitivity, specificity and NPV compared with ICA and should be recognized as an accurate and noninvasive method for evaluation of graft patency in symptomatic CABG patients. Furthermore, the continuous technological improvement of CT scanners enables the assessment of challenging patients, such as those with high heart-rate,[75] while reducing radiation exposure and contrast media volume.[76–79] Finally, the prognostic utility of CCT in CABG patients has been demonstrated[80–82]: patients with two or more unprotected coronary territories are at higher risk for cardiac events.

Coronary cardiac computed tomography as a tool for planning percutaneous coronary intervention and optimal revascularization strategy

In comparison to ICA, the inherently three-dimensional nature of coronary CCT has an advantage in providing incremental anatomic information, such as lesion length and true vessel diameters,[83,84] helping us in better lesion coverage and optimal stent sizing,[85,86] as well as in identifying "high-risk" plaque features (e.g. low-attenuation plaque with positive remodeling)[87] for tailoring revascularization strategies.[88,89] In setting of coronary chronic total occlusion (CTO), the CT-based J-CTO, the CT-RECTOR and the KCCT score, showed better predictive performance of successful CTO recanalization compared with the angiographic J-CTO score.[90–92] Moreover, the use of CT-derived SYNTAX score, as alternative to the ICA-SYNTAX score, may guide revascularization strategy among multivessel CAD patients,[93,94] with a fair agreement with ICA and good reproducibility. Finally, a recent trial demonstrated a strong agreement of a Heart Team treatment decision-making based on CTA-derived SYNTAX II score with the decision derived from ICA, among de novo left main or three-vessel CAD (correlation coefficient of 0.98), resulting in a similar treatment recommendation in 93% of the cases.[95] Before the translation of these findings in patient-oriented outcomes, further larger randomized clinical trials are needed.[79,96] In the foreseeable future, the multimodal image integration of both noninvasive and invasive anatomic and functional coronary data,[97] the periprocedural use of CCT in the catheterization suite,[84,98] and the use of simulation modeling for CAD will support a personalized decision-making process of anatomically complex CAD.[99] Most recently, the FORECAST investigators[100] set out to determine the cost implications of FFRCT in 1400 patients with stable chest pain undergoing coronary CCT, compared with standard of care in the UK. No significant difference in cost over 9 months between the two groups of patients was observed. In addition, in the experimental arm, the observed reduction of the ICA rate and the coronary revascularization rate were not enough to balance the costs of the CCT and the FFR-CT. Moreover, the trial found no significant difference in MACCE, angina symptoms, quality of life or requirement for coronary revascularization. Importantly, the study was only designed to investigate resource allocation between those randomized to CCT with selective FFR-CT and those randomized to usual care, not to investigate cost benefits or patient care benefits of specific alternative investigation strategies, such as stress echocardiography. Finally, the FORECAST trial did not address the critical question regarding when exactly FFR-CT should be utilized in the clinical care pathway. FFR-CT may be of most use when CCT has been performed for stable chest pain, and angina symptoms persist despite optimal medical therapy. FFR-CT could be retrospectively assessed on the original CCT with the goal to assess suitability for revascularization. Thus, taking into account that FFR-CT is financially demanding, further randomized trials are needed to elucidate the possible cost-effectiveness of FFR-CT in this setting.

Limitations of coronary cardiac computed tomography

In clinical practice, it is important to recognize several pitfalls in interpreting the degree of coronary stenosis. Severe calcifications represent a main obstacle in interpreting the degree of stenosis in a coronary vessel, because of the blooming artifact.[5,14–18] A sharper kernel can be used for the reconstruction of the dataset and thus help reduce the blooming artifact. A higher BMI (>30 kg/m^2) could reduce the accuracy of a CCT scan, mainly because of reduced signal-to-noise ratio secondary to increased X-ray scatter. Several approaches, such as increased tube voltage, very good heart rate preparation, and administration of contrast with a higher rate (up to 7 ml/s) can improve the quality of the CCT. Depending on the protocol used, step or stitch artifacts can also reduce diagnostic image quality. Selecting the appropriate protocol depending on the heart rate variability is, therefore, of paramount importance to avoid these types of problems. Whenever the heart rate is very stable and less than 65/min, a high-pitch spiral protocol might be more appropriate. Whenever many extrasystoles are present or the heart rate shows high variability, such as in atrial fibrillation, acquisitions in systole should be favored.[14–18,69] Of note, the high-pitch spiral protocol is not without drawbacks, even when the patient has a low heart rate with a minimal heart rate variability.[69] Lastly, care should be taken when analyzing certain segments of the coronary arteries, which have a very curved trajectory. This applies for the distal segment of the right coronary artery and origin of the posterior descending artery, the proximal segment of the left anterior descendent artery with the origin of the first diagonal branch, and origin of the first obtuse marginal branch.

Cardiac computed tomography for planning of surgical and transcatheter valve procedures

In addition to the role as an alternative to ICA before surgical valve procedures for evaluation of coronary arteries,[101] as described in the part 1 of the present document, CCT is emerging as a valuable complementary imaging method to assess valvular morphology and function.[102,103] Nowadays, CCT can be used in patients with inadequate echocardiographic image quality or with severe aortic stenosis and discordant mean aortic gradient as CCT can confirm the severity of aortic stenosis by quantifying the calcification load.[17,104]

In the setting of transcatheter aortic valve replacement (TAVR), CCT plays a critical role in providing detailed anatomic assessment of aorta and ileo-femoral vessels (nongated CT) and of aortic root and valve annulus (diameters and area), valve leaflet length and degree of calcification, and distance between aortic annulus and coronary ostia (gated-CT).[105,106] Furthermore, coronary CCT may also rule out significant CAD in TAVR candidates.[107] Another emerging indication is the assessment of surgical and transcatheter aortic valve replacement complications, namely bioprosthetic valve disfunction because of pannus or thrombus. In fact, CCT can detect subclinical leaflet thrombosis manifesting as hypo-attenuating leaflet thickening (HALT), possibly associated to the more severe hypo-attenuation affecting motion (HAM), leading to start an appropriate anticoagulant strategy.[108]

More recently, CCT is emerging as a key imaging modality for planning transcatheter mitral (TMVR) and tricuspid (TTVR) valve procedures in patients with prohibitively high surgical risk. In TMVR candidates, CCT may provide paramount data regarding morphology of mitral annulus (using a simplified D-shape model), extent and location of annular calcifications, landing zone and myocardial shelf (to ensure proper device capture and positioning), circumflex artery and coronary sinus course, aorto-mitral angle and neo-LVOT obstruction.[102,109,110]

In TTVR candidates, CCT depicts tricuspid annulus morphology, identifies the landing zone, measures diameters of inferior and superior vena cava and their angulation towards tricuspid annular plane and the distance between the valve annulus and the right coronary artery.[111,112]

Cardiac computed tomography for evaluation of distinct phenotypes of cardiomyopathies: dilatative, hypertrophic and arrhythmogenic

Cardiomyopathies are defined as myocardial diseases associated with mechanical and/or electrical dysfunction in the absence of underlying ischemic, hypertensive, valvular or congenital heart disease[113] Due to its high NPV for ruling out CAD, CCT is accepted as first-line imaging modality in the initial evaluation of known or suspected heart failure patient, even without angina, to exclude ischemic cardiomyopathy. Furthermore, CCT can quantify left ventricle (LV) volumes and global systolic function and assess regional wall motion abnormalities.[114,115] Nowadays, retrospectively gated cardiac CT is considered an accurate and reproducible alternative to echocardiography and CMR for the evaluation of biventricular volumes and function when this information cannot be achieved because of suboptimal acoustic windows, claustrophobia, significant artifact from metallic implants limiting the utility of echocardiography and CMR.[116] CCT-derived ventricular volumes and ejection fraction have been shown to correlate well with CMR as a gold standard and may be superior to both 2D and 3D echocardiography.[115] It is a quicker scan, requires shorter and fewer breath holds and is often better tolerated than CMR. Furthermore, recent development in scanners and acquisition techniques allows achieving high-quality images with lower radiation doses, making the technique more attractive in population with cardiomyopathy associated with several comorbidities.[117] In the setting of dilated phenotype, CCT, by simultaneously assessing presence of CAD, demonstration of fatty replacement and/or of LIE with ischemic pattern may favor the diagnosis of ischemic cause. Otherwise, absence of CAD and/or CCT features suggesting ischemic scars may orient diagnosis towards nonischemic causes. Moreover, in selected patients with contraindication to CMR, it has been suggested that CCT can detect noncompaction cardiomyopathy.[118]

In patients with hypertrophic phenotype, CCT is always recommended when CAD needs to be excluded. Furthermore, in this setting, CCT may provide in-depth assessment of myocardial changes with demonstrated capability to support the diagnosis of cardiac amyloidosis by quantifying the extracellular volume fraction.[119] Moreover, in patients with obstructive hypertrophic cardiomyopathy (HCM), CCT can assess intramyocardial fibrosis and represents a useful guide for planning of surgical or percutaneous intervention.[120]

In patients with arrhythmogenic right ventricular dysplasia, CCT can reliably detected RV wall motion abnormalities, dilation and dysfunction,[121] together with fibro-fatty RV replacement (with/without LV involvement).

Cardiac computed tomography electrophysiological applications

Left atrium

Pulmonary vein isolation, either by radiofrequency or cryoablation, is the most common ablation technique for atrial fibrillation.[122] The integration of 3D CT-derived cardiac images into electro-anatomical maps (EAM) allows ablation procedures designed specific to patient anatomy.[123] Furthermore, CCT is routinely used to assess postprocedural complications, such as esophageal injury and pulmonary vein stenosis.[124] In patients with atrial fibrillation, CCT has been proposed as an alternative to transesophageal echocardiography to exclude left atrium and left atrial appendage (LAA) thrombosis, using dual phase CCT acquisition to avoid false-positive findings.[125,126] In patients scheduled for percutaneous LAA exclusion because of contraindications for long-term anticoagulant treatment,[122] CCT can accurately evaluate LAA morphology and sizing before device deployment to avoid complications.[127] In addition, CCT can identify device malposition, leaks and thrombus at follow-up.[128,129] The use of CT-derived 3D printing LAA models may further increase the accuracy of CCT in sizing the LAA occluding devices.[130]

Cardiac venous system

The evaluation of cardiac venous anatomy by CCT prior to cardiac resynchronization therapy (CRT) may improve the clinical outcome.[131,132] Considering the huge variability of venous anatomy,[133] CCT may help in correct delivery of CRT,[134] as well as in proper placement of the left electrode into the target vein.[135] Venous CCT images should be preferablly acquired in the systolic phase of cardiac cycle,[136] and when a combined evaluation of coronary arteries is required, a single angiographic scan with a 4 s delay with respect to conventional angiographic phase might be acquired.[124] Efficacy of CRT is impaired by the scar[137–139] in the posterolateral LV wall, common site for LV lead placement.[139] Whenever the gold-standard CMR is contraindicated, CCT may identify myocardial scar,[44] thus, in combination with venous system anatomy, potentially accurately guiding lead placement.

Left and right ventricles

Catheter ablation is aimed to electrically isolate arrhythmogenic myocardium responsible of ventricular tachycardia onset, previously identified as areas of endocardial or epicardial surface with altered electrical pathway at the electro-anatomical voltage map (EAM). Due to several limitations of EAMs, several studies documented that noninvasive imaging guidance for ventricular tachycardia

Table 1 Recommendation of cardiac computed tomography in acute chest pain: rule-out CAD, triple rule-out, acute myocarditis, myopericarditis and tako-tsubo

Clinical setting	Diagnostic step	Recommendation	Indication
Patients with acute chest pain, low-to-intermediate likelihood of ACS and inconclusive triage based on troponin and ECG testing	First diagnosis	B	Rule-out of CAD. Use of CCT possibly restricted in settings with older technology and low expertise.
	First diagnosis (during pandemic)	A	
Triple rule-out (combined rule-out of ACS, acute aortic syndromes and pulmonary embolism)	First diagnosis	E	Available data generally suggest utility and advantages in using TRO CT instead of SOC in these patients. However, CT protocol standardization and large trials of validation are missing, and further research is recommended in this area. Moreover, current use of CT-based TRO could be restricted in some ED realities, due to limitation in state-of-the-art scanner and fully trained operator availability.
	First diagnosis (during pandemic)	B	
Rule-out ACS combined with investigation of other cardiac causes of acute chest pain, through CT-based global and regional ventricular function assessment and myocardial characterization (LIE – ECV)	First diagnosis	E	This is a very attracting and promising approach when CT is already clinically indicated or CMR contraindicated/not available but balance of benefits and harms cannot be determined at this moment, because of insufficient data. Interesting field for future research.
	First diagnosis (during pandemic)	B	

ACS, acute coronary syndrome; CAD, coronary artery disease; CMR, cardiac magnetic resonance; CT, computed tomography; ECV, extracellular volume fraction; ED, emergency department; SOC, standard of care; TRO. triple rule-out.

ablation is able to improve efficacy and safety of ablation.[140–143] The main advantage of CCT is its higher spatial resolution and the possibility to be performed in patient with cardiac devices.[44] Importantly, CCT is able to depict myocardial scars, which represent the substrate of ventricular arrhythmias, as areas characterized by severe wall thinning (wall thickness <5 mm),[144] typically in case of postischemic scar,[145] or characterized by LIE.[44]

Cardiac computed tomography for evaluation of cardiac masses, cardio-oncology and pericardial disease

Cardiac masses

Cardiac masses are categorized as either neoplastic or nonneoplastic. Primary cardiac tumors are rare (prevalence: 0.001–0.03%) whereas metastases are reported to be 20–40 times more common.[146] Echocardiography plays a pivotal role in the diagnosis of cardiac masses, mainly by differentiating tumors from thrombi, which are more common,[147,148] and in surgical resection planning. In case of poor acoustic windows, CMR or CCT can be performed synergistically with echocardiography. CCT can be used to characterize the mass, especially if calcified, to depict its anatomical relations with cardiac structures, to assess possible chest and lung concomitant lesions and corresponding vascular structures, and to exclude obstructive CAD or coronary involvement by the mass before surgery.[149]

Cardio-oncology

Cardiovascular disease is the leading cause of death in cancer survivors.[150] Anticancer therapies may cause myocardial fibrosis, congestive heart failure, pericardial or valvular disease, CAD and arrhythmias[151,152] by multiple

Table 2 Recommendations of coronary cardiac computed tomography at least 64 slice or more for evaluation of stent and graft patency

Clinical setting	Diagnostic step	Recommendation	Indication
Evaluation of ISR by last generation, whole organ high-definition CT scanner, including SAFIRE software	Follow-up	A	Several studies support the use of last generation CCT scan for the assessment of ISR, with SAFIRE software on board as it is able to maintain diagnostic accuracy, reducing radiation doses
Left main drug eluting stent in symptomatic patients or after 2 years	Follow-up	A	Patients with ostium and body LM stent
		B	Patients with bifurcation LM-LAD-Circumflex stent
Drug eluting stent at least 3 mm in symptomatic patients or after 2 years	Follow-up	A	single drug eluting stent $\geq$3 mm
		B	Multiple/long drug eluting stent $\geq$3 mm
Multiple/long drug eluting stent less than 3 mm in symptomatic patients or after 2 years	Follow-up	C	single drug eluting stent $<$3 mm
		D	Multiple/long drug eluting stent $<$3 mm
Evaluation of ISR with CCT stress perfusion	Follow-up	E	This is a very attracting and promising approach, as it may increase specificity, positive predictive value, and diagnostic accuracy over regular CTA, especially in case of suboptimal CTA quality or prior revascularization. However, current lack of methodological standardization, limited validation data, technological requirements, and dose concerns hamper widespread clinical application.
Evaluation of patency of BVS	Follow-up	E	It is appropriate to perform CCT as an alternative to invasive coronary angiography for BVS evaluation in selected experimental setting
Evaluation of stent patency in venous graft	Follow-up	A	Single drug eluting stent $\geq$3 mm
		B	Single drug eluting stent $<$3 mm
		B	Multiple/long drug eluting stent $\geq$3 mm
		C	Multiple/long drug eluting stent $<$3 mm
Evaluation of stent patency in arterial graft	Follow-up	B	Single drug eluting stent $\geq$3 mm
		C	Single drug eluting stent $<$ 3 mm
		C	Multiple/long drug eluting stent $\geq$3 mm
		D	Multiple/long drug eluting stent $<$ 3 mm
Evaluation of CABG patency in symptomatic patients	Follow-up	A	Patients with venous grafts
		A	In case of ICA failure in evaluating LIMA or RIMA patency
		B	Patients with arterial or mixed grafts
		C	Evaluation of native vessels (reduced image quality due to high burden of atherosclerosis and consequent artifacts)
Evaluation of CABG patency in asymptomatic patients	Follow-up	A	After 5 years
		B	Patients with new onset left ventricular systolic dysfunction
Routine use of coronary CCT before clinically indicated ICA after CABG	Follow-up	E	It is appropriate to perform CCT for evaluation of patients with prior CABG, particularly if graft patency is the primary objective. More data need for this strategy
Evaluation of CABG course before redo interventions	Procedural planning	A	Identification of LIMA and RIMA course
Evaluation of prognosis in CABG patients	Follow-up	A	Patients with two or more unprotected coronary territories are at higher risk of cardiac events

BVS, bioabsorbable vascular scaffold; CABG, coronary artery bypass grafting; CCT, cardiac computed tomography; ICA, invasive coronary angiography; LAD, left arterial descending; LAMI, left internal mammary artery; LM, left main; RAMI, right internal mammalian arterial.

pathways: inflammation, prothrombotic state, myocardial toxicity, coronary vasospasm and hypertension.[153] According to current guidelines, patients are screened using clinical, echocardiographic and serological biomarkers.[154–156] The growing volume of patients living with cancer, the advent of new technological opportunities to improve diagnosis, and the necessity of early recognition of cancer therapy-related toxicity mandate integrative multidisciplinary approach and care in a specialized environment, whereby cardiac CCT will strongly be involved.[157] Specifically, CCT can be used to screen patients undergoing RT as it allows for the identification of CAD and has a prognostic utility in identifying subjects at increased risk for all-cause death[158] whereas a negative CCT portends an extremely low risk of cardiac death.[159] Current guidelines suggest screening for CAD 5–10 years after chest irradiation as part of surveillance for late cardiovascular toxicity.[150] Approaches for early detection of CAD include anatomical and/or functional assessment. CCT allows direct visualization of coronary artery atherosclerosis and is particularly suitable for detecting CAD at an early stage.[159] Importantly, the assessment and diagnosis of ACS in cancer patients can be complicated by hematological abnormalities, such as anemia, thrombocytopenia, and coagulation disorders, which portent a higher risk of invasive angiography complications. CCT may, therefore, represent a valid alternative for the diagnosis of significant CAD, even in the settings of ACS.[160] Finally, where surgical revascularization is warranted, CCT provides a further assessment of potential RT-induced damage to mediastinal structures, such as the pericardium, and atherosclerotic disease to the internal mammary arteries,[161] which may complicate the surgery. Other than CAD, valvular heart disease (VHD) can be a complication of chest irradiation, and the risk of VHD is related to the radiation dose.[162]

Table 3 Recommendations of coronary cardiac computed tomography for planning percutaneous coronary intervention and transcatheter valve procedures

Clinical setting	Diagnostic step	Recommendation	Indication (#)
LM and no-LM coronary artery cross-sectional size at the target lesion site (MLD and MLA)[a]	Procedural planning	E	Lesion length and true vessel diameters 'High-risk' plaque features Plaque location and burden Vessel tortuosity Bifurcation involvement # The use of CCT in this clinical setting can assist interventional cardiologists, favoring tailored revascularization strategies. Interesting field for future research.
CCT characteristics to guide CTO PCI	Procedural planning	E	3D spatial orientation and course of the occluded segment, Length of the occlusion and number of occlusion sites, Grade of calcifications (site, extension and arc of circumference) and stump morphology (tapered or blunt), Vessel shrinkage, presence of side branches and bridging collaterals # The use of CCT in this clinical setting can assist interventional cardiologists with selective catheter placement, appropriate guidewire choice, accurate stent size selection, and, most importantly, development of a stepwise revascularization strategy plan.
Planning of surgical valve procedures	First diagnosis	([a])	Evaluation of coronary arteries
Planning of SAVR or TAVR	First diagnosis	A	Diagnosis of aortic stenosis by quantifying calcium load in patients with inadequate echocardiographic image quality or severe aortic stenosis and discordant mean aortic gradient
Planning of TAVR	First diagnosis	A	Evaluation of aortic valve annulus, aortic root, valve leaflet length and degree of calcification, distance between aortic annulus and coronary ostia Evaluation of aorta and ileo-femoral vessels Evaluation of previous CABG
		B	Evaluation of native coronary arteries and stents on a case-per-case basis considering local availability of technology and expertise
		C	In patients with chronic kidney disease
Assessment of SAVR and TAVR complications	Follow-up	A	Diagnosis of hypo-attenuating leaflet thickening (HALT) and hypo-attenuation affecting motion (HAM) in TAVR recipients Diagnosis of pannus or thrombosis in SAVR recipients
Planning of TMVR	First diagnosis	A	Evaluation of mitral annulus, extent and location of annular calcifications, landing zone and myocardial shelf, left ventricle outflow tract, circumflex artery and coronary sinus course, and aorto-mitral angle Evaluation of coronary arteries
Planning of TTVR	First diagnosis	A	Evaluation of tricuspid annulus, landing zone, right coronary artery course, and inferior and superior vena cava diameters and angle with annular plane Evaluation of coronary arteries

CCT, cardiac computed tomography; CTO, chronic total occlusion; LM, left main; MLA, minimal luminal area; MLD, minimal luminal diameter; PCI, percutaneous coronary intervention. *, Intravascular ultrasound (IVUS)-derived MLD of less than 2.8 mm or MLA of less than 6 mm^2 for US population and MLA of 4.5 mm^2 or less for Asian population suggests a physiologically significant lesion according to fractional flow reserve (FFR); CABG, coronary artery bypass grafting; HALT, hypo-attenuated leaflet thickening; HAM, hypo-attenuated leaflet motion; ICA, invasive coronary angiography; TAVI, transcatheter aortic valve implantation; TMVR, transcatheter mitral valve implantation. [a] See Part I.

CCT is increasingly used as an adjunct for the diagnosis and evaluation of VHD, particularly in the setting of aortic stenosis. Aortic calcium quantification has become a vital component of the diagnosis of low-flow, low-gradient aortic stenosis with preserved ejection fraction[101] where the aortic calcium score has been shown to correlate with the degree of severity. CCT is also crucial to surgical planning as RT is frequently associated with mediastinal fibrosis and a porcelain aorta, impacting the suitability for conventional surgical treatment of VHD.[163] Transcatheter aortic valve implantation (TAVI) may represent a more favorable treatment option, and CCT also plays a significant role in the work-up and preprocedural planning of TAVI procedures.[101] Finally,

Table 4 Recommendation of cardiac computed tomography for electrophysiological applications, cardiac masses, cardio-oncology and pericardial disease evaluation

Clinical setting	Diagnostic step	Recommendation	Indication
Atrial fibrillation catheter ablation	Procedural planning	A	Anatomy depiction and integration of 3D CT-derived images into electro-anatomical maps - Exclusion of left atrium or left atrial appendage thrombosis when echocardiography is inconclusive or as an alternative to transesophageal echocardiography
	Follow-up	A	Assessment of postprocedural complications (e.g. esophageal injury or pulmonary vein stenosis)
Left atrial appendage exclusion	Procedural planning	A	Evaluation of left atrial appendage morphology, device sizing, and exclusion of thrombosis
		C	Evaluation of left atrial appendage morphology and device sizing with CT-derived 3D-printed models
	Follow-up	B	Assessment of postprocedural complications (e.g., device malposition or peri-device leaks) and evaluation of treatment efficacy (i.e. appendage complete thrombosis) in order to guide antiaggregation strategy
Cardiac resynchronization therapy	Procedural planning	B	Evaluation of cardiac vein anatomy to guide LV lead placement
		C	Identification of postero-lateral LV scar when CMR is contraindicated
		B	Identification of procedural complications (e.g. perforation or dissection of coronary sinus)
Ventricular tachycardia catheter ablation	Procedural planning	A	Integration of CT-derived 3D anatomy with ventricular electro-anatomical maps especially in complex procedures (e.g. identification of coronary arteries in epicardial procedures, previous failure, large ventricular aneurysm)
		E	Preoperative myocardial substrate characterization
		B	Preoperative myocardial substrate characterization in patients with cardiac devices and contraindication to CMR
Functional evaluation of cardiomyopathies (ventricular and atrial volume quantification; wall motion abnormalities qualitative evaluation)	First diagnosis or follow-up	B	In patients with poor echocardiographic image quality and contraindication to CMR
Exclusion of CAD as concomitant or causative feature of cardiomyopathies	First diagnosis	A	Rule out of CAD
Myocardial tissue characterization	First diagnosis	B	When CMR is contraindicated CCT could be considered as an alternative
Hypertrophic phenotype	Procedural planning	A	Planning of surgical or percutaneous alcoholization intervention
Cardiac mass	First diagnosis	A	For the assessment of mass characteristics and relations with surrounding structures, especially when CMR is contraindicated For exclusion of coronary involvement by the mass and of obstructive CAD before surgery
	Follow-up	A	For the evaluation of postchemotherapy or surgical treatment
Cardio-oncology	First diagnosis	A	In case of suspected chemotherapy and radiotherapy-induced CAD in cancers survivors
	Follow-up	A	
	First-diagnosis	E	For myocardial tissue characterization when CMR is contraindicated
Pericardial disease	First diagnosis	C	For diagnosis when CMR is contraindicated
		B	In case of significant pericardial effusion (without tamponade) to exclude aortic dissection, after trauma, or if echocardiography is inconclusive
		A	In case of constrictive pericarditis (with or without effusion) to confirm diagnosis if echocardiography is inconclusive and for pericardiotomy planning
		A	In case of masses, tumors, or cysts to confirm diagnosis
		A	In case of congenital absence of pericardium to confirm diagnosis and to detect associated malformations, especially when CMR is contraindicated
	Follow-up	B	For the evaluation of postmedical therapy or surgical treatment

AF, atrial fibrillation; CA, catheter ablation; CAD, coronary artery disease; CCT, cardiac computed tomography; CRT, cardiac resynchronization therapy; LAA, left atrial appendage; VT, ventricular tachycardia.

mediastinal irradiation can be complicated by acute and chronic radiation pericarditis,[164] easily assessed on CCT images, being average pericardium thickness measures 0.7–2 mm.

Pericardial disease

Many diseases can affect the pericardium, including infections, neoplasms, traumas, primary myocardial diseases and congenital diseases. Echocardiography is the first-line imaging modality, especially in unstable patients with pericardial effusion or tamponade, thanks to its ability to visualize pericardial leaflets and efficiently evaluate the hemodynamic effect of the disease.[165] However, CCT may be useful in specific settings. For example, in calcific pericarditis, CCT may identify calcifications, pericardial thickening and effusion.[166] Calcifications are often segmentally distributed but they can as well be absent: in this case, the diagnosis of restrictive cardiomyopathy becomes more likely. CCT is invaluable in surgical planning of pericardiectomy as well as for follow-up. Moreover, CCT allows to distinguish between hemorrhagic, purulent or malignant pericardial effusions and simple serous/chylous effusions (Tables 1–4).[167]

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Conflicts of interest

There are no conflicts of interest.

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