ORIGINAL PAPER

Utility of cardiac computed tomography scanning in the diagnosis and pre-operative evaluation of patients with infective endocarditis

Jason R. Sims[1] · Nandan S. Anavekar[2,3] · Krishnaswamy Chandrasekaran[2,3] · James M. Steckelberg[4] ·
Walter R. Wilson[4,5] · Bernard J. Gersh[2] · Larry M. Baddour[2,4] · Daniel C. DeSimone[4]

Abstract

Transesophageal echocardiography (TEE) is the gold standard imaging study used in the diagnosis of infective endocarditis (IE). Computed tomography angiography (CTA) has undergone rapid advancement as a cardiac imaging technique and has previously shown promise in small non-randomized studies for evaluation of IE. We hypothesized that cardiac CTA would perform similarly to TEE in the detection of endocarditic lesions and that there would be no difference in clinical outcomes whether the coronary arteries were evaluated by CTA or invasive coronary angiography (ICA). 255 adults who underwent surgery for IE at the Mayo Clinic Rochester between January 1, 2006 and June 1, 2014 were identified retrospectively. 251 patients underwent TEE and 34 patients underwent cardiac CTA. TEE had statistically higher detection of vegetations (95.6 vs. 70.0%, $p < 0.0001$) and leaflet perforations (81.3 vs. 42.9%, $p = 0.02$) as compared to cardiac CTA. For detection of abscess/pseudoaneurysm TEE had a similar sensitivity to cardiac CTA (90.5 vs. 78.4%, $p = 0.21$). There was no significant difference in peri-operative outcomes whether coronary arteries were evaluated by CTA or ICA. The greatest advantage of cardiac CT in the setting of IE is its ability to couple the detection of complex cardiac anatomic abnormalities with coronary artery delineation, serving two important components of the diagnostic evaluation, particularly among patients who will require surgical intervention due to IE complications. Cardiac CTA may be considered as an alternate coronary artery imaging modality in IE patients with low to intermediate risk of disease but meet guideline recommendations for coronary artery imaging.

Keywords Cardiac CT · Infective endocarditis · Pre-operative evaluation · Valvular heart disease · Coronary artery disease

✉ Jason R. Sims
Sims.Jason@mayo.edu

1 Department of Internal Medicine, Mayo Clinic, 200 1st St SW, Rochester, MN 55905, USA

2 Department of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA

3 Department of Radiology, Mayo Clinic, Rochester, MN, USA

4 Division of Infectious Diseases, Mayo Clinic, Rochester, MN, USA

5 Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, USA

Introduction

Transesophageal echocardiography (TEE) is the gold standard diagnostic tool for identifying structural abnormalities in infective endocarditis (IE) [1–3]. Classic features of IE on TEE include vegetations, ring abscess, pseudoaneurysm, fistula, leaflet perforation, and valvular dehiscence [4]. In recent years, rapid advancement in computed tomography (CT) scanning has led to markedly improved utility in cardiac and coronary artery imaging since it was first shown to be of use in quantifying coronary calcium over 25 years ago [5, 6]. Prior to surgery for IE, a proportion of patients will undergo invasive coronary angiography (ICA) to determine if there is a need for intra-operative coronary artery bypass grafting (CABG). Current indications for coronary assessment include: men > 40 years old, post-menopausal women, and those with a history of coronary artery disease (CAD) or multiple risk factors for CAD [7, 8].

Although there have been improvements in the safety of angiography, it remains an invasive procedure with associated risks, particularly in critically ill patients with IE who require urgent surgery [9]. Of particular concern in patients with IE, are reports of fatal coronary embolization of mobile vegetative material that occurred during ICA [10]. Cardiac CT angiography (CTA) has been validated previously as a non-invasive option to evaluate for CAD [11]. Prospective clinical trials as well as meta-analyses have repeatedly demonstrated high sensitivity and negative predictive values (NPV) of cardiac CTA for excluding coronary stenoses > 50% in intermediate and low-risk patients [11–17].

Therefore, the current investigation sought to compare the diagnostic accuracy of cardiac CTA with TEE for detecting imaging features of IE and compare perioperative outcomes of patients who underwent cardiac CTA vs. ICA for assessment of coronary anatomy prior to surgery for IE.

Methods

A retrospective cohort of 255 adult (18 and older) consecutive patients who underwent cardiac surgery for IE between January 1, 2006 and June 1, 2014 at Mayo Clinic Rochester was identified.

Cardiac CT scanners over the study period ranged from 64 to 128 slice dual-source machines. All scans were ECG-gated and 3D post-processing was performed. Multiphase datasets were obtained in the majority of cases. Beta-blocker use was part of the cardiac CT protocol but was excluded if the patient had a contraindication to their use. All reading physicians had received advanced training in cardiac CT imaging (SCCT Level 3 certified). All echocardiographers were COCATS level III trained. Echo machines were GE, Phillips, or Acuson devices.

The comprehensive TEE closest to the time of cardiac surgery was used for comparison. Cardiac CT data was included only if both coronary artery and IE findings were assessed on the same study (i.e. if a CTA was ordered solely for coronary assessment and IE findings were not assessed, the study was excluded). The IE features of interest on echocardiogram included vegetations, abscess/pseudoaneurysm, fistula, leaflet perforation, and valvular dehiscence. Surgical observations were established by review of operative and pathology reports. Findings were reported on a per-patient basis.

For patients who underwent cardiac CTA or ICA, coronary arteries were evaluated for the number of vessels with > 50% stenosis. ICA was further evaluated to determine if it changed management. A change in management was defined as the decision to pursue revascularization at the time of cardiac surgery regardless of whether bypass was aborted at the time of procedure for technical reasons. For evaluation of acute kidney injury (AKI), the pre-angiogram serum creatinine level was compared to a 3 day post-angiogram creatinine level. An increase of greater than or equal to 0.3 mg/dL was defined as AKI. Patients who underwent surgery during this time were excluded from this analysis. Additionally, patients on dialysis were excluded from this analysis.

For statistical analysis, the diagnostic accuracy of cardiac CTA for IE as compared with operative findings was assessed. The same analysis was performed for TEE to serve as a reference in this patient population. Second, clinical outcomes were assessed for patients undergoing cardiac CTA as compared with ICA. Third, coronary artery disease findings were compared between patients undergoing cardiac CTA compared with ICA. Sensitivity and specificity analyses were performed. Population proportions were compared using the Pearson Chi square test. A value of $p < 0.05$ was considered significant for all tests (These values have been made bold in the tables). All analyses were performed using JMP (SAS Institute, Cary, NC, United States). This study was approved by the Mayo Clinic Institutional Review Board.

Results

Of the 255 patients with IE undergoing surgery, 34 (13%) had cardiac CTA pre-operatively and 103 (40%) underwent ICA. Baseline characteristics for these groups were similar except for a statistically significant younger age (54.0 vs. 64.1 years, $p < 0.001$) and larger male predominance (91.2% CTA vs. 74.8% ICA, $p = 0.04$) in the cardiac CTA group as shown in Table 1.

There were no significant differences among cardiac risk factors. The CTA group had a larger proportion of aortic valve involvement than the ICA group (82.4 vs. 58.3%, $p = 0.01$). Fig. 1 depicts the number of patients undergoing each method of preoperative coronary evaluation. The group of patients that did not have documented preoperative coronary evaluation was heterogeneous and included 4 main clinical scenarios: (1) young patients with no risk factors; (2) urgent or emergent timing of surgery; (3) recent coronary evaluation performed for an unrelated reason; (4) coronary evaluation was performed at outside facility but textual report was not available in the medical record. Of note, 7 patients proceeded to ICA after CTA. Additionally, 5 patients had contraindications to ICA and 23 patients did not undergo coronary evaluation for unclear reasons.

Among 34 patients who underwent pre-operative cardiac CTA, the median number of days from CT to surgery was 4 and 47.1% had prosthetic valves. Sensitivity and specificity for detection of vegetations were 70 and 92.9%, respectively (Table 2). However, for detection of abscess/pseudoaneurysm, these were 90.5 and 92.3%, respectively. Sensitivity

Table 1 Study population (n = 255)

	All patients	ICA group (n = 103)	CTA group (n = 34)	p value
Mean age at surgery (years)	57.6	64.1	54.0	**< 0.001**
Male	78.4 (200)	74.8 (77)	91.2 (31)	**0.04**
Female	21.7 (55)	25.2 (26)	8.8 (3)	**0.04**
Caucasian	92.9 (237)	93.2 (96)	94.1 (32)	0.85
Diabetes mellitus	19.2 (49)	18.4 (19)	14.7 (5)	0.62
Hypertension	50.2 (128)	60.2 (62)	55.9 (19)	0.66
Hyperlipidemia	45.9 (117)	53.4 (55)	44.1 (15)	0.35
Current smoker	12.9 (33)	6.8 (7)	17.6 (6)	0.06
Former smoker	27.5 (70)	33 (34)	23.5 (8)	0.30
History of CAD	20.4 (52)	21.4 (22)	20.6 (7)	0.92
History of MI	6.3 (16)	2.9 (3)	5.9 (2)	0.42
History of revascularization	16.9 (43)	18.4 (19)	20.6 (7)	0.78
CABG	81.4 (35)	84.2 (16)	100 (7)	0.26
PCI	23.3 (10)	15.8 (3)	0 (0)	0.26
On aspirin	45.1 (115)	49.5 (51)	32.4 (11)	0.08
On P2Y12 inhibitor	3.9 (10)	3.9 (4)	5.9 (2)	0.62
On anticoagulation	28.2 (72)	23.3 (24)	32.4 (11)	0.29
Prosthetic valve	42.4 (108)	37.9 (39)	47.1 (16)	0.34
Aortic valve involvement	68.4 (172)	58.3 (60)	82.4 (28)	**0.01**

Baseline characteristics of the study population are presented

ICA invasive coronary angiography, *CTA* computed tomography angiography, *CAD* coronary artery disease, *MI* myocardial infarction, *CABG* coronary artery bypass grafting, *PCI* percutaneous coronary intervention

Fig. 1 Pre-operative evaluation of coronary artery anatomy. The number of patients undergoing various coronary artery evaluation strategies are presented. *CTA* computed tomography angiography. *ICA* invasive coronary angiography
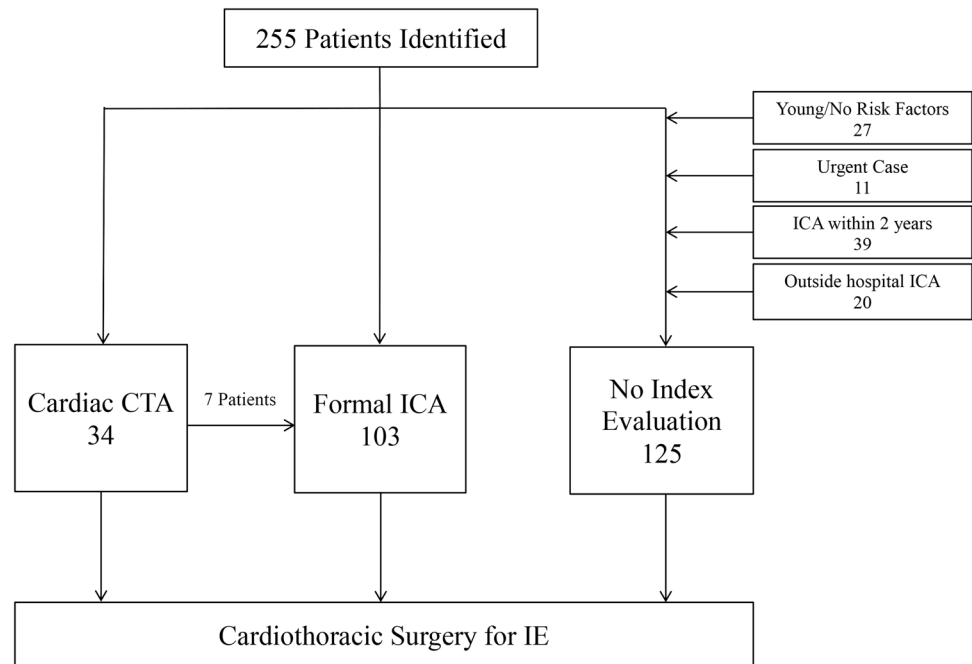
for detection of fistula, leaflet perforation, or dehiscence ranged from 40 to 50%. Specificity of cardiac CTA was high (> 90%) for all endocarditic findings. Figure 2 demonstrates a perivalvular abscess identified by cardiac CTA. Figure 3 compares the CTA and TEE imaging of a patient with periprosthetic abscess/pseudoaneurysm. Figure 4 depicts a pseudoaneurysm of the intervalvular fibrosa and an aortic valve vegetation imaged by both CTA and TEE.

Table 2 Diagnostic performance of CTA and TEE compared to intraoperative findings

Endocarditic lesion	CTA	TEE	p value
Vegetation	n = 20	n = 180	
Sensitivity	70.0 (48.1–85.4)	95.6 (91.4–97.7)	**< 0.0001**
Specificity	92.9 (68.5–98.7)	93.0 (84.6–97.0)	0.99
Leaflet perforation	n = 7	n = 63	
Sensitivity	42.9 (15.8–75.0)	81.3 (70.0-88.9)	**0.02**
Specificity	96.3 (81.7–99.3)	95.7 (91.8–97.8)	0.89
Abscess/pseudoaneurysm	n = 25	n = 88	
Sensitivity	90.5 (71.1–97.3)	78.4 (68.7–85.7)	0.21
Specificity	92.3 (66.7–98.6)	98.8 (95.6–99.7)	0.08
Dehiscence	n = 7	n = 39	
Sensitivity	57.1 (25.0-84.2)	70.0 (54.6–81.9)	0.50
Specificity	100.0 (87.5–100.0)	100.0 (98.2–100.0)	1.00
Fistula	n = 2	n = 13	
Sensitivity	50.0 (9.5–90.5)	78.6 (52.4–92.4)	0.38
Specificity	96.9 (84.3–99.4)	98.7 (96.3–99.6)	0.41

Diagnostic utility for endocarditic findings is reported for cardiac CTA and TEE. 95% confidence intervals are reported in parentheses. Sensitivity and specificity are reported as percentages

CTA computed tomography angiography, *TEE* transesophageal echocardiography

Fig. 2 Perivalvular abscess identified by cardiac CTA

Of the 255 patients included, 251 underwent pre-operative TEE and 42.9% had prosthetic valves. The median number of days from TEE to surgery was 1. Sensitivity and specificity for detection of vegetations were 95.6 and 93.0%, respectively. For the detection of abscess/pseudoaneurysm, these were 78.4 and 98.8%, respectively. For the other endocarditic findings, sensitivities ranged from 70 to 80%. Specificity of TEE for detection of fistula, leaflet perforation, and dehiscence were all high (> 90%).

When comparing the performance of cardiac CTA and TEE, statistically significant differences were demonstrated in the sensitivity for detection of vegetations and leaflet perforations with TEE performing superiorly. The sensitivity for detection of abscess/pseudoaneurysm, fistula, and dehiscence did not differ significantly between the two groups. The findings remained unchanged when an analysis was

limited to the subgroup of patients with prosthetic valve IE (Data not shown).

Table 3 compares the CAD findings between patients undergoing CTA and ICA. The proportion of patients with less than 50% coronary stenosis in the cardiac CTA group was 70.6% compared with 60.2% in the ICA group (p = 0.28). Of all the patients who underwent ICA, including the 7 previously evaluated by CTA, the proportion whose management was changed by the study was 17.5% (10.0–24.9%, 95% CI). Patients undergoing cardiac CTA were less likely to have an elevated serum creatinine (> 1.5 mg/dL) at baseline (2.9 vs. 18.4%, p = 0.03). The mean difference in serum creatinine after contrast exposure was 0.03 mg/dL in the CT group and − 0.02 mg/dL in the catheterization group (p = 0.30). The percent of patients with a serum creatinine increase > 0.3 mg/dL after contrast

Fig. 3 Perivalvular abscess/pseudoaneurysm imaged by cardiac CTA and TEE. **a** Axial cut at the level of the aortic valve. **b** Sagittal cut demonstrating a long-axis view of the left ventricle. **c** Right ventricular outflow view via TEE. **d** Left ventricular long-axis view via TEE. *Ao* aorta, *AV* aortic valve, *LA* left atrium, *LV* left ventricle, *PSA* pseudoaneurysm, *RA* right atrium, *RVOT* right ventricular outflow tract
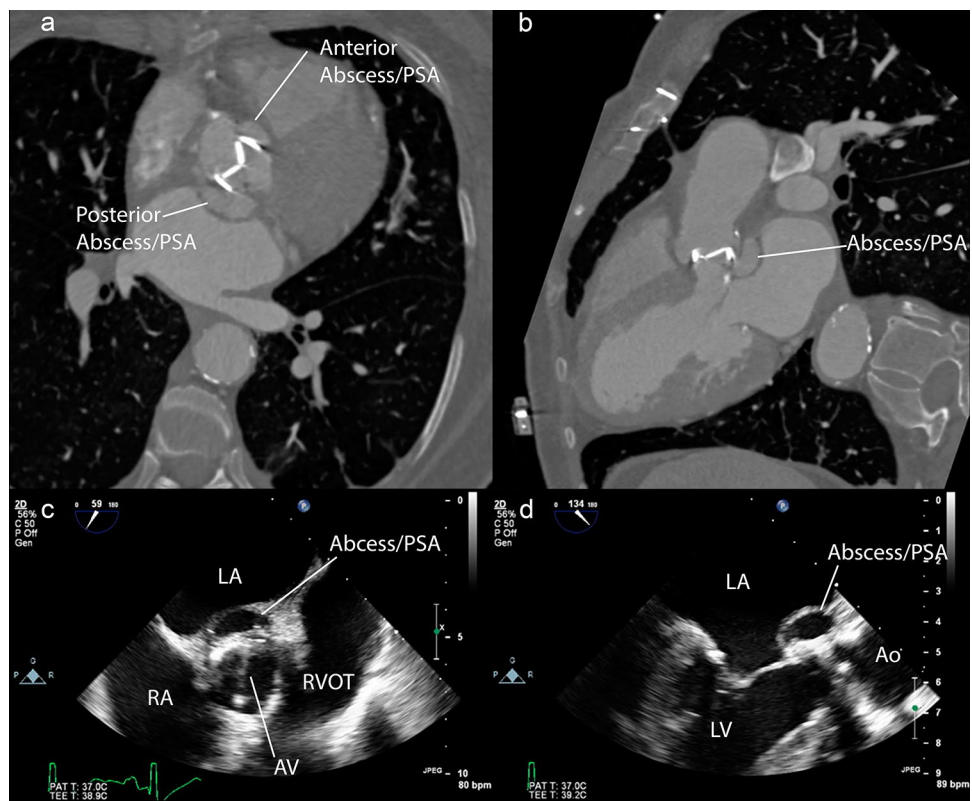
Fig. 4 Pseudoaneurysm and associated aortic valve vegetation imaged by cardiac CTA and TEE. **a, b** CTA images in oblique and sagittal sections. **c, d** TEE images of the left ventricular outflow tract, intervalvular fibrosa, and aortic valve with and without color flow doppler. *Ao* aorta, *Comm* communication, *LA* left atrium, *LV* left ventricle, *PSA* pseudoaneurysm, *Veg* vegetation
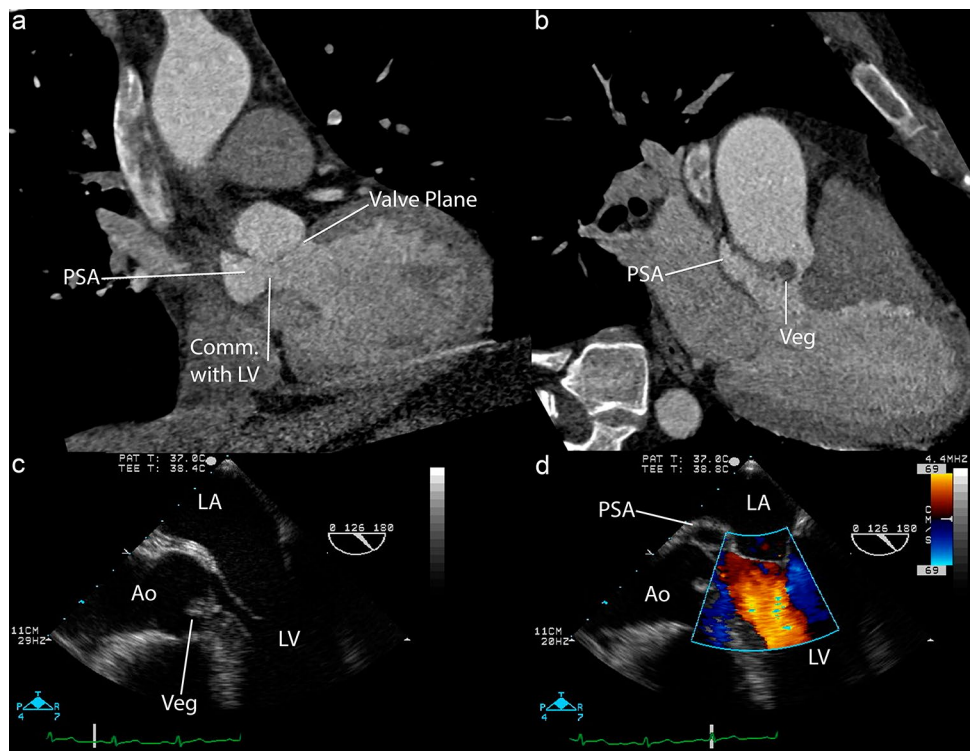
exposure was 3.5 and 3.3% respectively (p = 0.97). There was one adverse event documented in the ICA group that was an allergic reaction attributed to iodinated contrast. There were no adverse events attributed to cardiac CTA.

Table 3 CAD findings and clinical outcomes

	All patients (n = 255)	CTA group (n = 34)	ICA group (n = 103)	p value
< 50% stenosis	–	70.6 (24)	60.2 (62)	0.28
> 50% stenosis	–	29.4 (10)	39.8 (41)	0.28
Single vessel	–	50.0 (5)	41.5 (17)	0.63
Multi vessel	–	50.0 (5)	58.5 (24)	0.63
Intraoperative CABG	10.6 (27)	14.7 (5)	18.4 (19)	0.62
Perioperative mortality	6.7 (17)	2.9 (1)	2.9 (3)	0.99
Perioperative stroke	2.0 (5)	0.0 (0)	2.9 (3)	0.31
1 year mortality	14.9 (38)	5.9 (2)	11.7 (12)	0.34

Frequency of coronary artery disease in the study population is reported and stratified by pre-operative coronary artery evaluation strategy. Values are reported as percentages with number of cases in parentheses

CAD coronary artery disease, *CTA* computed tomography angiography, *ICA* invasive coronary angiography

Post-operative clinical outcomes in patients undergoing cardiac CTA vs. ICA are listed in Table 3. The rate of intraoperative bypass grafting for coronary disease was 14.7% in the cardiac CTA group (n = 5) and 18.4% in ICA group with no statistically significant difference. Of the 5 patients in the CTA group who underwent intra-operative CABG, 4 were also evaluated with ICA pre-operatively. The remaining patient underwent CABG due to anatomical complications of IE rather than due to obstructive CAD. The 1-year mortality rate post-operatively was low at 5.9 and 11.7% (p = 0.34) for the cardiac CTA and ICA groups, respectively. There was no significant difference in peri-operative stroke (n = 0 and n = 3, respectively) or mortality (n = 1 and n = 3, respectively) between the CTA and ICA groups. No peri-operative myocardial infarctions were noted in either group. Patients without a preoperative coronary evaluation demonstrated increased peri-operative and 1 year all-cause mortality rates of 10.4 and 20.0%, respectively. This difference in peri-operative mortality was statistically significant compared with ICA (p = 0.03) but not with CTA (p = 0.17). When peri-operative mortality was excluded from the 1-year mortality analysis, there were no longer any statistically significant differences between the CT group, the ICA group, and the no index evaluation group (3.0 vs. 9.0 vs. 10.7%, respectively; p = 0.42).

Discussion

The current study is the largest to date comparing cardiac CTA to TEE in IE patients. Cardiac CTA was similar to TEE in identification of abscess/pseudoaneurysm in the current investigation, while, as expected, TEE demonstrated significantly higher sensitivity for vegetations and leaflet perforation. Of note, the specificity of both tests for all IE lesions was > 90%. This is despite almost onehalf of patients having prosthetic valves with recent evidence demonstrating that CTA has the ability to change diagnosis/treatment with echocardiography in 20–25% of prosthetic IE cases [18]. In patients with difficult to characterize perivalvular extension of infection by TEE, cardiac CTA is a reasonable next diagnostic step with the ability to define the coronary arterial anatomy concomitantly, thus avoiding an additional procedure (ICA) and contrast exposure.

With regard to preoperative coronary evaluation, both groups had similar cardiac risk factors. Cardiac CTA has excellent negative predictive value in low to intermediate CAD risk patients. The evidence has been less robust in high risk patients with some studies demonstrating a continued high NPV while others maintaining a high sensitivity, but a decline in NPV due to the increased prevalence of disease [19–23]. Among patients undergoing ICA, 60% had no coronary stenosis > 50% and over 80% had no change in management. This implies that there are opportunities to increase the utilization of cardiac CTA and decrease the proportion of patients requiring an invasive procedure prior to cardiac surgery for IE. A cost effectiveness study incorporating CTA as a first line test in pre-operative coronary evaluation for non-cardiac surgery demonstrated a decreased cost associated with the work-up and perioperative period [24]. Therefore, in addition to avoiding an invasive procedure with a low risk for adverse events, this strategy may be fiscally prudent as well.

The low rate of cardiac CTA utilization in the current study population is noteworthy. While this fluctuated from year-to-year, there was no clear trend towards increased utilization from 2007 to 2014, even after the 2009 prospective study by Feuchtner et al. suggested its utility [25]. Potential factors that account for this low rate of utilization are likely uncertainty about the clinical value of cardiac CTA given the small studies to date, a long history of preoperative evaluation of coronaries by cardiac catheterization, and an understandable desire to avoid a double contrast load if a study is positive or non-diagnostic, particularly in severely ill patients with renal dysfunction.

Figure 5 displays an algorithm adapted from the 2014 AHA/ACC guideline for valvular heart disease by Nishimura et al. and our proposal for the approach to preoperative coronary assessment for patients with IE [26]. Unless patients have symptoms of active ischemic coronary disease or are at high pre-test probability, then performing a cardiac CTA may be reasonable. This will reliably exclude significant CAD, potentially avoid ICA with its associated costs/potential complications, and may assist with surgical planning.

There are several studies published to date to support this strategy of pre-operative CTA in non-cardiac as well as cardiac surgery [27]. Jakamy et al. evaluated 48 patients who underwent elective valve surgery and found that CTA had an NPV of 91% and ICA could have been avoided in 65% of patients [28]. Ciolina et al. demonstrated the additive value of cardiac CTA for assessing the aortic valve in pre-operative work-up for aortic stenosis [29]. In 42 patients, CTA correctly graded aortic valve calcification, sized the aortic annulus and sinotubular junction, detected thoracic aortic aneurysms, and correctly assessed aortic valve area over 90% of the time while also being used to assess coronary status. The ability of cardiac CTA to simultaneously provide additive diagnostic information and reliably assess coronary status makes it a versatile diagnostic test with significant yield in the pre-operative work-up of patients with IE and other valvular disorders.

Our study has limitations that deserve address. The study of IE has been hindered for decades by its relatively uncommon nature and the vast heterogeneity in microbiology, clinical presentation, disease manifestations, and patient factors. This has historically resulted in small study populations and a general lack of prospective randomized studies (Online Resource 1). Therefore, while the current investigation is limited by its size and retrospective nature, this is in line with how IE has historically been studied. Next, by identifying patients who underwent surgery for IE, we excluded patients who may have had a rarely reported fatal coronary embolic event during ICA or other severe complications including AKI resulting in dialysis dependence. Therefore, our study did not include identification of significant adverse events at the time of cardiac catheterization. Finally, the rates of perioperative mortality, stroke, and MI were low for both groups, accounting for a reduced statistical power for detecting differences.

Conclusion

The greatest advantage of cardiac CT in the setting of IE is its ability to couple the detection of complex cardiac anatomic abnormalities with coronary artery delineation. Cardiac CTA may be considered as an alternate coronary artery imaging modality in IE patients with low to intermediate risk of disease but meet guideline recommendations for coronary artery imaging.

Fig. 5 Proposed algorithm for pre-operative coronary artery evaluation for patients with infective endocarditis. *CAD* coronary artery disease, *CTA* computed tomography angiography
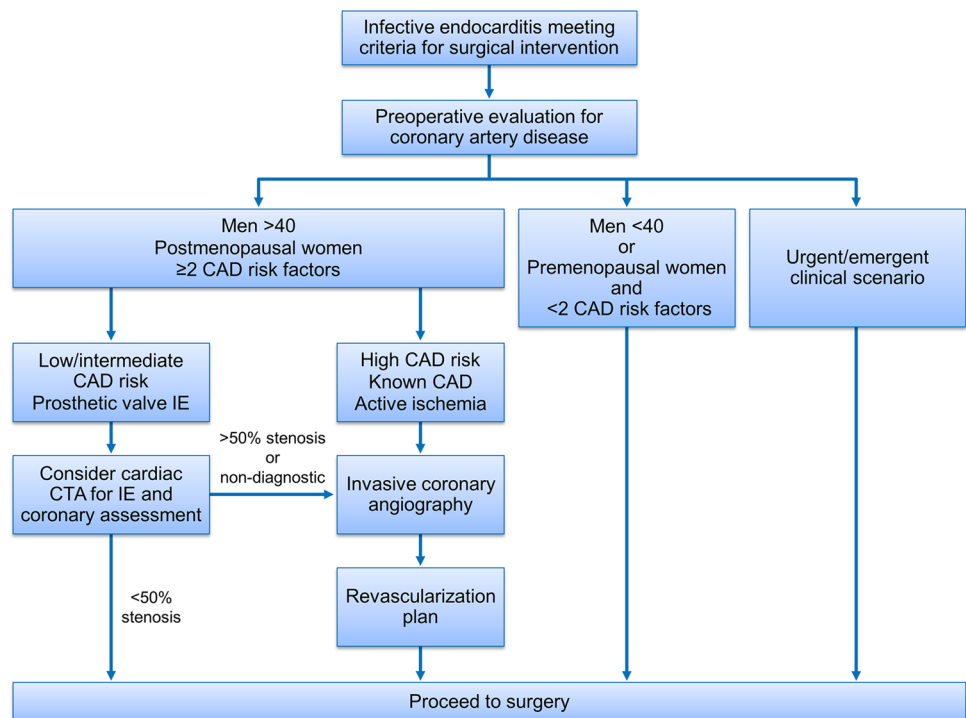
Compliance with ethical standards

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