Diagnostic Performance of Transesophageal Echocardiography and Cardiac Computed Tomography in Infective Endocarditis

Islem Sifaoui, MD, Leopold Oliver, MD, Vania Tacher, MD, PhD, Antonio Fiore, MD, Raphael Lepeule, MD, Amina Moussafeur, Raphaelle Huguet, MD, Emmanuel Teiger, MD, PhD, Etienne Audureau, MD, PhD, Haytham Derbel, MD, Alain Luciani, MD, PhD, Hicham Kobeiter, MD, PhD, Pascal Lim, MD, PhD, Julien Ternacle, MD, PhD, and Jean-François Deux, MD, PhD, *Créteil, France*

Background: Multimodality imaging is essential for infective endocarditis (IE) diagnosis. The aim of this work was to evaluate the agreement between transesophageal echocardiography (TEE) and cardiac computed tomography (CT) findings in patients with surgically confirmed IE.

Methods: Sixty-eight patients (mean age 63 ± 2 years) with a definite diagnosis of left-side IE according to the modified European Society of Cardiology Duke criteria, on both native and prosthetic valves, underwent TEE and cardiac CT before surgery. The presence of valvular (vegetations, erosion) and paravalvular (abscess, pseudoaneurysm) IE-related lesions were compared between both modalities. Perioperative inspection was used as reference.

Results: TEE performed better than CT in detecting valvular IE-related lesions (TEE area under the curve [AUC_{TEE}] = 0.881 vs AUC_{CT} = 0.720, *P* = .02) and was similar to CT with respect to paravalvular IE-related lesions (AUC_{TEE} = 0.830 vs AUC_{CT} = 0.816, *P* = .835). The ability of TEE to detect vegetation was significantly better than that of CT (AUC_{TEE} = 0.863 vs AUC_{CT} = 0.693, *P* = .02). The maximum size of vegetations was moderately correlated between modalities (Spearman's rho = 0.575, *P* < .001). Computed tomography exhibited higher sensitivity than TEE for pseudoaneurysm detection (100% vs 66.7%, respectively) but was similar with respect to diagnostic accuracy (AUC_{TEE} = 0.833 vs AUC_{CT} = 0.984, *P* = .156).

Conclusions: In patients with a definite diagnosis of left-side IE according to the modified European Society of Cardiology Duke criteria, TEE performed better than CT for the detection of valvular IE-related lesions and similar to CT for the detection of paravalvular IE-related lesions. (J Am Soc Echocardiogr 2020;33:1442-53.)

Keywords: Endocarditis, Cardiac computed tomography, Transesophageal echocardiography, Paravalvular complications, Cardiac surgery

Infective endocarditis (IE) is a serious infection of the endocardial surface of the heart that most commonly involves the valves, and it requires urgent treatment including cardiac surgery in 75% of cases.[1-3] In addition to microbiological investigations, the noninvasive imaging evaluation is the cornerstone of IE diagnosis.[4] Identification of IE-related valvular (i.e., vegetation and leaflet erosion) and/or paravalvular lesions (i.e., abscess and pseudoaneurysm) is one of the two major Duke criteria. The first-line modality includes echocardiography using both transthoracic (TTE) and transesophageal (TEE) approaches because they provide a dynamic, precise, and complementary analysis

From the Radiology Department (I.S., V.T., H.D., A.L., H.K., J.-F.D.), Cardiology Department, SOS Endocardites unit (L.O., A.M., R.H., E.T., P.L., J.T.), Cardiac Surgery Department (A.F.), Antimicrobial Stewardship Team (R.L.), and Public Health Department (E.A.), Henri Mondor Hospital, Assistance Publique-Hôpitaux de Paris, INSERM U955, Team 8 (L.O., A.F., R.H., E.T., H.K., P.L., J.T., J.-F.D.), and INSERM U955, Team 18 (V.T., A.L.), Paris-Est Creteil University, Val-de-Marne, Créteil, France.

J.T. and J.-F.D. should be considered joint senior authors.

Conflicts of Interest: P.L. and J.T. are consultants for General Electric, but this study did not receive financial support from the industry. The remaining authors have no conflicts of interest.

Reprint requests: Dr. Islem Sifaoui, Service d'imagerie médicale, Henri Mondor Hospital 51 avenue Du Maréchal de Lattre de Tassigny, 94010 Créteil, France (E-mail: *islem.sifaoui@aphp.fr*).

0894-7317/$36.00

https://doi.org/10.1016/j.echo.2020.07.017

Abbreviations

2D = Two-dimensional

3D = Three-dimensional

AUC = Area under curve

CT = Computed tomography

ECG = Electrocardiogram

ESC = European Society of Cardiology

IE = Infective endocarditis

NPV = Negative predictive value

NVE = Native valve endocarditis

PPV = Positive predictive value

PVE = Prosthetic valve endocarditis

ROC = Receiver operating characteristic

TEE = Transesophageal echocardiography

TTE = Transthoracic echocardiography

of the valves.[5-8] However, TEE accuracy for detecting local and regional complications may be limited, especially in patients with prosthetic valve endocarditis (PVE). Cardiac computed tomography (CT) is recommended to detect valvular and mainly paravalvular lesions in patients with PVE or when echocardiography is inconclusive and to accurately assess IE-related cardiac lesions for better surgical procedure planning.[4,9,10] However, most studies evaluating the performance of cardiac CT for the detection of IE included a relatively small number of patients,[11-19] and the surgical confirmation was not systematically performed in these series. Therefore, the aim of our study was to compare the performance of TEE and cardiac CT in the detection of IE-related cardiac lesions according to surgery findings in a large series of patients with a definite diagnosis of left-side IE based on the modified European Society of Cardiology (ESC) Duke criteria.

METHODS

Study Population

The Cardiology Department of Henri Mondor Hospital includes a unit specializing in the management of IE, which prospectively and consecutively enrolled all patients with a definite diagnosis of IE. The diagnosis of IE was based on the modified ESC Duke criteria[4] and validated by our local endocarditis team. All patients referred to our center with a definite diagnosis of IE systematically had a multimodality imaging evaluation including TTE, TEE, and whole-body CT with a cardiac acquisition. In these patients, CT was performed routinely to provide the surgeon with a comprehensive multimodality assessment of the valve in question. We retrospectively identified in this database patients with a definite diagnosis of IE according to the modified ESC Duke criteria who had TTE, TEE, CT, and cardiac surgery (n = 141) between November 2015 and August 2017. Exclusion criteria were patients with right heart IE (n = 12), patients explored with nongated cardiac CT (n = 51), or a delay >7 days between imaging and surgery (n = 10). Finally, 68 patients were included. Our institutional review board approved the protocol. All patients were informed of the benefit and risk of the management and treatment decision, and they gave their written consent.

Echocardiography Imaging Acquisition and Analysis

All patients underwent both TTE and TEE evaluation as per the recommendations of the European Society of Cardiovascular Imaging guidelines using commercially available equipment (Vivid e9 and e95 systems, General Electric Vingmed Ultrasound, Horten, Norway). Comprehensive TEE was performed by cardiologists using a two- (2D) and three-dimensional (3D) transesophageal probe (6VT-D, General Electric Vingmed Ultrasound). Recordings were electrocardiogram (ECG) -gated and systematically included 2D and 3D acquisitions with and without color Doppler focused on both the aortic and the mitral valves (four-dimensional zoom acquisition using one- or multibeat modality).

Study analysis was performed by consensus by two cardiologists aware that the patient had a confirmed left-side IE according to the modified ESC Duke criteria, but without further information on the patient's clinical, CT, and biological status, at least 6 months after the initial acquisition. In order to calculate reproducibility, a second analysis of 20 randomly selected patients was performed more than 2 months after the first one. Quality of cardiac TEE images was scored on a three-point scale: 1: good (good image quality, view plane, and Doppler settings); 2: intermediate (adequate but not optimal image quality, view plane, or Doppler settings); 3 weak (poor image quality, view plane, and Doppler settings). Transesophageal echocardiography image interpretation consisted of a new 2D and 3D acquisition analysis combined with systematic 3D multiplanar reconstruction using dedicated offline software (ECHOPac, ver. 12, General Electric Medical). The presence of vegetation, leaflet erosion, paravalvular abscess, and pseudoaneurysm was classified. Definitions of these IE-related cardiac lesions are reported in Table 1.[18] The TEE was considered positive for the detection of IE-related cardiac lesion if at least one of these signs was present. Measurements of vegetation were performed on the image presenting the largest vegetation size.

Cardiac CT Imaging

Acquisition Protocol. All patients were examined using a 256-row detector CT system (Revolution CT, General Electric Healthcare,

Table 1 Definition of lesions related to IE by TEE and cardiac CT

Findings	TEE	Cardiac CT
Vegetation	Oscillating or nonoscillating intracardiac mass on a valve or other endocardial structure	Hypodense, homogeneous, irregular mass on a valve or endocardial structure
Leaflet erosion	Interruption of endocardial tissue continuity traversed by color Doppler	Defect in a leaflet
Paravalvular abscess	Thickened, irregularly shaped inhomogeneous, paravalvular area or mass with echodense or echolucent appearance	Irregularly shaped, inhomogeneous paravalvular masses within periannular region, myocardium, or pericardium
Pseudoaneurysm	Pulsatile paravalvular echo-free space detected with color Doppler	Abnormal cavity close to a valve enhancing concomitantly with cardiac or aortic lumen

HIGHLIGHTS

- TEE performed better than CT for detection of valvular IE-related lesions.
- TEE and CT were similar in the detection of paravalvular IE-related lesions.
- CT may be useful when TEE is equivocal or not feasible in left-side IE.

Milwaukee, WI) using a standardized protocol. Cardiac exploration included two prospectively ECG-triggered acquisitions, each performed on single cardiac cycle: a low-dose nonenhanced cardiac acquisition (calcium scoring acquisition protocol) followed by a prospective acquisition (covering 30%-80% of the RR space) performed after contrast medium injection (60 mL of Iomeron 400 infused at a rate of 5 mL/sec followed by 30 mL normal saline by a dual-head power injector). Scanning parameters of the contrast-enhanced acquisition were collimation 256 × 0.625 mm, scan coverage was 160 mm, tube voltage was 100 kV, mA intensity was 150-500 mA, rotation time was 0.28 msec, matrix size was 512 × 512 pixels, and reconstruction section thickness and section interval were 0.625 mm. According to the acquisition protocol performed in our center, a brain CT (acquired before cardiac CT, without contrast medium injection) and a thoracoabdominopelvic CT performed 70 seconds after contrast medium injection were systematically performed to detect systemic embolisms. Mean dose length product for cardiac CT was 140 ± 50 mGy cm, and total dose length product (including brain and thoracoabdominopelvic CT) was 1,850 ± 250 mGy.cm.

CT Image Analysis. All CT analysis was performed 6 months after images acquisition, by the consensus of two cardiac radiologists, who were aware that the patient had a confirmed left-side IE according to the modified ESC Duke criteria but had no further information on the patient's clinical, TEE, and biological status. A second analysis session in 20 randomly selected patients, performed more than 2 months after the first one, was used to calculate reproducibility of the readers.

Table 2 Characteristics of the study population

Characteristics	*n* (%)
No. of patients	68
Age, years ± SD (range)	63 ± 2 (24-88)
Sex, male	53 (78)
Hypertension	35 (51)
Diabetes	18 (27)
Atrial fibrillation or flutter	13 (19)
Coronary artery disease	8 (12)
Dyslipidemia	18 (26)
Renal failure	7 (9)
Intravenous drug addiction	0 (0)
Neoplasia	13 (19)
Valve involved	
Prosthetic	15 (22)
Native	53 (78)
Aortic	42 (62)
Mitral	22 (32)
Multiple	4 (6)
Microbiology	
Culture positive	60 (88)
Staphylococcus	19 (28)
Streptococcus	26 (38)
Enterococcus	10 (15)
Others	5 (7)

Data are reported as *n* (%) unless otherwise indicated.

Table 3 Surgical findings

Surgical data	*n* (%)
Operated patients	68 (100)
IE-related lesions surgically confirmed	63 (93)
Valvular lesion (vegetation or erosion)	56 (82)
Vegetation	56 (82)
Native aortic valve	27 (40)
Prosthetic aortic valve	8 (12)
Native mitral valve	16 (24)
Prosthetic mitral valve	1 (1)
Bivalvular	4 (6)
Leaflet erosion	19 (28)
Native aortic valve	12 (18)
Prosthetic aortic valve	NA
Native mitral valve	5 (7)
Prosthetic mitral valve	NA
Bivalvular	2 (3)
Paravalvular lesion (abscess or pseudoaneurysm)	24 (35)
Abscess	22 (32)
Native aortic valve	11 (16)
Prosthetic aortic valve	4 (6)
Native mitral valve	4 (6)
Prosthetic mitral valve	1 (1)
Bivalvular	2 (3)
Pseudoaneurysm	6 (9)
Native aortic valve	4 (6)
Prosthetic aortic valve	2 (3)
Native mitral valve	0 (0)
Prosthetic mitral valve	0 (0)
Bivalvular	0 (0)

NA, Not available.

Table 4 Diagnostic performance of TEE and cardiac CT for the detection of cardiac lesions related to IE

Diagnostic performance	All patients (*N* = 68)		NVE (*n* = 53)		PVE (*n* = 15)	
	TEE	CT	TEE	CT	TEE	CT
Vegetation (*n* = 56), %						
Sensitivity	89.3	80.4	91.1	80.0	81.8	81.8
Specificity	83.3	58.3	87.5	62.5	75.0	50.0
PPV	96.1	90.0	97.8	92.3	90.0	81.8
NPV	62.5	38.9	63.6	35.7	60.0	50.0
Diagnostic accuracy	88.2	76.5	90.6	77.3	80.0	50.0
Leaflet erosion (*n* = 19), %						
Sensitivity	68.4	68.4	68.4	68.4	NA	NA
Specificity	89.8	73.5	85.3	64.7	NA	NA
PPV	72.2	50.0	72.2	52.0	NA	NA
NPV	88.0	85.7	82.9	78.6	NA	NA
Diagnostic accuracy	83.8	72.1	79.2	66.0	NA	NA
Abscess (*n* = 22), %						
Sensitivity	72.7	77.3	73.3	80.0	71.4	71.4
Specificity	89.1	80.4	92.1	86.8	75.0	50.0
PPV	76.2	65.4	78.6	70.6	50.0	55.6
NPV	87.2	88.1	89.7	91.7	66.7	66.7
Diagnostic accuracy	83.8	79.4	86.8	84.9	73.3	60.0
Pseudoaneurysm (*n* = 6), %						
Sensitivity	66.7	100	50.0	100	75.0	100
Specificity	100	96.8	100	96.8	100	100
PPV	100	75.0	100	100	100	100
NPV	96.9	100	98.1	100	91.7	100
Diagnostic accuracy	97.0	97.1	98.1	96.2	93.3	100

NA, Not appropriate.

Quality of cardiac CT images was scored on a three-point scale: 1: good (cardiac valves and other cardiac structures clearly visible, no kinetic artifacts, excellent opacification of cardiac cavities); 2: intermediate (some kinetic/motion artifacts on cardiac structures or weak opacification of cardiac cavities); 3 weak (kinetic/motion artifacts and weak opacification of cardiac cavities).

From raw data sets, images were generated using an iterative technique (Adaptive Statistical Iterative Reconstruction 50%). For all patients, 10 transverse data sets were reconstructed for every 5% of the cardiac cycle (30%-80%). Reconstructed images were analyzed using a dedicated platform (Advantage Workstation 4.7; Revolution CT, General Electric Healthcare). Aortic and mitral valves were analyzed on diastolic and systolic images. Multiphasic reconstructions images were also used to perform a dynamic analysis of the movement of the valves. The presence of vegetation, leaflet erosion, paravalvular abscess, and pseudoaneurysm were classified. Definitions of these IE-related cardiac lesions are reported in Table 1. Computed tomography was considered positive for the detection of IE-related

Table 5 Comparison of AUC for cardiac CT, TEE, and both modalities for the detection of cardiac lesions related to IE

	AUC TEE	AUC CT	AUC CT + TEE	*P**	*P*†
Vegetations	0.863	0.693	0.765	.018	.143
Leaflet erosion	0.791	0.709	0.831	.368	.500
Vegetations + leaflet erosion	0.881	0.720	0.783	.024	.143
Abscess	0.809	0.789	0.835	.762	.600
Pseudoaneurysm	0.833	0.984	0.984	.156	.156
Abscess + pseudoaneurysm	0.830	0.816	0.845	.835	.746

Surgery was considered as the gold standard.
*AUC TEE vs AUC CT.
†AUC TEE vs (TEE + CT).

Table 6 Diagnostic performance of TEE and cardiac CT for the detection of cardiac lesions related to IE in aortic and mitral valve

	Aortic valve (*n* = 42)		Mitral valve (*n* = 22)	
Diagnostic performance	TEE	CT	TEE	CT
Vegetation, %				
Sensitivity	88.6	85.7	94.1	70.6
Specificity	85.7	71.4	80.0	40.0
PPV	96.9	93.8	94.1	80.0
NPV	60.0	50.0	80.0	28.6
Diagnostic accuracy	88.1	83.3	90.1	63.6
Leaflet erosion, %				
Sensitivity	75.0	58.3	60.0	80.0
Specificity	86.7	80.0	94.1	58.8
PPV	69.2	53.8	75.0	36.4
NPV	89.7	82.8	88.9	90.9
Diagnostic accuracy	83.3	73.8	86.4	63.6
Abscess, %				
Sensitivity	86.7	86.7	40.0	60.0
Specificity	85.2	77.8	94.1	82.4
PPV	76.5	68.4	66.7	50.0
NPV	92.0	91.3	84.2	87.5
Diagnostic accuracy	85.7	81.0	81.8	77.3
Pseudoaneurysm, %				
Sensitivity	66.7	100	NA	NA
Specificity	100	94.4	100	100
PPV	100	75.0	NA	NA
NPV	94.7	100	100	100
Diagnostic accuracy	95.2	95.2	100	100

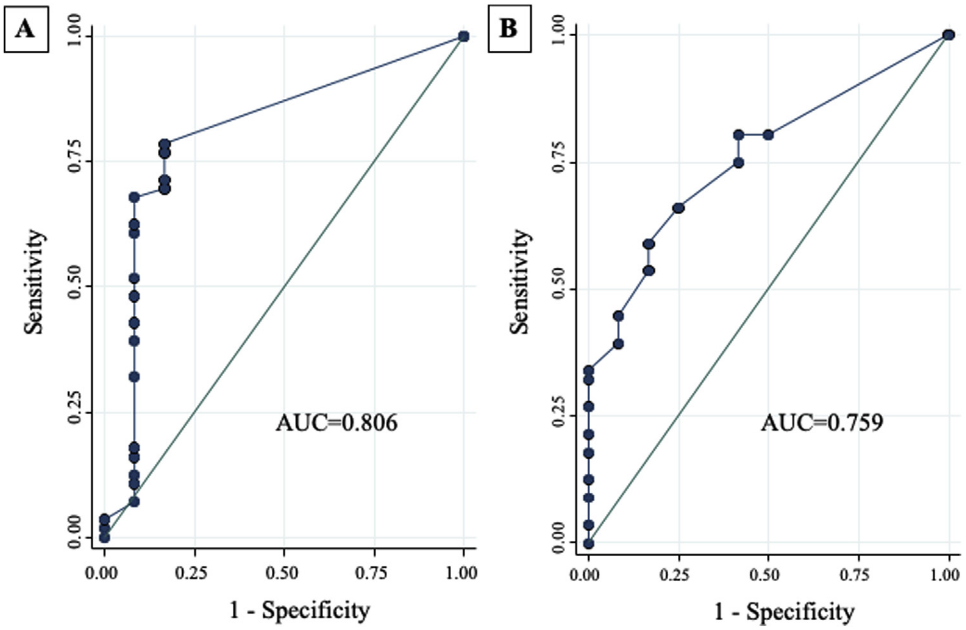

Figure 1 ROC curves that illustrates the performance of TEE **(A)** and cardiac CT **(B)** for the detection of vegetation.

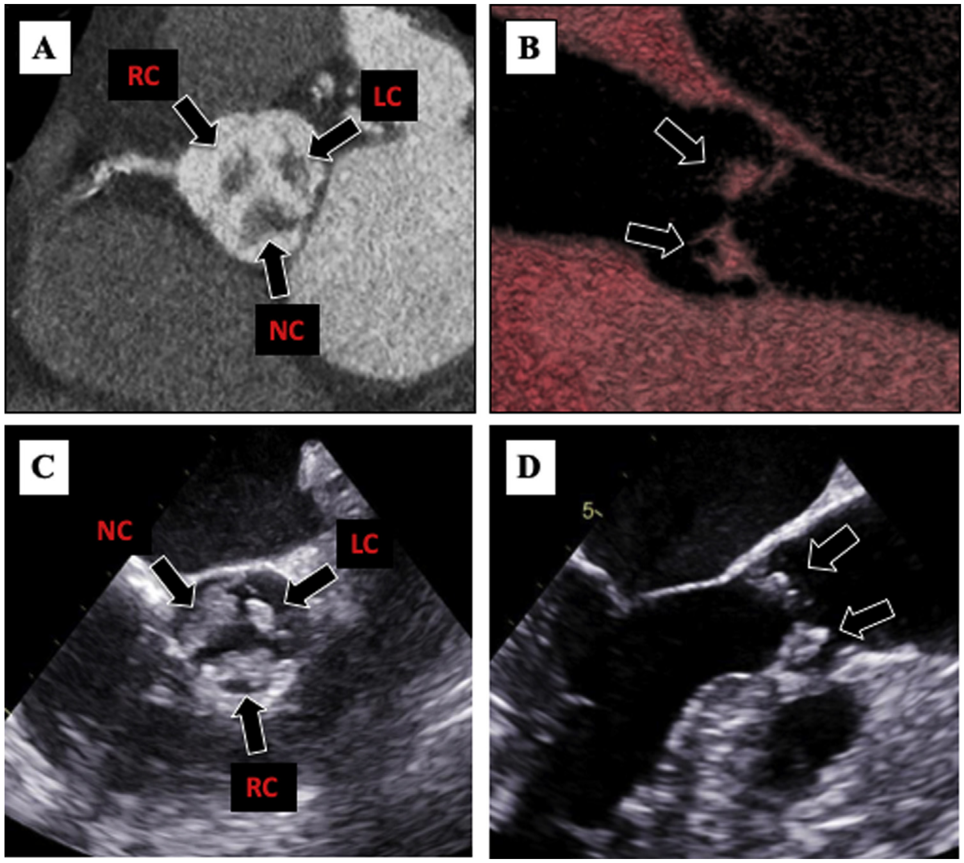

Figure 2 Example of a 76-year-old patient with an IE of the native aortic valve. Large vegetations (*arrows*) were observed on the three aortic leaflets by CT from the en face view **(A)** and the volume-rendered image of the left ventricular outflow tract (**B**; image quality: 1). Similar findings were observed by TEE from the short-axis **(C)** and the long-axis **(D)** views of the aortic valve (image quality: 1). *LC*, Left coronary; *NC*, noncoronary; *RC*, for right coronary.

cardiac lesion if at least one of these signs was present. Measurements of vegetation were performed on the image presenting the largest vegetation size.

Surgical Findings

All patients were referred to cardiac surgery. Infective endocarditis–related cardiac lesions were recorded by review of the operation records. These included the presence and location of vegetation, leaflet erosion, paravalvular abscess, and pseudoaneurysm.

Statistical Analysis

Continuous variables are presented as means ± SD or median (25%-75% interquartile range), and categorical variables are expressed as percentages. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracies of CT and TEE were calculated for each lesion separately. Regarding the diagnostic performance of cardiac CT and TEE to detect the presence of any IE-related cardiac lesions, sensitivity and PPV were calculated. Specificity and NPV were not calculated because of the low number of real negative cases. Areas under receiver operating characteristic (ROC) curves were compared using the approach by DeLong *et al.*[20] to account for the correlation between ROC areas obtained from applying two or more test modalities to the same sample. Cohen's kappa coefficients were estimated to assess the diagnosis agreement between the two test modalities (TEE and CT) for detecting vegetation and paravalvular complications. Interrater reliability for echocardiography and CT imaging findings were calculated with the Cohen's kappa test. The kappa coefficient of 0-0.40 was considered poor agreement, 0.41-0.60 was considered moderate agreement, 0.61-0.80 was considered good agreement, and 0.81-1.00 was considered very good agreement of the findings. Spearman correlation coefficients were estimated to compare the magnitude of the association between vegetation size by CT and TEE. A value of $P < .05$ was considered significant. All statistical analyses were performed using SPSS v. 25.0 (SPSS, Chicago, IL).

RESULTS

Population Characteristics

Overall, 68 patients with a definite diagnosis of left-side IE according to the modified ESC Duke criteria who underwent TEE, cardiac CT, and surgery were enrolled. All clinical and microbiological characteristics of patients are shown in Table 2. The mean age was 63 ± 2 years, and 78% of patients were men. Before surgery, IE was detected on the aortic valve in 62% of cases and on the mitral valve in 32% of cases, and four patients (6%) had a bivalvular involvement. Native valve endocarditis

(NVE) and PVE were observed in 78% and 22% of cases, respectively. Twelve percent of patients had negative blood cultures. *Streptococcus* (38%) and *Staphylococcus* (28%) were the two most common microbiological agents identified. Infective endocarditis–related cardiac lesions were surgically confirmed in 63 (93%) patients. All surgical findings are reported in Table 3. The median intervals between TEE and CT, between CT and surgery, and between TEE and surgery were 1.0 (0-1), 2.0 (1-3), and 2.0 (1-3.7) days, respectively.

Quality of TEE and CT Images

The mean quality score of TEE images was 1.2 ± 0.4 (1-3). Fifty-four patients (79%) exhibited a good image quality (grade 1). Image quality was judged intermediate in 12 patients (18%; grade 2) and weak in the remaining two patients (3%, grade 3). The mean quality score of CT images was 1.7 ± 0.8.[1-3] Thirty-four patients (50%) exhibited a good image quality (grade 1). Image quality was judged intermediate in 21 patients (31%; grade 2) and weak in the remaining 13 patients (19%, grade 3).

Comparison between TEE and Cardiac CT

Diagnostic performances of TEE and cardiac CT for the detection of IE-related cardiac lesions according to the presence of vegetation, leaflet erosion, abscess, and pseudoaneurysm are reported in Tables 4 and 5. No patients had paravalvular fistula.

Detection of IE-Related Cardiac Lesions. Transesophageal echocardiography and CT exhibited similar accuracy to detect IE-related cardiac lesions (92.6% both for TEE and CT). The diagnostic performance of each modality did not differ significantly according to the image quality score: for TEE, diagnostic accuracy was 90.7%, 100%, and 100%, respectively, for patients with good (grade 1), intermediate (grade 2), and weak (grade 3) image quality score ($P = .49$); for CT, diagnostic accuracy was 88.2% for grade 1, 100% for grade 2, and 92.3% for grade 3 ($P = .31$). Sensitivity and PPV of TEE (93.6% and 95.3%, respectively) and CT (96.8% and 98.3%, respectively) were similar. Transesophageal echocardiography performed better than CT regarding detection of valvular (vegetations + leaflet erosion) IE-related lesions and was similar with respect to paravalvular (abscess + pseudoaneurysm) ones (Table 5). Compared with TEE alone, the combination of both modalities for the detection of valvular IE-related lesions slightly increased sensitivity (98.2% vs 92.8%) but markedly decreased specificity (58.3% vs 83.3%), without significant variation of the area under the curve (AUC; 0.783 vs 0.881; $P = .143$). Regarding paravalvular IE-related lesions, the combination of both modalities increased sensitivity (91.6% vs 75.0%) but decreased specificity (79.5% vs 90.9%), without significant variation of the AUC (0.845 vs 0.830; $P = .746$; Table 5).

Detection of Vegetation. Fifty-six patients (82%) exhibited vegetations that were confirmed by cardiac surgery. Fifty cases (74%) were correctly detected with TEE, and 45 cases (66%) with CT. There were

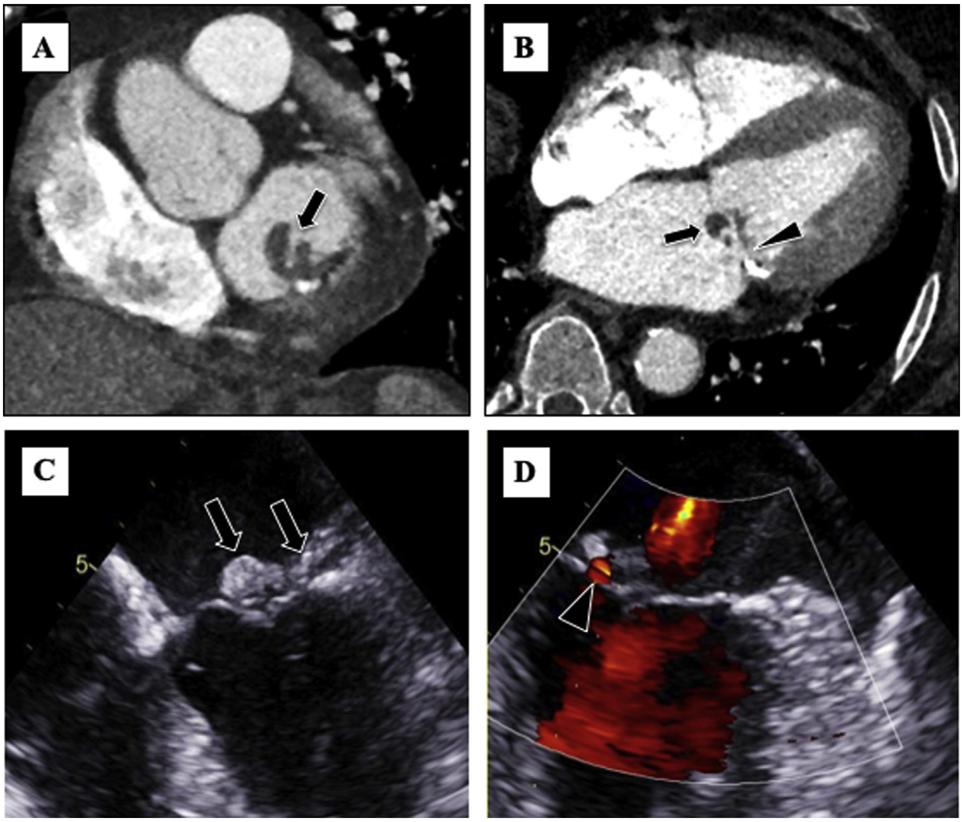

Figure 3 Example of an 85-year-old patient with an IE of the native mitral valve. A large nodular vegetation of the posterior leaflet (*arrows*) was observed by CT from the short-axis **(A)** and four-chamber **(B)** views (image quality: 1). A defect on the posterior leaflet (*arrowhead*) suggesting erosion of the mitral valve was also observed. The large vegetation was associated with a posterior leaflet infiltration on TEE images (**C**, *arrows*), and the color Doppler images confirmed the erosion of the posterior leaflet **(D**, *arrowhead*; image quality: 1).

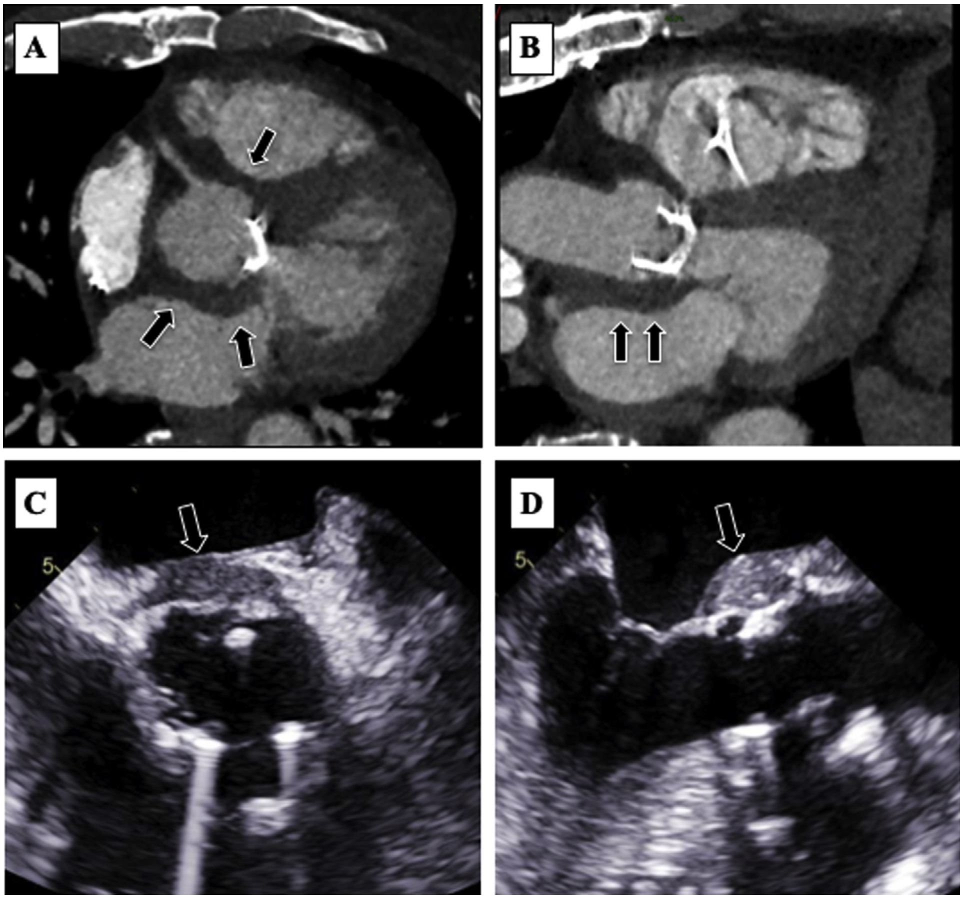

Figure 4 Example of a 72-year-old patient with an IE of the aortic bioprosthesis valve complicated by an abscess. The axial **(A)** and long-axis **(B)** views from CT revealed a circumferential thickening (*arrows*) surrounding the aortic bioprosthesis (image quality: 1). Transesophageal echocardiography also evidenced the thickening of the periprosthetic valve but only at the posterior part (**C and D**, *arrows*; image quality: 1).

two false positives with TEE (aortic NVE [$n = 1$], mitral PVE [$n = 1$]) and five false positives with CT (aortic NVE [$n = 1$] and PVE [$n = 1$]; mitral NVE [$n = 2$] and PVE [$n = 1$]). Sensitivity, specificity, and accuracy of TEE were higher than CT (Table 4), and the AUC of TEE was significantly higher than that of CT (Table 5). Transesophageal echocardiography was similar for vegetation detection in aortic (AUC = 0.870) and mitral (AUC = 0.871, $P = .950$) IE. Computed tomography was also similar for vegetation detection in aortic (AUC = 0.786) and mitral IE (AUC = 0.553, $P = .162$; Table 6). The interrater agreement for the detection of vegetation was moderate on CT images (kappa = 0.496, $P < .01$) and on TEE (kappa = 0.549, $P < .02$). The agreement between CT and TEE was moderate (kappa = 0.452, $P < .001$). The agreement was poor between CT and surgery (kappa = 0.323; $P < .01$) and good between TEE and surgery (kappa = 0.642; $P < .0001$). Combining TEE and CT did not improve the ability to detect vegetation compared with TEE alone (Table 5).

Regarding the size of the 56 vegetations measured during surgery, 33 (58.9%) were larger than 10 mm, 45 (80.3%) were larger than 7 mm, and 53 (94.6%) were larger than 4 mm. The correlation between TEE and CT was moderate (Spearman's rho = 0.575, $P < .0001$) and not improved when only large vegetations (≥10 mm) were considered. For TEE, the higher Youden index was obtained for a vegetation size of 4 mm, with 76.8% sensitivity and 83.3% specificity. For CT, a vegetation size of 7 mm was associated with the best pairing of sensitivity (66.1%) and specificity (75.0%). The AUC of TEE (0.806) and CT (0.759) did not exhibit statistical difference ($P = .465$; Figure 1). An example of a patient with vegetation related to an aortic NVE is shown in Figure 2.

Detection of Leaflet Erosion. Nineteen patients (28%) exhibited leaflet erosion at surgery, all located on native valve. Thirteen (68%) of 19 were correctly diagnosed with TEE and CT. There were five false positives with TEE (aortic NVE [$n = 4$] and mitral NVE [$n = 1$]) and 14 false positives with CT (aortic NVE [$n = 7$] and mitral NVE [$n = 7$]). Specificity and accuracy of leaflet erosion detection by TEE were higher than by CT, while sensitivity was similar for both modalities (Table 4). The AUCs were similar between modalities (Table 5). Transesophageal echocardiography and CT also performed similarly in both aortic ($AUC_{TEE} = 0.808$ vs $AUC_{CT} = 0.692$, $P = .284$) and mitral IE ($AUC_{TEE} = 0.771$ vs $AUC_{CT} = 0.694$, $P = .697$; Table 6). The interrater agreement for the detection of leaflet erosion was moderate on CT images (kappa = 0.465, $P < .02$) and on TEE (kappa = 0.549; $P < .02$). The agreement between CT and TEE was poor (kappa = 0.351, $P < .003$). The agreement was poor between CT and surgery (kappa = 0.376; $P < .02$) and moderate between TEE and surgery (kappa = 0.592; $P < .0001$). The association of TEE and CT increased slightly AUC (Table 5), but no significant difference was detected. An example of patient with mitral IE and leaflet erosion is reported in Figure 3.

Detection of Paravalvular Abscess. Twenty-two patients (32%) had a paravalvular abscess confirmed by surgery. Sixteen cases were correctly diagnosed with TEE (72.7%) and 17 cases with CT (77.3%). There were five false positives with TEE (aortic NVE [$n = 2$] and PVE [$n = 2$] and mitral NVE [$n = 1$]) and nine false positives with CT (aortic NVE [$n = 3$] and PVE [$n = 3$]; mitral NVE [$n = 2$] and PVE [$n = 1$]). Transesophageal echocardiography and CT were similar in the detection of paravalvular abscess in the overall population and in NVE (Tables 4 and 5). The performance of TEE trended higher (diagnostic accuracy, 73.3%) than that of CT (60.0%) in PVE but without statistical significance ($AUC_{TEE} = 0.732$ vs $AUC_{CT} = 0.607$, $P = .451$). Transesophageal echocardiography and CT performed worse in PVE than in NVE. Computed tomography and TEE were similar for the detection of abscess in both aortic ($AUC_{TEE} = 0.859$ vs $AUC_{CT} = 0.822$, $P = .654$) and mitral ($AUC_{TEE} = 0.671$ vs $AUC_{CT} = 0.712$, $P = .830$) IE. Both techniques exhibited lower sensitivities for mitral (≤60%) than aortic IE (>85%; Table 6). The interrater agreement for the detection of abscess was good on CT images (kappa = 0.617, $P < .001$) and very good on TEE (kappa = 1, $P < .0001$). The agreement between TEE and CT was moderate (kappa = 0.522, $P < .001$), and the agreement with surgical findings was in the same range between TEE (kappa = 0.578, $P < .001$) and CT (kappa = 0.556, $P < .001$). Combining TEE and CT increased the sensitivity, which reached 90.9% (vs 72.7% for TEE and 77.3% for CT), and decreased specificity (76.1% vs 89.1% for TEE and 80.4% for CT), without significant difference with respect to AUC (Table 5). An example of a patient with a paravalvular abscess detected both on TEE and CT is reported in Figure 4. An example of a false negative of CT is reported in Figure 5.

Detection of Pseudoaneurysm. Six patients (9%) had a pseudoaneurysm at surgery (all located on the aortic valve), confirmed in four cases by TEE and in all cases by CT. No false positive was noticed with TEE, and two false positives were present with CT (aortic NVE [$n = 1$] and PVE [$n = 1$]). Both modalities performed well for detection of pseudoaneurysm: CT exhibited higher sensitivity than TEE (100% vs 66.7%), but diagnostic accuracy was similar between modalities (97% both for TEE and CT). Similar results were observed in both NVE and PVE (Table 4), as well as in aortic and mitral IE (Table 6). The AUCs of TEE and CT were in the same range (Table 5). The interrater agreement for the detection of pseudoaneurysm was very good on CT images (kappa = 0.855, $P < .0001$) and

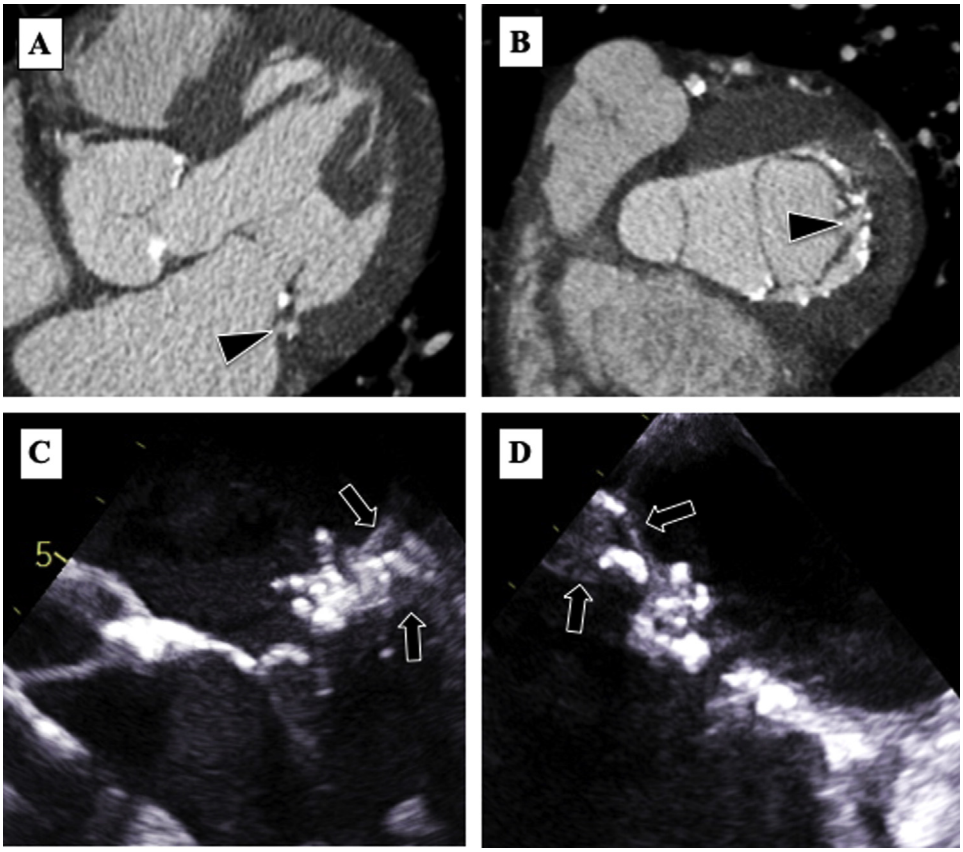

Figure 5 Example of a 60-year-old patient with an IE of the mitral valve complicated by an abscess. The axial **(A)** and basal short-axis **(B)** views from CT revealed an erosion (*arrowhead*) of the posterior leaflet. The posterior leaflet was calcified and thickened and was interpreted to be degenerative. No paravalvular collection suggesting an abscess was detected (image quality: 1). Transesophageal echocardiography identified the posterior leaflet erosion but also revealed a hypoechogenic thickening of the posterior annulus related to an abscess (**C and D**, *arrows*; image quality: 1).

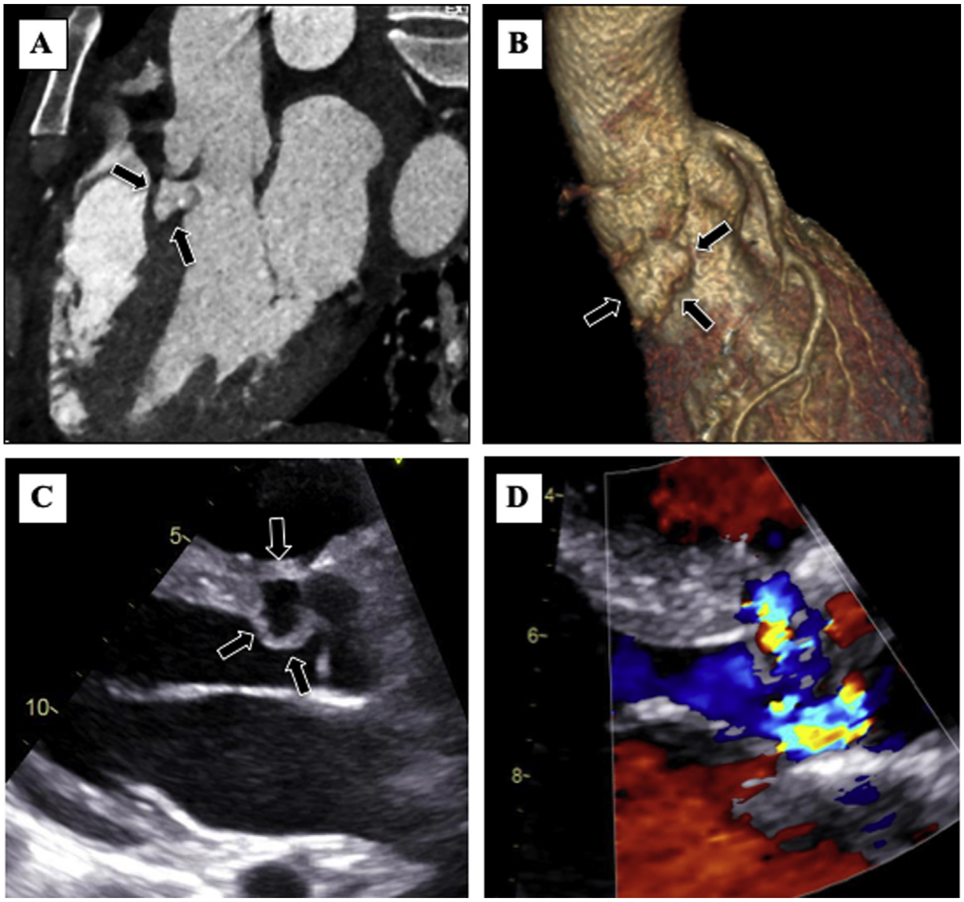

Figure 6 Example of a 43-year-old patient with an IE of the native aortic valve complicated by an anterior pseudoaneurysm. Long-axis view by CT **(A)** revealed a circulating cavity communicating with left ventricular outflow tract (*arrows*) corresponding to a pseudoaneurysm. Three-dimensional volume-rendered CT image **(B)** confirmed an abnormal nodular structure located next to the right aortic sinus (*arrows*; image quality: 1).The pseudoaneurysm was also observed by TTE from the parasternal long-axis view at the anterior part of the aortic annulus (**C**, *arrows*). The color Doppler confirmed that the pseudoaneurysm was circulating (**D**; image quality: 1).

good on TEE (kappa = 0.767; $P < .001$). The agreement between TEE and CT was good (kappa = 0.685, $P < .001$). The agreement with surgical findings was very good for both TEE (kappa = 0.785, $P < .001$) and CT (kappa = 0.852, $P < .001$). The combination of both modalities did not significantly increase the AUC in comparison to CT alone (Table 5). An example of a patient with a pseudoaneurysm detected by both modalities is reported in Figure 6. An example of a false negative of TEE is reported in Figure 7.

DISCUSSION

In this study, TEE was superior to CT to detect valvular IE-related lesions, while the ability to detect paravalvular complications was similar between both modalities. Compared with TEE alone, a combination of both modalities did not significantly improve diagnostic performance. Both TEE and CT exhibited lower diagnostic performance in PVE than in NVE.

In the present study, we observed that CT performed similarly for the detection of vegetation compared with previous studies, which report a rate between 70%[16] and 96%,[12] except for one study,[19] where the low reported rate of detection (16%) was mainly related to the single-phase ECG-gated protocol and the use of thick CT sections. As expected,[14-16,19] TEE performed better than CT for the detection of vegetation, probably due to its higher temporal resolution. In contrast to previous published data[13,16,18] our study noticed only a moderate correlation between TEE and CT for the evaluation of the vegetation size even in vegetation > 10 mm. Interestingly, the diagnostic performance and especially the specificity of CT tend to be lower in the mitral than in the aortic valve. This difference may be due to two specific states of the mitral valve: the dynamic motion during the cardiac cycle and the complex anatomy (subvalvular apparatus and nonpathological focal leaflet thickening), which can lead to misdiagnosis (false positive or negative). Transesophageal echocardiography also better detected leaflet erosion compared with CT. Such difference in performance was previously observed[15-18] and may be explained by the contribution of color Doppler during TEE that helps to confirm leaflet erosion.

The presence of paravalvular extension of IE is a serious complication that requires cardiac surgery because of worse prognosis,[21] but its diagnosis by TEE may be challenging mostly in PVE cases. The previously reported sensitivity of TEE for abscess detection was often <60%,[11,14,15,19] while it was significantly better in our study (72.7%). This difference may be explained by the systematic utilization of 3D reconstructions during TEE that enhanced anatomic understanding of adjacent structures[6,22] and also by the unique design of our endocarditis unit. Indeed, all patients with a suspected or confirmed IE in our hospital are admitted in this unit to undergo a complete evaluation (including TTE and TEE) by a dedicated team. Previous studies also reported higher performance of CT compared with TEE for abscess detection,[11,13] while the combination of both modalities improved the diagnostic performance.[14,19] In our study, CT performed well but was similar to TEE in detecting abscess. Both techniques performed worse for the detection of abscess in PVE than in NVE. The difference was more important for the CT probably because of beam-hardening artifacts that decrease image quality. Interestingly, both TEE and CT sensitivity for abscess detection was lower in mitral than in aortic IE, which may be related to unclear imaging delineation between mitral annulus and myocardium. The combination of both modalities did not significantly improve diagnostic performance. Conversely, CT performed very well for pseudoaneurysm detection, with 100% sensitivity, higher than TEE (66.7%), which missed two pseudoaneurysms. Such high performance has been reported in the literature.[16,18,19] Although our results apply only to surgically confirmed IE, we believe that the similar performance of TEE and CT for the detection of paravalvular complications suggests that for this indication the two techniques can be considered equivalent. Thus CT can be of value to detect paravalvular complications of IE when TEE is equivocal or not feasible. However, its use in all-comers remains to be defined especially in light of the limited improvement of diagnostic performance when TEE and CT are combined and radiation exposure is taken into consideration.

Some limitations have to be mentioned. First, this study was conducted in a single institution and multicenter studies are required to confirm such results. Second, only IE patients with a surgical indication were included to provide a robust confirmation of TEE and CT findings. However, these patients could have more extensive IE lesions than all-comers, which may lead to overestimating the performance of both modalities. Third, bias may have existed during the analysis of images because the readers of the TEE and CT images knew that examinations were performed in patients with a definite diagnosis of IE. It would have been interesting to include cardiac imaging performed for suspicion of IE to avoid this bias and to evaluate the ability of CT to rule out IE. Nevertheless, our aim was to have surgical confirmation to increase the confidence in our results. It would also have been interesting to interpret TEE and CT images using the clinical and biological data, but we decided to be blind to it in order to

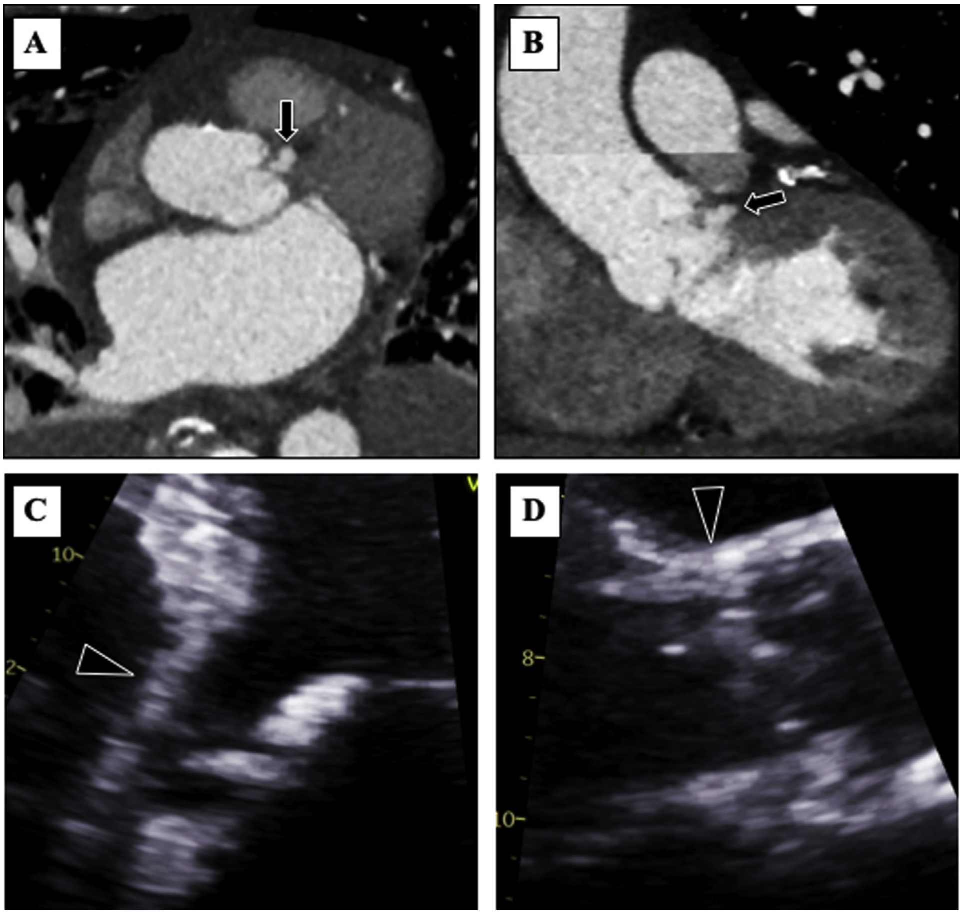

Figure 7 Example of an 82-year-old patient with an IE of the aortic valve complicated by a pseudoaneurysm. The axial **(A)** and coronal **(B)** views from CT revealed a small contrast-enhanced cavity at the anterior part of the aortic annulus (*arrows*) suggesting a pseudoaneurysm (image quality: 1). Transthoracic echocardiography **(C and D)** did not detect any abnormality in the anterior annulus area (*arrowhead*). The presence of a small anterior pseudoaneurysm was confirmed by surgery (image quality: 1).

be more reproducible and not influenced by the physician experiences. Fourth, with such a small number of IE-related cardiac lesions, there is high likelihood of missing a significant difference between techniques. Fifth, it is possible that relevant information was not recorded during the initial TEE, and that may have affected the diagnostic performance. However, the systematic 3D acquisition with a subsequent analysis may have limited this problem. Finally, only left-side IEs were included in our study because of the difficulty in analyzing right cavities on CT (inhomogeneous opacification frequently observed and imaging artifacts induced by leads of cardiac devices).

CONCLUSION

In patients with a definite diagnosis of left-side IE according to the modified ESC Duke criteria, TEE performed better than CT for the detection of valvular IE-related lesions, while the ability to detect paravalvular IE-related lesions was similar between the two modalities.

REFERENCES

1. Hoen B, Duval X. Infective endocarditis. N Engl J Med 2013;368:1425-33.
2. Iung B, Doco-Lecompte T, Chocron S, Strady C, Delahaye F, Le Moing V, et al. Cardiac surgery during the acute phase of infective endocarditis: discrepancies between European Society of Cardiology guidelines and practices. Eur Heart J 2016;37:840-8.
3. Thuny F, Grisoli D, Cautela J, Riberi A, Raoult D, Habib G. Infective endocarditis: prevention, diagnosis, and management. Can J Cardiol 2014;30:1046-57.
4. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, 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;36:3075-128.
5. Bai A, Steinberg M, Showler A, Burry L, Bhatia R, Tomlinson G, et al. Diagnostic accuracy of transthoracic echocardiography for infective endocarditis findings using transesophageal echocardiography as the reference standard: a meta-analysis. J Am Soc Echocardiogr 2017;30:639-46.
6. Afonso L, Kottam A, Reddy V, Penumetcha A. Echocardiography in infective endocarditis: state of the art. Curr Cardiol Rep 2017;19:127.
7. Guner A, Kalcik M, Ozkan M. Fundamental role of echocardiographic evaluation in the diagnosis of prosthetic valve endocarditis. Echocardiography 2019;36:815-6.
8. Vilacosta I, Olmos C, de Agustin A, Lopez J, Islas F, Sarria C, et al. The diagnostic ability of echocardiography for infective endocarditis and its associated complications. Expert Rev Cardiovasc Ther 2015;13:1225-36.
9. Gomes A, Glaudemans AWJM, Touw DJ, van Melle JP, Willems TP, Maass AH, et al. Diagnostic value of imaging in infective endocarditis: a systematic review. Lancet Infect Dis 2017;17:e1-14.
10. Erba P, Pizzi M, Roque A, Salaun E, Lancellotti P, Tornos P, et al. Multimodality imaging in infective endocarditis: an imaging team within the endocarditis team. Circulation 2019;140:1753-65.
11. Chaosuwannakit N, Makarawate P. Value of cardiac computed tomography angiography in pre-operative assessment of infective endocarditis. J Cardiothorac Surg 2019;14:56.
12. Fagman E, Flinck A, Snygg-Martin U, Olaison L, Bech-Hanssen O, Svensson G. Surgical decision-making in aortic prosthetic valve endocarditis: the influence of electrocardiogram-gated computed tomography. Eur J Cardiothorac Surg 2016;50:1165-71.
13. Feuchtner GM, Stolzmann P, Dichtl W, Schertler T, Bonatti J, Scheffel H, et al. Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. J Am Coll Cardiol 2009;53:436-44.
14. Hryniewiecki T, Zatorska K, Abramczuk E, Zakrzewski D, Szymanski P, Kusmierczyk M, et al. The usefulness of cardiac CT in the diagnosis of perivalvular complications in patients with infective endocarditis. Eur Radiol 2019;29:4368-76.
15. Koo HJ, Yang DH, Kang JW, Lee JY, Kim DH, Song JM, 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.
16. Ouchi K, Sakuma T, Ojiri H. Cardiac computed tomography as a viable alternative to echocardiography to detect vegetations and perivalvular complications in patients with infective endocarditis. Jpn J Radiol 2018;36:421-8.
17. Sims JR, Anavekar NS, Chandrasekaran K, Steckelberg JM, Wilson WR, Gersh BJ, et al. Utility of cardiac computed tomography scanning in the diagnosis and pre-operative evaluation of patients with infective endocarditis. Int J Cardiovasc Imaging 2018;34:1155-63.
18. Kim IC, Chang S, Hong GR, Lee SH, Lee S, Ha JW, 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.
19. Koneru S, Huang SS, Oldan J, Betancor J, Popovic ZB, Rodriguez LL, et al. Role of preoperative cardiac CT in the evaluation of infective endocarditis: comparison with transesophageal echocardiography and surgical findings. Cardiovasc Diagn Ther 2018;8:439-49.
20. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837-45.
21. Chu VH, Park LP, Athan E, Delahaye F, Freiberger T, Lamas C, et al. Association between surgical indications, operative risk, and clinical outcome in infective endocarditis: a prospective study from the International Collaboration on Endocarditis. Circulation 2015;131:131-40.
22. Tanis W, Teske AJ, van Herwerden LA, Chamuleau S, Meijboom F, Budde RP, et al. The additional value of three-dimensional transesophageal echocardiography in complex aortic prosthetic heart valve endocarditis. Echocardiography 2015;32:114-25.