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Invited review

Cardiac computed tomography in the contemporary evaluation of infective endocarditis

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A B S T R A C T

Increasing data have accumulated on the role of Cardiac Computed Tomography (CCT) in infective endocarditis (IE) with high accuracy for large vegetations, perivalvular complications and for exclusion of coronary artery disease to avoid invasive angiography. CCT can further help to clarify the etiology of infective prosthetic valve dysfunction (e.g. malposition, abscess, leak, vegetation or mass). Structural interventions have increased the relevance of CCT in valvular heart disease and have amplified its use. CCT may be ideally integrated into a multimodality approach that incorporates a central role of transesophageal echocardiography (TEE) with 18-FDG PET and/or cardiac magnetic resonance in individually selected cases, guided by the Heart Team. The coronavirus-19 (COVID-19) pandemic has resulted in renewed attention to CCT as a safe alternative or adjunct to TEE in selected patients. This review article provides a comprehensive, contemporary review on CCT in IE to include scan optimization, characteristics of common IE findings on CCT, published data on the diagnostic accuracy of CCT, multimodality imaging comparison, limitations and future technical advancements.

1. Introduction

Infective endocarditis (IE) is a complex entity caused by damage to the valvular endothelium that causes platelet and fibrin deposition leading to vegetations; accurate imaging is essential to improve prognosis. Traditionally IE has been evaluated by echocardiography (transthoracic (TTE) and transesophageal (TEE)) as the first line diagnostic testing modality.[1] However, important data on the diagnostic accuracy of cardiac computed tomography (CCT) have accumulated during recent years.[2–5] Structural interventions have increased the relevance of CCT in valvular heart disease and have amplified its use.[6–8] The non-invasive nature of CCT and the minimal person-to-person contact have also renewed interest in CCT amidst the coronavirus disease 2019 (COVID-19) pandemic as a means to reduce the risk to healthcare workers (HCW) of high risks of exposure with TEE as an aerosol generating procedure.[9]

This review article provides a comprehensive, contemporary review on CCT in IE to include scan optimization, characteristics of common IE findings on CCT, published data on the diagnostic accuracy of CCT, multimodality imaging comparison, limitations and future technical advancements.

2. CCT imaging principles, scan optimization and clinical indications in infective endocarditis

2.1. CCT imaging principles and scan optimization

CCT is a robust modality for cardiac anatomy evaluation given the sub-millimeter (~0.5 mm) "isotropic" resolution that is superior when compared to other imaging modalities.[10] As a full 3D cardiac dataset, the use of post-processing multiplanar reconstruction (MPR) techniques enables structures to be interrogated from any angle allowing for accurate assessment of pathologic location (anterior, posterior, medial, lateral). This allows, for example, an anterior vegetation or abscess to be better

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visualized when compared to transesophageal echocardiography (TEE), whereas far-field structures (anterior aortic annulus, tricuspid valve) may suffer from acoustic shadowing. Additionally, calcium can be much more clearly differentiated from tissue on CCT in comparison to echocardiography. With the high spatial resolution of CCT, paravalvular abscesses may be clearly seen due to excellent tissue-contrast differentiation highlighting heterogeneous regions. An important benefit of CCT angiography is for coronary artery evaluation in patients requiring surgery, potentially avoiding invasive cardiac catheterization. This may be of important benefit to avoid interaction of invasive catheters with an infected valve that could lead to vegetation embolization or associated abscess tissue. Although higher radiation dose is received with retrospective ECG-gated acquisition (3–7 mSv) in comparison to prospective ECG-gated acquisition, retrospective is the preferred method in IE to assess for vegetations, valve mobility and dehiscence.

Retrospective ECG-gated acquisition should be performed with scan coverage of the entire heart as per SCCT guidelines.[11] A sufficient IV contrast volume rate should be administered to provide differentiation between contrast-enhanced blood pool and surrounding structures. A coronary artery volume contrast flow rate (5–6 ml/s) is advisable for the best visualization of small abscesses and pseudoaneurysms, while tailoring to local scanner characteristics. If evaluating only the left or right side of the heart, triggering or timed-bolus should be protocoled for the specified region. However, in the usual circumstances, both left and right sided opacification would be ideal to evaluate all cardiac valves and surfaces. This may require a longer contrast bolus to increase time of opacification. A triphasic contrast protocol, which can mitigate streak artifact and prolong contrast time, is recommended when opacifying the right heart.[7] Multiphase CCT acquisition, reconstructed at 5–10% increments, is ideal to maximize temporal distinction of vegetations, pseudoaneurysms, and paravalvular abscesses across the cardiac cycle (See Fig. 1). For the assessment of aneurysms and pseudoaneurysms, the use of pre- and post-contrast images may further allow for identification of an intramural hematoma showing a low attenuation coefficient (60–70 HU) in the aortic wall in non-contrast images.[12] For optimal prosthetic valve visualization a medium smooth tissue reconstruction kernel is typically utilized.[13]

2.2. *Clinical indications for CCT in IE*

CCT doesn't have the high temporal resolution that 2D-Echocardiography has, and potentially could miss small highly mobile vegetations, however it can identify large vegetations and although less common, abscesses in patients with suspected native valve IE. If a cardio-embolic event in the coronaries is suspected in the context of IE, CCT can help in diagnosing and identifying it. For patients with suspected IE that may have a relative contraindication for TEE, such as esophageal pathology or concerns for contagion as with COVID, CCT may be considered as an alternative. For patients with IE undergoing surgical valve replacement, CCT could help identify presence of obstructive CAD that may benefit from surgical revascularization. As for surgical planning for aortic IE, CCT may help defining the size, anatomy and calcification of the aortic valve, root and ascending aorta for surgical planning. In right-sided endocarditis, CT may reveal concomitant pulmonary disease, including abscesses and infarcts. For prosthetic valves it can be used to detect abscesses/pseudoaneurysms with a diagnostic accuracy similar to TEE, and is superior in the detecting the extent and consequences of any perivalvular extension, including the anatomy of pseudoaneurysms, abscesses and fistulae as it will be discussed further.

3. CCT findings and characterization of infective endocarditis

Important imaging findings in IE may be categorized into valvular (valvular vegetations, valve perforations) and perivalvular (abscesses, pseudoaneurysms, prosthetic dehiscence, and fistulas) abnormalities. Vegetations may be seen on any of the valves or any other structure in the heart (Fig. 1) and often exhibit mobility which can be appreciated through multiphase CCT imaging. Valve perforations may be difficult to

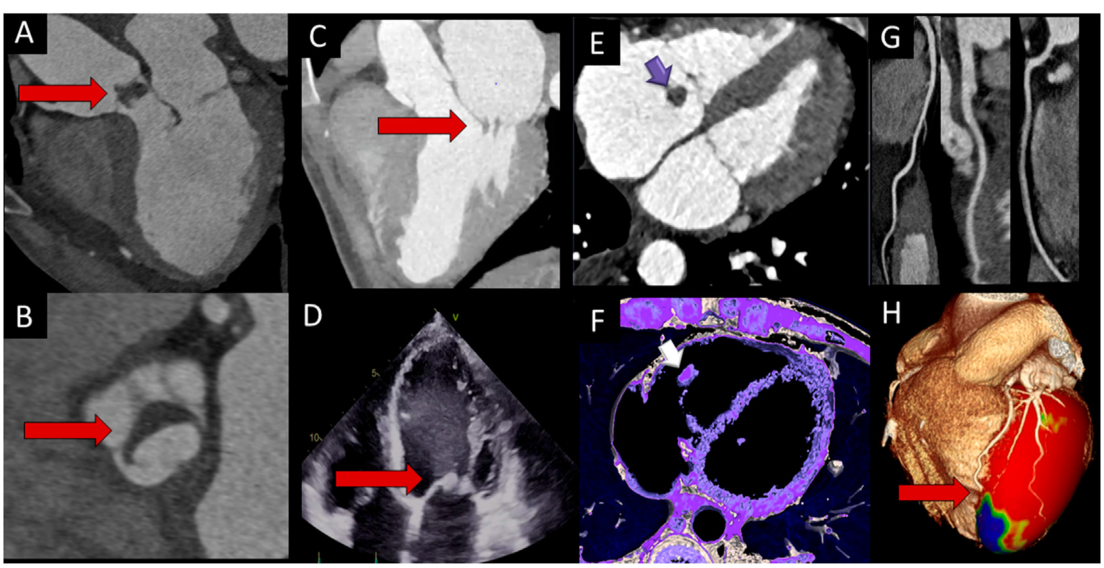

Fig. 1. Aortic, Mitral and Tricuspid vegetations on cardiac computed tomography. A and B. 75-year man with *Streptococcus pneumoniae* aortic endocarditis with severe aortic regurgitation underwent CT to assess coronary arteries prior to surgical intervention. An irregularly shaped 1.3 cm × 1.3 cm mobile vegetation (A) was identified downstream to the valve with (B) non-coronary cusp ballooning and leaflet perforation. **C and D.** 39-year-old woman with a pelvic malignancy. A **(D)** transthoracic echocardiogram showed classic findings of "marantic endocarditis" or also known as non-bacterial thrombotic endocarditis. **(C)** CCT confirms findings of "marantic endocarditis" with vegetations attached to both mitral valve leaflet tips. **E and F.** Round-shaped mass-like mobile vegetation attached to the posterior side of septal tricuspid valve leaflet. Pedunculated lesion of >1 cm size indicates risk of embolization. **(E)** Multiplanar reformat during systole shows the mass on posterior surface (arrow) floating into the downstream chamber, the right atrium. **(F):** 3D volume-rendered reformat during diastole shows anterior mass movement over tricuspid valve orifice towards the right ventricle). **G and H.** (G) Normal coronary arteries in Case (A, B) that allowed the patient to avoid invasive angiography. **H.** Coronary embolism suspected to have arisen from mitral valve lesions in Case (C, D) causing abrupt cut-off (arrow) of the left anterior descending artery with color map of resting perfusion abnormality (as shown in blue) in the apex of the left ventricle. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

visualize on CCT, especially when small in size due to limited temporal resolution. Volume-rendering techniques may be helpful as a supplementary technique to evaluate for perforation, but volume dropout is common and these must be interpreted carefully and informed by the 2-dimensional slices.[14]

Perivalvular complications of IE are typically well-visualized on CCT. Perivalvular extension of IE has been noted in up to 35% of patient undergoing operation for IE and abscess is a risk factor for adverse outcomes including operative death.[15] The perivalvular complications of pseudoaneurysm, dehiscence, and fistula can be co-existent with or the result of perivalvular abscess. Abscess typically appears as a low CT attenuation with liquid density (20–50 HU) or heterogeneous collection adjacent to the valve, depending on the degree and extent of necrosis (Figs. 2 and 3; Video 1). Abscess may – or may not – present with an outer hyperenhancing rim (abscess "capsule"), which indicates active inflammation. A hyperintense rim is more suspicious of an acute abscess than an exclusive liquid collection, especially after surgery or in patients without clinical signs of IE. Hyperenhancement is best seen at a delayed scan of either 70 s, or very late after 2–3 min.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.jcct.2021.02.001.

In particular, the aortic root is usually surrounded by periaortic fatty tissue (<0 up to – 100 HU). The loss of the periaortic lipid layer, and an increase of HU above 0 into positive ranges (1-30HU), should always raise the concern of periaortic abscess in native valves, without prior cardiac surgery intervention. In case of suspicion and no consistency with clinical presentation and echocardiography, a 18FDG –PET CT should be considered to confirm (or rule out) abscess, which has a higher accuracy.[16]

A pseudoaneurysm typically appears as a cavity adjacent to the valve which communicates with surrounding structures, and in the case of prosthetic valves typically occur in conjunction with a perivalvular dehiscence (Fig. 4, Video 2). Pseudoaneurysms are cavities filled with contrast agent (200–400 HU) and can be differentiated from periaortic abscesses using HU from cavity contents. In periaortic abscess the content of cavity will be fluid and necrotic tissue (0–50 HU) and may be surrounded or not by peripheral hyperenhancing rim.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.jcct.2021.02.001.

Multi-phase CCT can further elucidate the pulsatile nature of pseudoaneurysms throughout the cardiac cycle. As the abscess or pseudoaneurysm extends, fistulation into other cavities may occur. Whereas flow cannot be directly visualized, contrast flow into areas of prosthetic dehiscence and fistula formation can be seen. Contrast-based findings can be elucidated and further characterized through several techniques, including maximum-intensity projection and volume-rendering. As findings such as leaflet perforation and fistula may not exist in a single plane, expanding the field of view beyond a single slice may be helpful (Fig. 5). CCT findings may help in deciding whether surgical treatment is indicated or not based on size of vegetation, qualitative mobility (>1 cm and mobile likely favors surgery), presence and extent or periannular or periprosthetic complications may help define if management will lean more towards surgical or conservative approaches.

4. CCT role in coronary and extra cardiac embolic evaluation

A distinct advantage of CCT angiography is the high diagnostic accuracy to reliably exclude obstructive coronary artery disease in patients with lower pre-test probability of CAD and in younger individuals to avoid unnecessary invasive angiography.[17] In a study by Sims et al. in patients who underwent both CCT and invasive coronary angiography, over 80% had no change in management based on invasive angiography. In some instances, particularly aortic valve vegetation, CCT may allow for dual visualization of vegetation and coronary anatomy in a single scan for patients with IE may need prompt surgical treatment with prosthetic valve infection, invasion beyond valve leaflet and at risk recurrent systemic embolization due to large mobile vegetations, or persistent sepsis.[18] In patients with prior valve replacement or coronary bypass CCT may further provide important information on the status of surgical adhesions that may complicate the procedure.[19] In addition, a CT based evaluation may allow for assessment of septic emboli in a single scan. In the study by Kim et al. focused on cardiac evaluation, in 4 out of 75 patients (5.3%) extracardiac emboli (1 pulmonary, 3 splenic) were identified.[3] As for mycotic aneurysms, CCT allows for visualization of the wall of the aorta and surrounding structures to appreciate prominence of inflammatory soft tissue surrounding aorta and fat stranding,[20] which

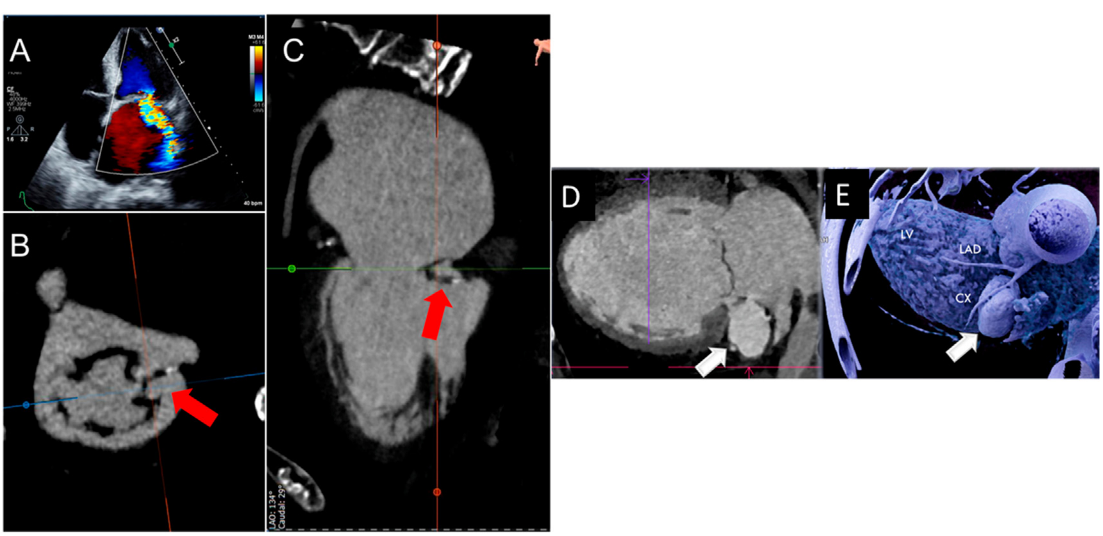

Fig. 2. Mitral valve abscess and annulus pseudoaneurysm. An elderly male was referred for evaluation of transcatheter mitral intervention in the setting of new dyspnea. **A.** TTE imaging shows significant mitral regurgitation explaining patient symptoms. **B** and **C.** CCTA performed as part of transcatheter intervention workup shows a contrast filled space at the P3 scallop with calcification in the leaflet (red arrows), most consistent with healed leaflet abscess. Based on these findings, patient was referred for surgery. **D.** 58-year-old man presenting to the emergency department with fever and elevated C-Reactive Protein of 21 mg/dl. Transthoracic echocardiogram (TTE) during initial screening was normal. CTA showed posterior mitral annulus paravalvular pseudoaneurysm.: 2-Chamber view by multiplanar reformat: White arrow pointing at left circumflex coronary artery adjacent to the cavity. **E.**: 3D volume rendered image with the left circumflex circumventing the pseudoaneurysm. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

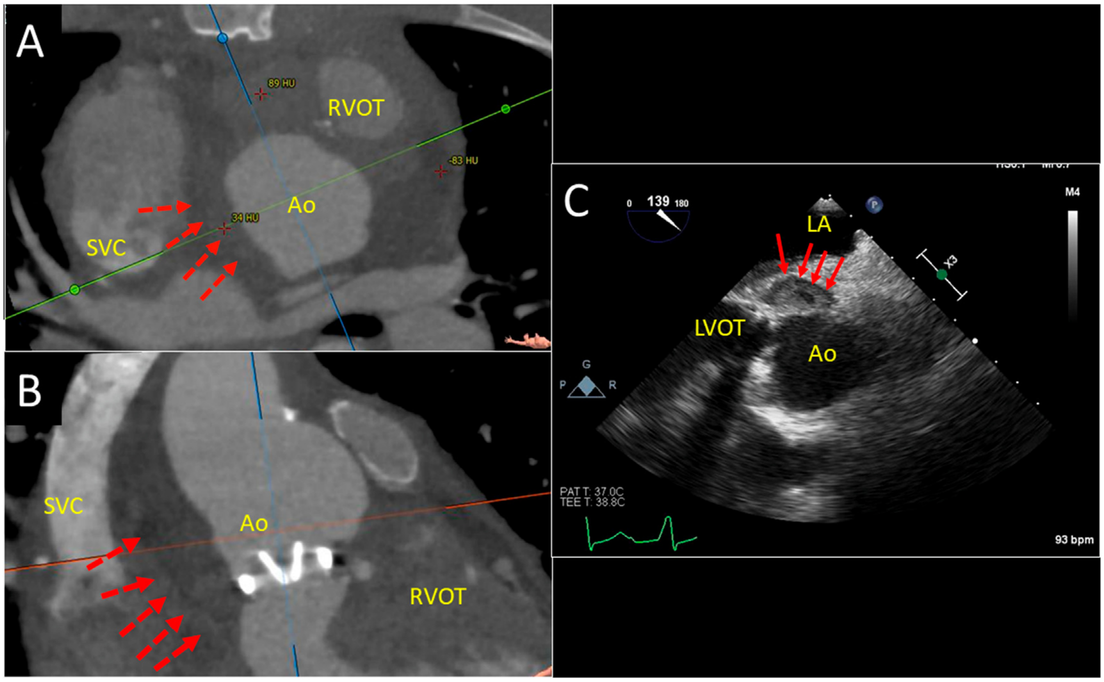

Fig. 3. Perivalvular Aortic Abscess. A 25-year-old man with history of congenital aortic valve disease requiring surgical aortic valve replacement, presenting with fatigue and found to have *Streptococcus mitis* bacteremia. A. Extensive aortic root abscess is seen posteriorly as a hypoattenuating collection (red arrows). CT number measures 34 HU compared to 89 for myocardial tissue and −84 for epicardial fat. B. Long-axis image shows cranio-caudal extent of abscess from LVOT to ascending aorta. There was associated valve dehiscence (refer to Video 1). C. Correlative TEE image of abscess with necrotic core is shown. Abbreviations: Ao = aorta; CT = computed tomography; HU = Hounsfield Unit; RVOT = right ventricular outflow tract; SVC = superior vena cava; TEE = transesophageal echocardiogram.. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

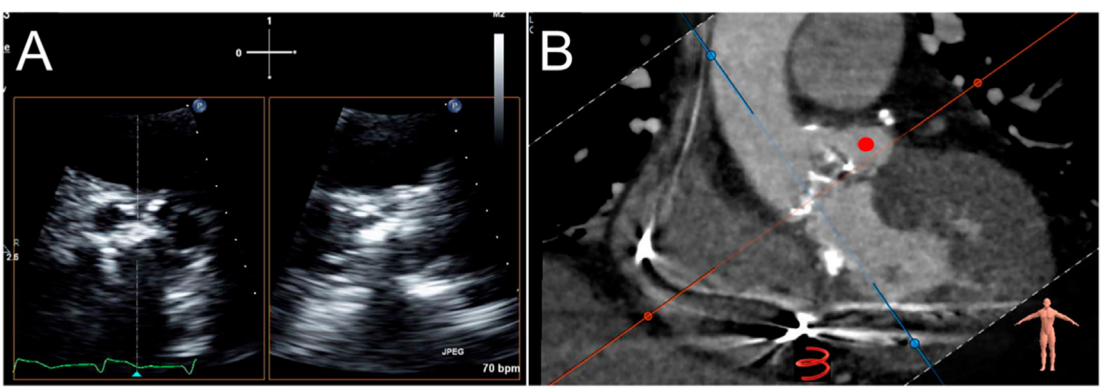

Fig. 4. Pseudoaneurysm in a patient with prior surgical aortic valve replacement and recurrent endocarditis. A. TTE demonstrates severely thickened leaflets and severe bioprosthetic aortic stenosis. B. CCT performed for TAVR evaluation demonstrates a large pseudoaneurysm originating at the LVOT aspect of the bioprosthetic sewing ring (red circle), not seen by TTE. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

may be visualized with magnetic resonance angiography, but not with invasive angiography.

5. Diagnostic performance of CCT vs transesophageal echocardiography

5.1. Native valves

In native valves, the most important assessment is to determine whether there is presence or absence of vegetations, the integrity of the valve and although rare if there is development of a para-valvular abscess, for which CCT provides very good spatial and temporal resolution to detect. Prior data have shown excellent diagnostic performance of CCT and high intermodality agreement with TEE. In a prospective study of 37 patients the initial seminal study by Feuchtner et al. demonstrated excellent diagnostic accuracy of 64-slice dual-source CCTA for detection of vegetations, abscess, and pseudoaneurysms with sensitivity, specificity, PPV and NPV of >95% compared to surgical findings.[2] On a per-valve basis, CCTA and TEE accuracy for detection of vegetations and abscess/pseudoaneurysm showed no statistical difference, although this comparison was limited by small numbers. CCT missed five small vegetations, one was missed due to CT artifacts. Three were small mitral valve vegetations (≤4 mm in size) and one was a tricuspid valve vegetation that was missed due to low right ventricular contrast enhancement and artifacts due to a pacemaker. TEE missed 2 vegetations on a mechanical valve which were seen on CCT, due to metal artifacts. Subsequent studies have confirmed the overall similar ability of CCTA and TEE for general IE diagnosis, with the caveat of superior ability of CCT to diagnose

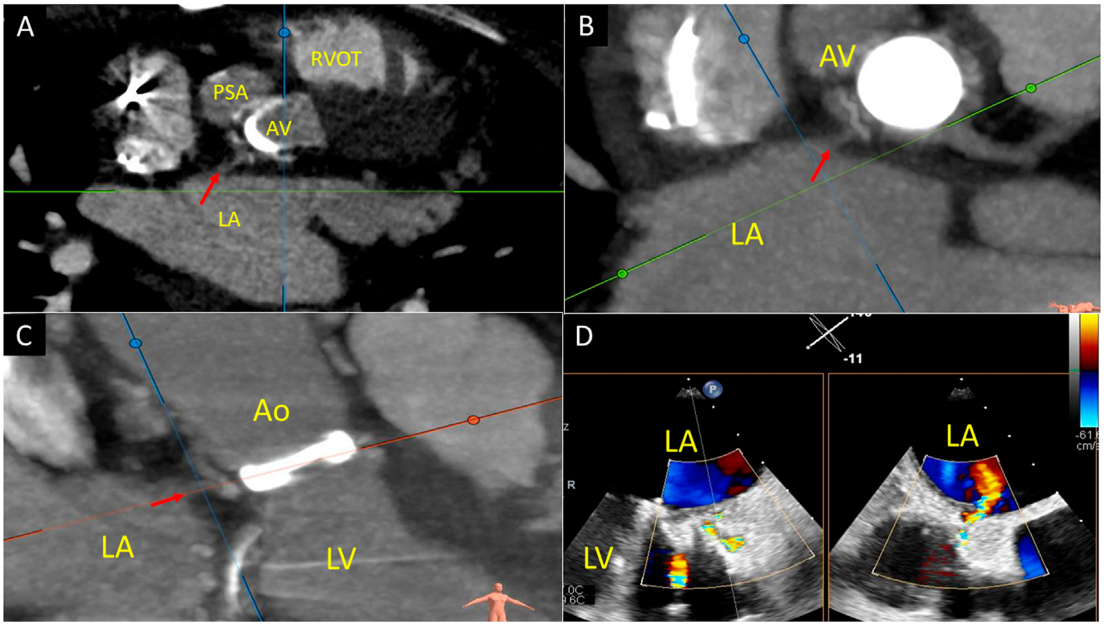

Fig. 5. Aortic Root to Left Atrial Fistula in the Setting of Multiple Surgeries for IE. A 35-year-old female with a history of multiple surgeries presented with dyspnea. A. CCTA axial images suggested aortic root to left atrial fistula (red arrow) and an LVOT pseudoaneurysm is seen. Short-axis (B) and long-axis (C) MIP images elucidate the fistula tract further given its serpiginous path (red arrows). D. Correlative TEE color Doppler biplane image demonstrates a color Doppler jet originating from the aortic root and exiting into the left atrium. As this fistula was small, hemodynamic consequences were minimal. Abbreviations: Ao = aorta; AV = aortic valve; CCTA = cardiac computed tomography angiography; LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; MIP = maximum-intensity projection; PSA = pseudoaneurysm; TEE = transesophageal echocardiogram. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

paravalvular abscess and pseudoaneurysm, and of TEE to diagnose smaller vegetations (<10 mm) and valve perforations (Table).[3,4,21–25] A recent meta-analysis included 8 studies comparing diagnostic performance of CCT and TEE for identifying IE valvular complications validating it with surgical findings. They found CCT with a higher sensitivity to diagnose pseudoaneurysm or abscess (CCT: 78% vs. TEE: 69%).[26] For vegetations, valve perforations and paravalvular leakage the sensitivities were higher for TEE. Another recent meta-analysis showed that CCT, when compared to TEE, performs better in identifying prosthetic valve infection and showed a trend of improved detection of periannular complications.[27]

5.2. Prosthetic valves

CCT often allows for enhanced diagnostic assessment of prosthetic valves, both surgical and transcatheter, particularly when the acoustic shadowing during a TEE assessment may obscure or conceal important pathology in the peri-prosthetic tissue, such as prosthetic dehiscence or para-valvular abscesses.

Regarding visualization of prosthetic dehiscence, CCT has been shown in several studies to have excellent specificity and/or positive predictive value in comparison to surgical findings, with modest sensitivity compared to TEE.[4,21,24] When referenced to intraoperative direct inspection, Hryniewiecki et al. demonstrated that a combination of echocardiography and CCT provided superior sensitivity for all valvular and perivalvular IE findings compared to either modality alone, strongly supporting a multimodality approach.[24] However, especially in the immediate post-surgical setting, liquid collections are common and do not indicate abscess. After a time period of 2–3 month after surgery, an 18-FDG PET/CT might be able to diagnose (or rule out) findings suspicious or periprosthetic abscess. Table 1 summarizes the relevant literature for the accuracy of CCT for the evaluation of IE in native and prosthetic valves. When considering CCT and TEE for IE, it is important to mention the only study looking at how CCT and TEE findings relate to in-hospital and follow-up mortality in patients undergoing surgery for IE by Ming Wang et al.[28] TEE findings of pseudoaneurysm or abscess were the only prognostic findings that predicted in-hospital mortality, however CCT findings of pseudoaneurysm, abscess or fistula were the only predictors of mortality during follow up.[28]

6. Multimodality comparison to PET/CT and cardiac magnetic resonance

PET/CT has been used to detect valvular and Cardiovascular Implantable Electronic Devices (CIED) infections.[29] The data regarding the use of ^{18}F-FDG PET as an adjunctive diagnostic tool to diagnosis infective endocarditis and CIED related infections are comprised mostly of small observational studies.[30–34] There have been a few large meta-analyses evaluating the data collectively; however, there were no standardized PET/CT criteria for diagnosis of infectious endocarditis, as many of them incorporated qualitative or semiquantitative evidence of the PET/CT in the clinical Duke criteria, which was already influenced by echocardiographic findings. A meta-analysis of 6 studies involving 246 patients investigating the diagnostic value of ^{18}F-FDG PET for patients with infectious endocarditis found a pooled sensitivity and specificity of 61% and 88%, respectively.[35] Notably, 5 of the 6 studies used the Modified Duke Criteria as the reference standard, while only 1 used bacteriological data from CIED infections. In another meta-analysis of 13 studies involving 537 patients,[36] the pooled sensitivity and specificity of ^{18}F-FDG PET for diagnosis of IE was 76.8% and 77.9%, respectively. (Figs. 6 and 7 demonstrate ^{18}F-FDG PET imaging for IE evaluation). Disadvantages of ^{18}F-FDG PET are inability to image cardiac motion, inability to visualize valvular vegetations and requirement of dietary preparation, which may delay diagnosis when compared to CCT. Another disadvantage of ^{18}F-FDG PET is a lower spatial resolution of 5 mm in most scanners,[37] as compared to cardiac CT.

However, ^{18}F-FDG PET is an accurate modality for the detection of prosthetic valve endocarditis (PVE), especially for periprosthetic abscess or infection. The most accurate approach, however, is the multimodality interpretation: Both TEE, cardiac ECG-gated and PET/CT findings should

Table 1
Diagnostic accuracy of CCT of key studies for infective endocarditis detection in published literature in comparison with intraoperative findings.

Author	Year	Platform	N	Parameter	Comparison	Sensitivity	Specificity
Feuchtner et al.[2]	2009	64-slice or dual source (2 × 32 row) MDCT	37 patients 73 valves	Vegetation or Abscess/ pseudoaneurysm	TEE	98	88
				Vegetation	Intraoperative findings	96	97
				Abscess or pseudoaneurysm		100	100
				Dehiscence/Paravalvular leakage		88	100
Gahide et al.[23]	2010	16-slice or 64-slide MDCT	19 patients (Aortic only)	Vegetation (All)	Intraoperative findings	71	100
				Vegetation > 1.0 cm		100	100
				Pseudoaneurysm		92	100
Habets et al.[53]	2014	64-slide or 256-slide MDCT + Heart Team Consensus	28 patients	Vegetation	Intraoperative findings	100	100
				Aneurysm/Abscess		100	91
Koo et al.[4]	2018	Dual source (2 × 64 row) MDCT	49 patients	Vegetation	Intraoperative findings	91	98[a]
				Leaflet perforation		50	44[a]
				Abscess/pseudoaneurysm		60	75[a]
				Dehiscence/Paravalvular leakage		50	100[a]
Sims et al.[21]	2018	Dual source (2 × 32 and 2 × 64 row) MDCT	34 patients	Vegetation	Intraoperative findings	70	93
				Leaflet perforation		43	96
				Abscess/pseudoaneurysm		91	92
				Dehiscence/Paravalvular leakage		57	100
Kim et al.[3]	2018	Dual source (2 × 32 row or 2 × 64 row) MDCT	75 patients	Vegetation (All)	Intraoperative findings	[b]**Only diagnostic accuracy reported**	72[b]
				Vegetation (>10 mm)			90[b]
				Vegetation (<10 mm)			53[b]
				Leaflet perforation			91[b]
				Abscess			95[b]
Koneru et al.[25]	2018	Dual source (2 × 128 and 2 × 64 row) MDCT or 64- slice MDCT	122	Vegetation	Intraoperative findings	16	96
				Pseudoaneurysm/abscess		66	88
				Dehiscence		15	97
Hryniewiecki et al.[24]	2019	Dual source (2 × 64 row) MDCT	53 patients 71 valves	Vegetation	Intraoperative findings	89′	71′
				Abscess/pseudoaneurysm		81′	90′
				Inflammatory infiltration		46′	100′
				Leaflet perforation		43′	89′
Oliveira et al.[26]	2020	Meta-analysis; diverse MDCT	8 studies	Vegetation	Intraoperative findings	64′	88′
				Abscess/Pseudoaneurysm		78′	92′
				Leaflet perforation		41′	92′
				Paravalvular leakage		44′	97′
Jain et al.[27]	2020	Meta-analysis; diverse MDCT	10 studies	Vegetation		85′	84′
				Periannular complications		88′	93′
				Leaflet perforation		48′	93′
				Fistula		98′	98′
				Paravalvular leakage		85′	100′
				Dehiscence		46′	97′

Abbreviations: PVL = paravalvular leak.
‘ Pooled sensitivities and specificities.
[a] Only positive predictive value was reported.
[b] Only diagnostic accuracy was reported.

be interpreted head-to-head in adjunction, in order to rule-in or rule out a diagnosis (see Central Illustration, Fig. 8). Serial follow up of unclear but suspicious lesions, after antibiotic treatment, is a valuable strategy in clinical practice, which is usually recommended after 6–8 weeks up to 3 months (depending on lesion type). The sensitivity and specificity of ^{18}F-FDG PET in native valve IE is limited,[33,38] as it is more robust in prosthetic valve IE. ^{18}F-FDG PET should be utilized preferably in the context of suspected prosthetic valve infection in patients with limited echocardiographic images or contraindications to CCT.

For cardiac magnetic resonance (CMR), the level of data for IE is limited to case series[39] and a few case reports. However, the robust accuracy of CMR in valvular regurgitation quantification might be helpful in certain cases in which further assessment is needed.[40–42] CMR lacks the submillimeter spatial resolution of CCT to assess the perivalvular region when prosthetic valves are present, and the signal void generated by some prostheses may impair the assessment of prosthetic valve function. The data on usefulness of CMR in IE is limited, it may identify complications related to IE and might help in clarifying severity of valve regurgitation from IE in cases where that information could make a difference in clinical management.

7. CCT to improve safety of infective endocarditis imaging amidst COVID-19

Amidst the novel coronavirus disease (COVID-19) pandemic, it has become essential to balance the risk of virus aerosolization with HCW safety and optimal patient care. The Society of Cardiovascular Computed Tomography/American College of Cardiology (ACC) endorsed COVID-19 guidance statement suggests acute endocarditis, perivalvular extension or abscess as potential urgent CCT indications.[9] A *JACC: Cardiovascular Imaging*/ACC Imaging Council collaboration statement articulates CCT with the highest rating for invasive complications of endocarditis amongst the major cardiac imaging modalities to minimize risk, reduce resource use and maximize clinical benefit.[43] In acute phase COVID-19 patients, an ACC Imaging Council document supports the use of CCT instead of TEE in selected cases during the acute phase of COVID-19, to decrease the risk of exposure of HCW from aerosol-generating procedures and in cases where there is a suspicion of coronary embolism.[44] However, the increased risk of kidney dysfunction due to iodine contrast agent exposure has to be considered in critically ill COVID-19 patients, and carefully balanced to the urgency of the indication.

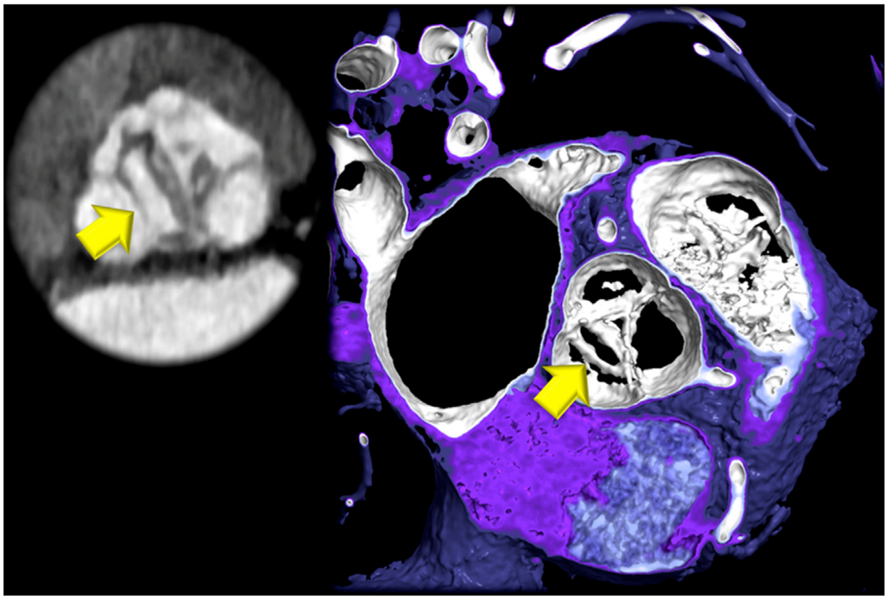

Fig. 6. Leaflet perforation: 63-year-old male with fever, previous sepsis (peritonitis) and definite infective endocarditis (positive blood culture: *Streptococcus m.*) CTA showed an irregular "hole" within non-coronary aortic cusp (yellow arrows), confirmed by TEE. (*Left*: axial oblique MPR. *Right*: 3D VRT) Note 3D VRT is advantageous over MRP for visualization of leaflet perforation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

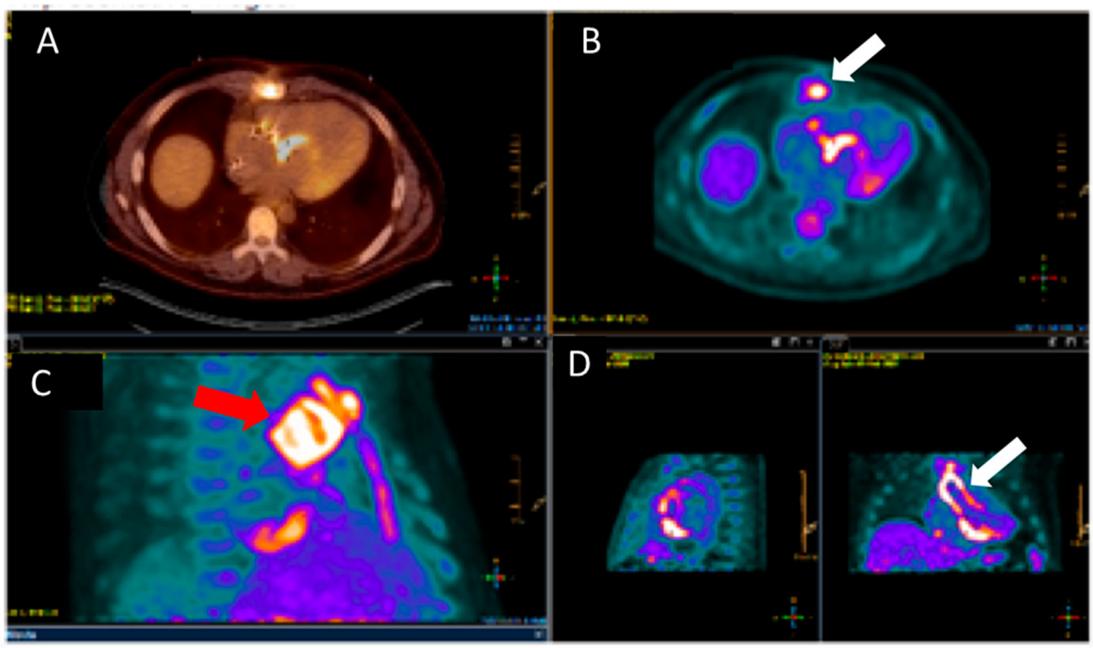

Fig. 7. PET-CT in patient with multiple cardiac prostheses (mechanical AVR, tricuspid annuloplasty ring, hemi-arch replacement) with strep bacteremia and unremarkable TEE. A 18F-FDG Cardiac PET after a high-fat/protein and low-carbohydrate prep demonstrates significant focal uptake involving the sternum (SUVmax = 15) (A), with extension to the ascending aorta (white arrows, B and D), and also focal uptake at the mechanical AVR and aortic root (SUVmax = 11.7) (red arrow, C), concerning for paravalvular abscess. SUV = standardized uptake value.. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

8. CCT in guidelines and new technical enhancements

Even with known advantages in the assessment of extravalvular IE findings, CCT has been historically underutilized for IE evaluation (14% in a recent retrospective study).[21] The most recent American Heart Association and European Society of Cardiology Guidelines mention CCT and other modalities as ancillary methods of evaluating IE with echocardiography as the only Class 1 imaging modality.[45,46] These guidelines have not been updated since 2015 to incorporate more contemporary data such as those cited in the current review. However, a recent survey published in 2020 by the European Association of Cardiovascular Imaging finds that 60% of surveyed sites are using CCT for diagnostic purposes, most often in those patients with complex prosthetic valve endocarditis and in cases when TEE is inconclusive.[47]

Currently, there are several new technologies available or in development which may further improve IE detection by CCT. The use of dual-energy CCT to improve tissue characterization via differentiation of high and low photon energies has been studied and is currently in limited clinical use.[48] Dual-energy CCT has been shown to reduce beam hardening and partial volume averaging artifacts.[49,50] Spectral CCT takes this a step further by ascertainment of multiple energy levels. Preclinical studies have shown the ability to differentiate multiple tissue

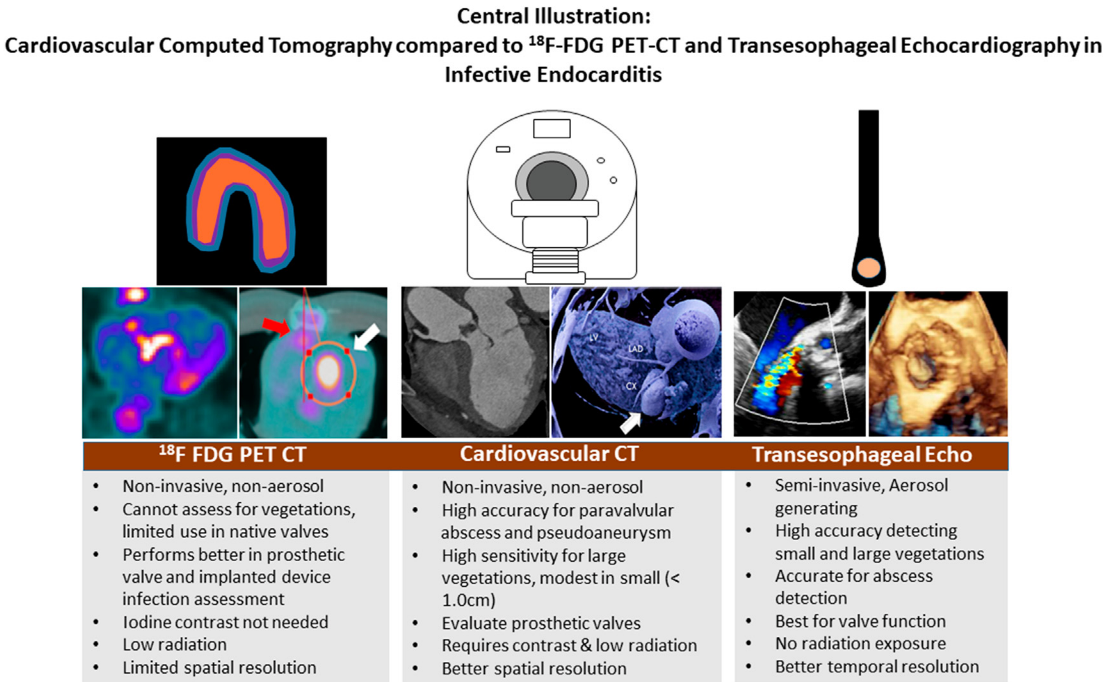

Fig. 8. Central Illustration. Cardiovascular Computed Tomography compared to ^{18}F-FDG PET-CT and Transesophageal Echocardiography in Infective Endocarditis.

atherosclerotic components using spectral CCT.[51] Improved tissue characterization may potentially help with early abscess or vegetation detection while reductions in stent artifacts can improve prosthetic evaluation. Ultra high-resolution CCT utilizes detector-rows of 0.25 mm in width to improve spatial resolution and is being studied for improved coronary artery disease evaluation.[52] Improved visualization of small vegetations traditionally less well-seen by CCT could be of benefit for IE evaluation.

9. Limitations of CCT in endocarditis evaluation

Despite the rising evidence presented in this paper, several important limitations of CCT in endocarditis require discussion. Acute kidney injury is a concern when giving iodinated contrast to patients with pre-existing renal insufficiency. In general, the risk of contrast-induced nephropathy increases with estimated glomerular filtration rate of <30 mL/min/1.73 m2, although the impact of intravenous contrast is debated. CCT has been found to have limited sensitivity and accuracy in patients with small (<10 mm) leaflet vegetations. Low temporal resolution and the absence of direct flow assessment limit the ability of CCT to evaluate for leaflet perforation or valvular dysfunction. There exists a selection bias in the literature as most studies have evaluated CCT in patients undergoing surgical valve repair or replacement in IE. Most of the data related to CCT in IE are from small, single center retrospective studies. Therefore, the evidence for CCT to exclude vegetations in persistently bacteremic patients with low risk TTE findings is unknown, though an emerging imaging approach at some centers, especially during the COVID-19 pandemic to avoid TEE. For patients with acute illness or heart failure with elevated heart rates and those who may not be able to perform a proper breath-hold may have lower diagnostic accuracy placing enhanced importance on optimizing scan parameters and heart rate control measures to achieve high diagnostic quality.

10. Conclusion

CCT has an important role in the contemporary assessment of IE, with high accuracy for large vegetations, perivalvular complications and for exclusion of coronary artery disease to avoid invasive angiography. In patients with suspected prosthetic valve dysfunction, CT can help to clarify the type of dysfunction (e.g. malposition, abscess, leak, vegetation or mass). CCT may be ideally integrated into multimodality approach that incorporates a central role of TEE with 18-FDG PET and/or CMR in individually selected cases that is guided by the Heart Team with an emphasis on high accuracy, high quality imaging while avoiding unnecessary testing to improve the diagnosis and outcomes of patients with IE.

Declaration of competing interest

Dr. Choi reports equity interest in Cleerly, Inc. Dr. Lopez-Mattei and other coauthors have no conflicts of interest to disclose related to the content of this manuscript.

References

1. Doherty JU, Kort S, Mehran R, Schoenhagen P, Soman P. ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR/STS 2017 appropriate use criteria for multimodality imaging in valvular heart disease. A report of the American College of Cardiology appropriate use criteria task force, American association for thoracic surgery, American heart association, American society of echocardiography, American society of nuclear Cardiology, heart rhythm society, society for cardiovascular angiography and interventions, society of cardiovascular computed tomography. *Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons*. 2017;70: 1647–1672.
2. Feuchtner GM, Stolzmann P, Dichtl W, et al. Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. *J Am Coll Cardiol*. 2009;53:436–444.
3. Kim IC, Chang S, Hong GR, et al. Comparison of cardiac computed tomography with transesophageal echocardiography for identifying vegetation and intracardiac complications in patients with infective endocarditis in the era of 3-dimensional images. *Circ Cardiovasc Imaging*. 2018;11, e006986.
4. Koo HJ, Yang DH, Kang JW, et al. Demonstration of infective endocarditis by cardiac CT and transoesophageal echocardiography: comparison with intra-operative findings. *Eur Heart J Cardiovasc Imaging*. 2018;19:199–207.
5. Choi AD, Feuchtner GM, Weir-McCall J, Shaw LJ, Min JK, Villines TC. Accelerating the future of cardiac CT: social media as sine qua non? *J Cardiovasc Comput Tomogr*. 2020.
6. Khalique OK, Pulerwitz TC, Halliburton SS, et al. Practical considerations for optimizing cardiac computed tomography protocols for comprehensive acquisition prior to transcatheter aortic valve replacement. *J Cardiovasc Comput Tomogr*. 2016; 10:364–374.

7. Pulerwitz TC, Khalique OK, Leb J, et al. Optimizing cardiac CT protocols for comprehensive acquisition prior to percutaneous MV and TV repair/replacement. *JACC Cardiovasc Imaging*. 2019.
8. Choi AD, Parwani P, Michos ED, et al. The global social media response to the 14th annual Society of Cardiovascular Computed Tomography scientific sessions. *J Cardiovasc Comput Tomogr*. 2020;14:124–130.
9. Choi AD, Abbara S, Branch KR, et al. Society of Cardiovascular Computed Tomography guidance for use of cardiac computed tomography admist the COVID-19 pandemic. Endorsed by the American College of Cardiology. *Journal of Cardiovascular Computed Tomography*. 2020.
10. Choi JW, van Rosendael AR, Bax AM, et al. The journal of cardiovascular computed tomography year in review - 2019. *J Cardiovasc Comput Tomogr*. 2020;14:107–117.
11. Abbara S, Blanke P, Maroules CD, et al. SCCT guidelines for the performance and acquisition of coronary computed tomographic angiography: a report of the society of cardiovascular computed tomography guidelines committee: endorsed by the north American society for cardiovascular imaging (NASCI). *J Cardiovasc Comput Tomogr*. 2016;10:435–449.
12. Chao CP, Walker TG, Kalva SP. Natural history and CT appearances of aortic intramural hematoma. *Radiographics*. 2009;29:791–804.
13. Faure ME, Swart LE, Dijkshoorn ML, et al. Advanced CT acquisition protocol with a third-generation dual-source CT scanner and iterative reconstruction technique for comprehensive prosthetic heart valve assessment. *Eur Radiol*. 2018;28:2159–2168.
14. Entrikin DW, Carr JJ. Blood pool inversion volume-rendering technique for visualization of the aortic valve. *J Cardiovasc Comput Tomogr*. 2008;2:366–371.
15. David TE, Regesta T, Gavra G, Armstrong S, Maganti MD. Surgical treatment of paravalvular abscess: long-term results. *Eur J Cardio Thorac Surg*. 2007;31:43–48.
16. Habib G, Erba PA, Iung B, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. *Eur Heart J*. 2019;40:3222–3232.
17. Williams MC, Newby DE, Nicol ED. Coronary atherosclerosis imaging by CT to improve clinical outcomes. *J Cardiovasc Comput Tomogr*. 2019;13:281–287.
18. Pettersson GB, Hussain ST. Current AATS guidelines on surgical treatment of infective endocarditis. *Ann Cardiothorac Surg*. 2019;8:630–644.
19. Malguria N, Hanley M, Steigner M, et al. Static and cine CT imaging to identify and characterize mediastinal adhesions as a potential complication for patients underdoing "redo sternotomy". *Am J Roentgenol*. 2013;201:W72–W74.
20. Lee W-K, Mossop PJ, Little AF, et al. Infected (mycotic) aneurysms: spectrum of imaging appearances and management. *Radiographics*. 2008;28:1853–1868.
21. Sims JR, Anavekar NS, Chandrasekaran K, et al. Utility of cardiac computed tomography scanning in the diagnosis and pre-operative evaluation of patients with infective endocarditis. *Int J Cardiovasc Imag*. 2018;34:1155–1163.
22. Fagman E, Perrotta S, Bech-Hanssen O, et al. ECG-gated computed tomography: a new role for patients with suspected aortic prosthetic valve endocarditis. *Eur Radiol*. 2012;22:2407–2414.
23. Gahide G, Bommart S, Demaria R, et al. Preoperative evaluation in aortic endocarditis: findings on cardiac CT. *AJR Am J Roentgenol*. 2010;194:574–578.
24. Hryniewiecki T, Zatorska K, Abramczuk E, et al. The usefulness of cardiac CT in the diagnosis of perivalvular complications in patients with infective endocarditis. *Eur Radiol*. 2019;29:4368–4376.
25. Koneru S, Huang SS, Oldan J, et al. Role of preoperative cardiac CT in the evaluation of infective endocarditis: comparison with transesophageal echocardiography and surgical findings. *Cardiovasc Diagn Ther*. 2018;8:439–449.
26. Oliveira M, Guittet L, Hamon M, Hamon M. Comparative value of cardiac CT and transesophageal echocardiography in infective endocarditis: a systematic review and meta-analysis. *Radiology: Cardiothoracic Imaging*. 2020;2, e190189.
27. Jain V, Wang TKM, Bansal A, et al. Diagnostic performance of cardiac computed tomography versus transesophageal echocardiography in infective endocarditis: a contemporary comparative meta-analysis. *Journal of Cardiovascular Computed Tomography*. 2020.
28. Wang TKM, Saeedan MB, Chan N, et al. Complementary diagnostic and prognostic contributions of cardiac computed tomography for infective endocarditis surgery. *Circulation: Cardiovascular Imaging*. 2020;13, e011126.
29. Ben-Haim S, Gacinovic S, Israel O. Cardiovascular infection and inflammation. *Semin Nucl Med*. 2009;39:103–114.
30. Pizzi MN, Roque A, Fernandez-Hidalgo N, et al. Improving the diagnosis of infective endocarditis in prosthetic valves and intracardiac Devices with 18F-fluordeoxyglucose positron emission tomography/computed tomography angiography: initial results at an infective endocarditis referral center. *Circulation*. 2015;132:1113–1126.
31. Ricciardi A, Sordillo P, Ceccarelli L, et al. 18-Fluoro-2-deoxyglucose positron emission tomography-computed tomography: an additional tool in the diagnosis of prosthetic valve endocarditis. *Int J Infect Dis*. 2014;28:219–224.
32. Saby L, Laas O, Habib G, et al. Positron emission tomography/computed tomography for diagnosis of prosthetic valve endocarditis: increased valvular 18F-fluorodeoxyglucose uptake as a novel major criterion. *J Am Coll Cardiol*. 2013;61:2374–2382.
33. de Camargo RA, Sommer Bitencourt M, Meneghetti JC, et al. The role of 18F-fluorodeoxyglucose positron emission tomography/computed tomography in the diagnosis of left-sided endocarditis: native vs prosthetic valves endocarditis. *Clin Infect Dis*. 2020;70:583–594.
34. San S, Ravis E, Tessonier L, et al. Prognostic value of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography in infective endocarditis. *J Am Coll Cardiol*. 2019;74:1031–1040.
35. Yan J, Zhang C, Niu Y, et al. The role of 18F-FDG PET/CT in infectious endocarditis: a systematic review and meta-analysis. *Int J Clin Pharmacol Ther*. 2016;54:337–342.
36. Mahmood M, Kendi AT, Ajmal S, et al. Meta-analysis of 18F-FDG PET/CT in the diagnosis of infective endocarditis. *J Nucl Cardiol*. 2019;26:922–935.
37. Kapoor V, McCook BM, Torok FS. An introduction to PET-CT imaging. *Radiographics*. 2004;24:523–543.
38. Wang TKM, Sánchez-Nadales A, Igbinomwanhia E, Cremer P, Griffin B, Xu B. Diagnosis of infective endocarditis by subtype using (18)F-fluorodeoxyglucose positron emission tomography/computed tomography: a contemporary meta-analysis. *Circ Cardiovasc Imaging*. 2020;13, e010600.
39. Dursun M, Yılmaz S, Yılmaz E, et al. The utility of cardiac MRI in diagnosis of infective endocarditis: preliminary results. *Diagn Interv Radiol*. 2015;21:28–33.
40. Uretsky S, Gillam L, Lang R, et al. Discordance between echocardiography and MRI in the assessment of mitral regurgitation severity: a prospective multicenter trial. *J Am Coll Cardiol*. 2015;65:1078–1088.
41. Lopez-Mattei JC, Ibrahim H, Shaikh KA, et al. Comparative assessment of mitral regurgitation severity by transthoracic echocardiography and cardiac magnetic resonance using an integrative and quantitative approach. *Am J Cardiol*. 2016;117:264–270.
42. Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European association of cardiovascular imaging and the American society of echocardiography. *J Am Soc Echocardiogr*. 2017;30:372–392.
43. Zoghbi WA, DiCarli MF, Blankstein R, et al. Multimodality cardiovascular imaging in the midst of the COVID-19 pandemic: ramping up safely to a new normal. *JACC Cardiovasc Imaging*. 2020;13:1615–1626.
44. Rudski L, Januzzi JL, Rigolin VH, et al. Multimodality imaging in evaluation of cardiovascular complications in patients with COVID-19. *J Am Coll Cardiol*. 2020:27553.
45. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American heart association. *Circulation*. 2015;132:1435–1486.
46. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European society of Cardiology (ESC). Endorsed by: European association for cardio-thoracic surgery (EACTS), the European association of nuclear medicine (EANM). *Eur Heart J*. 2015;36:3075–3128.
47. Holte E, Dweck MR, Marsan NA, et al. EACVI survey on the evaluation of infective endocarditis. *Eur Heart J Cardiovasc Imaging*. 2020;21:828–832.
48. Ohta Y, Kishimoto J, Kitao S, et al. Investigation of myocardial extracellular volume fraction in heart failure patients using iodine map with rapid-kV switching dual-energy CT: segmental comparison with MRI T1 mapping. *J Cardiovasc Comput Tomogr*. 2020;14:349–355.
49. Weir-McCall JR, Nicol E, Abbara S, et al. Highlights of the fourteenth annual scientific meeting of the society of cardiovascular computed tomography. *J Cardiovasc Comput Tomogr*. 2020;14:118–123.
50. Poulter R, Wood DA, Starovoytov A, Smith S, Chitsaz M, Mayo J. Quantified dual energy computed tomography perfusion imaging using myocardial iodine concentration: validation using CT derived myocardial blood flow and invasive fractional flow reserve in a porcine model. *J Cardiovasc Comput Tomogr*. 2019;13:86–91.
51. Symons R, Choi Y, Cork TE, et al. Optimized energy of spectral coronary CT angiography for coronary plaque detection and quantification. *J Cardiovasc Comput Tomogr*. 2018;12:108–114.
52. Symons R, De Bruecker Y, Roosen J, et al. Quarter-millimeter spectral coronary stent imaging with photon-counting CT: initial experience. *J Cardiovasc Comput Tomogr*. 2018;12:509–515.
53. Habets J, Tanis W, van Herwerden LA, et al. Cardiac computed tomography angiography results in diagnostic and therapeutic change in prosthetic heart valve endocarditis. *Int J Cardiovasc Imag*. 2014;30:377–387.