

## CARDIAC COMPUTED TOMOGRAPHY IN INFECTIVE ENDOCARDITIS

## KOMPJUTERIZOVANA TOMOGRAFIJA SRCA U INFEKTIVNOM ENDOKARDITITISU

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### Abstract

Infective endocarditis is a rare disease with an increasing incidence and an unchanged high mortality rate, despite the rapid medical development. Imaging plays integrative part in diagnosis of IE, with echocardiography as main diagnostic test. Rising research data in utility of Cardiac Computed Tomography (CCT) in diagnostic algorithm of IE, indicates its importance in detection of IE-related lesion along with the exclusion of coronary artery disease. The latest 2023 European Society of Cardiology Guidelines in management of IE classified CCT as class of recommendation I and level of evidence B in detection of both valvular and paravalvular lesions in native and prosthetic valve endocarditis. This review article provides comprehensive and contemporary review of role of CCT in diagnosis of IE, optimization of acquisition protocols, morphology characteristics of IE-related lesions, published data of diagnostic performance of CCT in comparison to echocardiography as the state-of-art method, limitation and future possibilities.

### Keywords:

infective endocarditis,  
cardiac computed  
tomography,  
transthoracic  
echocardiography,  
transesophageal  
echocardiography

## Sažetak

### Ključne reči:

infektivni endokarditis,  
kompjuterizovana  
tomografija srca,  
ehokardiografija

Infektivni endokarditis (IE) je retka bolest sa porastom incidencije obolevanja i nepromenjenom visokom stopom mortaliteta, uprkos brzom medicinskom razvoju. Imidžing ima integrativnu ulogu u dijagnozi IE, sa ehokardiografijom kao glavnim dijagnostičkim testom. U porastu je broj istraživačkih podataka o korisnosti kompjuterizovane tomografije srca (CCT) u dijagnostičkom algoritmu IE, ukazujući na njen značaj u otkrivanju morfoloških lezija IE uz isključivanje koronarne arterijske bolesti. Najnovije smernice Evropskog kardiološkog društva u lečenju IE iz 2023. godine klasifikovale su CCT kao klasu preporuke I i nivo dokaza B u otkrivanju valvularnih i paravalvularnih lezija kod IE nativnih i veštačkih valvula. Ovaj pregledni članak daje sveobuhvatan i savremeni pregled uloge CCT u dijagnozi IE, optimizaciju akvizicionih protokola, karakteristike morfoloških lezija IE, analizu do sada objavljenih istraživanja o dijagnostičkim performansama CCT u poređenju sa ehokardiografijom kao najsavremenijom metodom, postojeća ograničenja i buduće mogućnosti.

## Introduction

Infective endocarditis (IE) is the infection of cardiac native valves (NVE), prosthetic valves (PVE) and implantable electronic devices (CIED) (1-3).

It is a rare disease, which remains in the center of attention impermanent. Its incidence is rising and the mortality rate remains unaltered despite advances in medical field (4-5). The affected population is older with numerous comorbidities, but it isn't rare in children with congenital heart disease (CHD) (1,6). Along with the staphylococcus as the leading cause of IE in 31% of cases, there is increasing incidence of enterococcus species in elderly (7).

Diagnosis of IE is based on clinical suspicion sustained by microbiological confirmation and detection of IE-related lesion by imaging modalities (1,8-9). Echocardiography is first-line and key imaging method in diagnosis and decision-making process, monitoring patient during medical therapy, in peri- and postoperative period. Additional imaging modalities, such as cardiac computed tomography (CCT), are needed for confirmation of diagnosis in possible IE, detection of extent of invasive disease or extracardiac dissemination (9). In 2015 European Society of Cardiology (ESC) Guideline for the management of IE encouraged future usage of CCT in detection of paravalvular lesions as major criterion (8). The latest 2023 ESC Guidelines classifies CCT as class of recommendation I and level of evidence B in detection of both valvular and paravalvular lesions in NVE and PVE (9).

The aim of this article is to review the role of CCT in detection of IE-related lesion.

## Role of cardiac CT in imaging algorithm of Infective Endocarditis

Cardiac computed tomography is complementary imaging method to the echocardiography due to better spatial resolution. In diagnostic algorithm, both transthoracic echocardiography (TTE) and transesophageal

echocardiography (TOE) are recommended as first-line imaging modality in suspected IE, except in right-sided NVE where quality and conclusive TTE is sufficient. In cases of possible NVE and PVE, CCT is recommended to detect valvular lesions and confirm diagnosis. In cases of definite IE with suspected paravalvular complication or inconclusive TOE, CCT is recommended in both NVE and PVE (9).

## Cardiac CT protocol

### Acquisition

Electrocardiographic (ECG)-gated CCT is needed for analysis of cardiac structure. It is advisable not to perform dose modulation protocols, as low voltage image decrease spatial resolution in detection of IE-related lesions, regardless of image reconstruction protocols, filtered back projection (FBP) or iterative. All CT scans should be performed with three-phase biventricular contrast injection protocols. Time to exposition, from intravenous administration of contrast medium, should be calculated by time-bolus technique, with region-of interest (ROI) positioned at aortic root at the level of origin of left main artery. Retrospective image data should be reconstructed at 10% - 90% of R-R interval of cardiac cycle. In a case of irregular heart rhythm additional reconstruction around 300 ms should be performed (10, 11).

### Image analysis

Image analysis should be performed at workstation with dedicated cardiac application. Aortic and mitral valve are analyzed in diastolic phases, but if patient's heart rate is above 70 beats/min, systolic phase is advisable. From multiplanar reformations, double oblique reformation should be used in order to create cardiac valves planes in their longitudinal and transverse sections (10, 11).

### Infective Endocarditis Related Lesions

Causative microorganisms adhere to the damaged areas of the endocardium or foreign material. Its growth leads to thickening of valve cusps, with consecutive

development of valvular lesions: vegetations, perforations and aneurysms. With the development of an invasive form, the disease spreads along the annulus into the extravascular space, and forms perivalvular lesions: abscesses, pseudoaneurysms, fistulas and leaks. Correlation between morphological features of IE at surgery/autopsy, echocardiography and CCT are described in **table 1** (8, 10, 12).

easily detect vegetation mobility, but unfavorable patient's habitus, heavily valve calcification and prosthetic valves may impair its visibility (22). Adding CCT to the diagnostic algorithm improves vegetation detection. According to the heretofore available studies, CCT has sensitivity 70 - 96% and specificity 20 - 100%, as a single used test (14-20, 23). In 2013, Habets et al reported in 28 patients with

**Table 1.** Comparative description of IE-related lesion at Surgwery, Echocardiography and Cardiac CT

IE lesion	Surgery/Autopsy	Echocardiography	Cardiac CT
<b>Vegetation</b>	Infected mass attached to an endocardial structure or on implanted intracardiac material	Oscillating or non-oscillating intracardiac mass on valve or other endocardial structure, or on implanted intracardiac material	Hypodense mass attached to the valve, endocardium or prosthesis
<b>Aneurysm</b>	Saccular outpouching of valvular tissue	Saccular outpouching of valvular tissue	Saccular outpouching of valvular tissue
<b>Perforation</b>	Interruption of endocardial tissue continuity	Interruption of endocardial tissue continuity traversed by Color-Doppler flow	Interruption of endocardial tissue continuity confirmed in two planes
<b>Abscess</b>	Perivalvular cavity with necrosis and purulent material not communicating with cardiovascular lumen	Thickened, non-homogenous perivalvular area with echodense or echoluscent appearance	Hypodense zone with a vascular rim. Soft tissue thickening around the valve and great blood vessels as a sign of early abscess
<b>Pseudoaneurysm</b>	Perivalvular cavity communicating with the cardiovascular lumen	Pulsatile perivalvular echo-free space with Color-Doppler flow detected	Perivalvular contrast-filled cavity
<b>Fistula</b>	Communication between two neighboring cavities trough a perforation	Color-Doppler communication between two neighboring cavities trough a perforation	Contrast-filled communication between two neighboring cavities trough a perforation
<b>Leak</b>	Dehiscence of prosthesis	Paravalvular regurgitation identified with Color-Doppler with or without rocking motion of the prosthesis	Malalignment of the prosthesis and annulus with tissue defect. Rocking motion of more than 15° on cine CT images

Cardiac CT imaging of valvular lesions

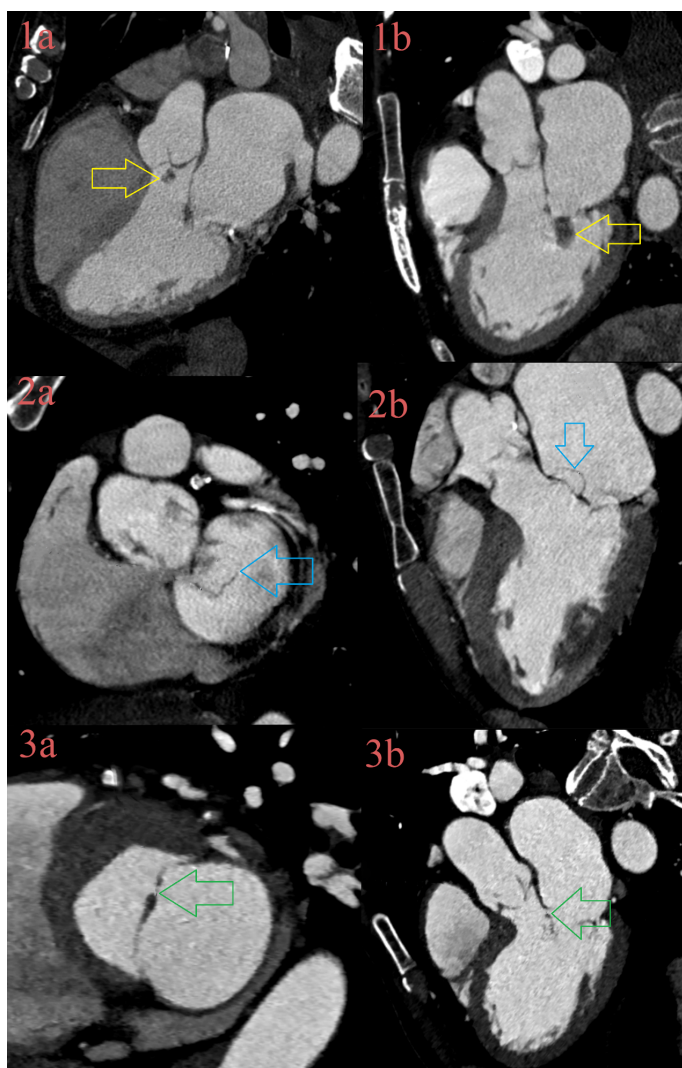
Vegetations

A vegetation appears as hypodense soft tissue lesion of variable size or focal thickening along the valve cusps or foreign material (**figure 1, images 1a - 1b**). They are localized to the low-pressure side - to the atrial side of mitral and tricuspid valve and to the ventricular side of aortic and pulmonary valve. The key to vegetation analysis is the assessment of embolic potential (10,11). Size and mobility are the most important independent risk factor, along with location on the mitral valve, size change during antibiotic therapy, particular microorganisms (*Staphylococcus species*), previous embolism, multivalvular involvement and biological markers. Cardiac CT may depict oscillating movement during cardiac cycle at cine images and if the length ≥ 10 mm, surgical treatment is required (9).

Sensitivity and specificity for detection of vegetations range for TTE 41 - 90% and 58 - 96%, whereas for TEE are higher 89.3 - 100% and 83.3 - 100% (13-21). Due to better temporal resolution, echocardiography can

PVE, that adding CCT to the standard imaging protocol (TTE + TEE), raised sensitivity to 100% versus 63% (24). In 2023, the latest study conducted 78 patients, with 88 vegetation at 85 valves, reported slightly higher sensitivity for CCT 92% versus TTE 80,7% and TEE 80,7%, but in mutual usage of all three imaging tests sensitivity raised to 92,4%. In NVE, CCT can better visualize vegetations in heavily calcified valves and make clearly differentiation from ruptured aneurysm. In PVE, due to metal reduction software, CCT can better depict vegetation, of anterior localization specifically. On contrary, in right-sided endocarditis CCT has limited visibility around pacemaker leads, when they present as coated thickening (11). By some authors sensitivity is in correlation to the vegetation's size. Ouchi et al., in 19 patients, detected length of 6 mm as cut-off value for vegetation detection (16). In 68 patients, Sifaoui et al. have found that a vegetation size of 7 mm was associated with the best pairing of sensitivity (66.1%) and specificity (75.0%) in CCT (19).

Differential diagnosis of vegetations includes thrombus, hypoattenuated leaflet thickening (HALT),



**Figure 1.** Cardiac CT of IE valvular lesion

Vegetations are depicted as hypodense mass lesions attached to the aortic valve (Image 1a, yellow arrow) and to the mitral valve (Image 1b, yellow arrow). Large aneurysm of A2 segment of anterior leaflet of mitral valve is depicted as saccular outpouching (Image 2a and 2b, blue arrow). There is perforation of A2 segment of anterior leaflet of mitral valve depicted as loss of continuation in transversal and longitudinal mitral plane (Image 3a and 3b, green arrow)

fibroelastoma, Lambl's excrescences and non-bacterial endocarditis (NBTE) (25-29). Thrombus is irregular, soft tissue lesion attached to the leaflets, sewing ring, or both, predominantly to the side of higher pressure (25). In transcatheter aortic valve implantation (TAVI) HALT affects whole leaflets from ring towards free margin uniformly (26). Echocardiography can depict thrombus as a mobile mass with signs of obstruction, but cannot detect small thrombosis or thin HALT, where CCT is superior in localization and characterization (25,26). Fibroelastoma are pedunculated lesions attached to the leaflet, rarely causing valve dysfunction or emboli due to thrombi adherence or disintegration (27). Lambl's excrescences are thinner, filiform lesions that arise in commissural valve zones (28). Non-bacterial endocarditis appears as small irregular lesions, commonly affecting left-sided valves and associated with malignancy, hypercoagulable states and autoimmune disease (Libman-Sacks endocarditis). It may be associated with embolism (29).

## Aneurysms

An aneurysm appears as saccular outpouching of leaflet with loss of homogenous curvature and could be the only present IE-related lesion (**figure 1, images 2a - 2b**) (10, 30). In 2018, Kim et al reported 100% agreement between TEE and CCT in aneurysm detection in five patients (31). The latest study reported that in detection of 42 aneurysms confirmed at surgery, sensitivity for TEE was 31,6% whereas for CCT 100%, with average aneurysm's depth  $7.16 \pm 2.65$  mm and width  $8.54 \pm 4.25$  mm (11).

## Perforations

A perforation is loss of leaflet continuity and may be associated with severe valve regurgitation. Echocardiography with the additional use of color doppler effect, detects two jet phenomena as a sign of perforation. Cardiac CT detects perforation as a defect that needs to be confirmed in longitudinal and transversal valve-planar reformation (**figure 1, images 3a - 3b**) (10,11). Previous studies reported superiority of TEE over CCT in perforation detection, with sensitivity of TEE in a range 68.4 - 81.3% whereas for CCT 41 - 68.4% (17-19). In detection of 26 perforation, Kim et al reported agreement between TTE and CCT 94.7% (31). Recent study, in detection of 50 perforations proven at surgery, reported higher sensitivity of CCT 83.7% in comparison to TEE 63.9%. Better spatial resolution allows CCT better depiction of valve perforation in hostile environment to the echocardiography, such as heavily calcified valve in attachment zones. If there are more than one perforation, CCT is more sensitive in their overall detection (11).

## Cardiac CT imaging of paravalvular lesions

### Abscess

An abscess is perivalvular cavity with necrosis and purulent material and requires surgical treatment. Echocardiography depicts abscess as non-homogenous hyperechogenic perivalvular thickening. Cardiac CT detects abscess as thick hypodense paravalvular lesion clearly demarcated from surrounded fat, which converts the density of perivalvular lipid layer from negative into positive values, approximately 20-50 HU (**figure 2, images 1a - 1b**) (30, 32). Hyperintense rim, as a sign of abscess capsule, is rarely seen in NVE, but in PVE, especially after surgery, is highly suspected to active inflammation rather than postoperative seroma (32). The CCT is superior to TTE and TEE in abscess detection. Sifaoui et al detected rather similar sensitivity and sensitivity of CCT versus TEE to be 77.3/72.7% vs. 72.7/ 89.1% (19). But, in 78 patients with aortic paravalvular IE, Ye et al. reported sensitivity and specificity of CCT 99/95% versus TEE 86/91% (20). In meta-analysis, Oliveira et al detected sensitivity and specificity of CCT in abscess detection 87% and 93% versus TEE 69% and 96% (18). The latest research, in NVE and PVE, reported

sensitivity of CCT in abscess detection to be 100% versus 44.4% for TEE. The CCT is superior in abscess detection around patches and grafts, whereas around the grafts the reader should keep in mind that hypodense thin rim <3 mm is considered normal finding due to graft material (11).

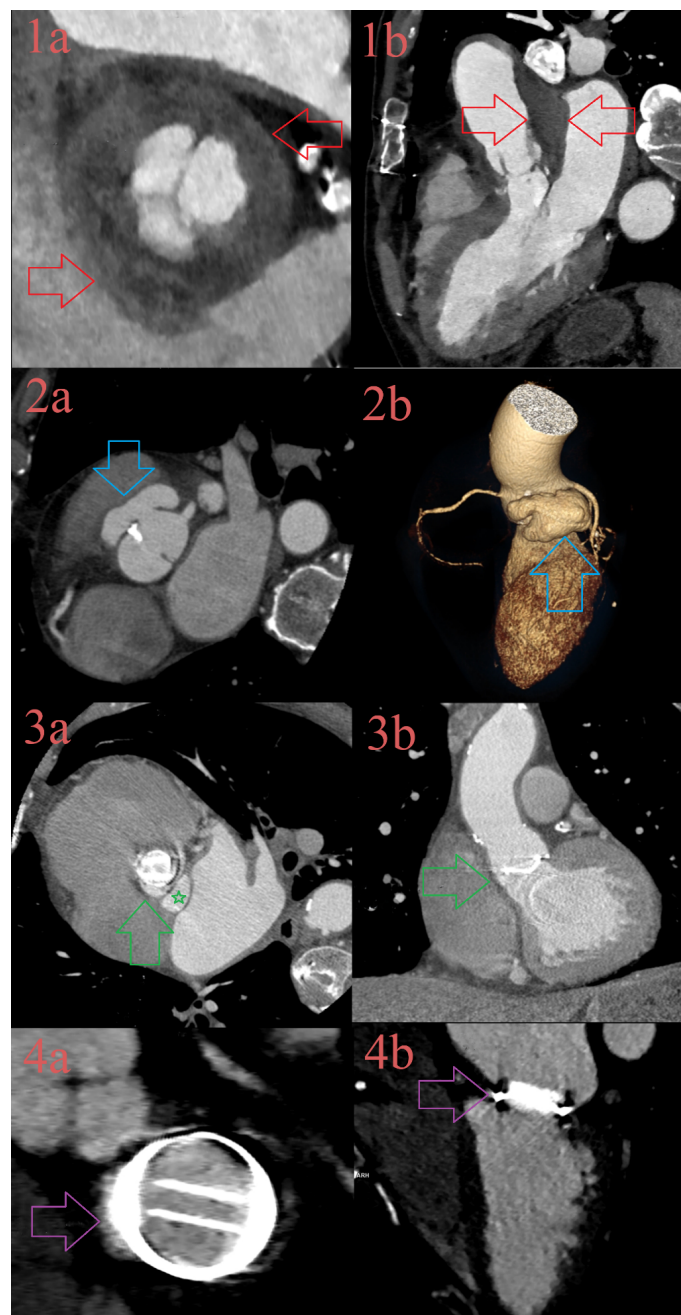
### Pseudoaneurysms

A pseudoaneurysm is drained abscess which communicate with cardiac chamber or aorta. In NVE, usually begins in subcommisural zone, where it expands from a small point of entry into the paravalvular space. It occurs almost exclusively in left-sided IE, probably due to high blood pressure and oxygenated blood. In PVE it usually begins from sewing ring and spreads along valve circumference (12). Echocardiography depicts pseudoaneurysm as pulsatile cavity with color Doppler flow. Cardiac CT depicts pseudoaneurysm as contrast filled paravalvular cavity, pulsatile on cine images (**figure 2, images 2a-2b and 3a**) (10, 30, 32). The TTE may visualize pseudoaneurysm in anterior position and to the right side, whereas TEE is superior in detection of pseudoaneurysm in posterior position, to the left side and in intervalvular fibrosa. However, lower spatial resolution, artifacts due to heavy calcification of valve annulus or vessel wall or metal artifacts from prosthetic material, diminishes detection of small pseudoaneurysm as well as depth and circumferential extension of larger ones (33). All abovementioned obstacles are surpassed with adding CCT to the IE imaging protocol due to better spatial resolution. Gahide et al reported sensitivity and specificity of CCT in detection of pseudoaneurysms are 100% and 87,5%, in aortic IE in 19 patients (23). Sifaoui et al, in 68 patients, reported sensitivity and specificity of CCT in pseudoaneurysm detection 100% and 96,8% in comparison to TEE 72.7% and 89.1% (19). Majority of studies report mutual sensitivity and specificity of CCT in detection of abscesses and pseudoaneurysms in a range 60 - 100% and 78.4 - 100% versus TEE 40 - 92.3% and 89 - 100% (14,15,17,21). Cardiac CT depicts pseudoaneurysms independent of their localization, accurately assess depth and size of its cavities and percentage of the circumference of the annulus involved, information relevant to the surgeon (11).

### Fistula

A fistula is communication between two neighboring cavities through an abnormal penetrating tract, usually as a consequence of abscess or pseudoaneurysm, and associated with poor clinical outcome. Echocardiography depicts fistula as paravalvular Color Doppler flow between two cavities. Cardiac CT depicts fistula as paravalvular contrast-filled tunnel between two neighboring cavities (**figure 2, images 3a - 3b**) (30). Sims et al reported lower sensitivity and specificity of CCT in fistula detection 50% and 96.9% versus TEE 78.6% and 98.7%, in 34 operated patients with preoperative CCT (17). Similarly, Ye et al, in 178 patients with aortic paravalvular IE, reported specificity

and sensitivity for CCT 100% / 98% and for TEE 100% / 96% (20). Meta-analysis of Jain et al reported higher sensitivity and specificity of CCT 98.% / 90% in comparison to TEE 85.7% / 98.6% (34). Cardiac CT provides additional information to TEE in precise depiction of fistula's morphology and dimensions due to better spatial resolution, especially in PVE (11).



**Figure 2.** Cardiac CT of IE paravalvular lesions

Abscess around aortic valve is depicted as thick hypodense lesion, that abuts its whole circumference, in aortic plane (Image 1a, red arrow) and its length from the intervalvular fibrosis to the middle of the ascending aorta in 3-chamber view (Image 1b, red arrows). In 2-sinus bicuspid aortic valve, there is large pseudoaneurysm towards RVOT, that drains in zone of anterior commissure, in aortic plane (Image 2a, blue arrow) and in VR reformation (Image 2b, blue arrow). Fistula around mechanic aortic valve depicted as thin contrast-opacified tunnel between aorta and left ventricle (Image 3a and 3b, green arrow) and pseudoaneurysm in intervalvular fibrosa (Image 3a, green star). Leak around mechanic mitral valve depicted as thin contrast-filled cavity (Image 4a and 4b, purple arrows)

## Leak

Destruction of the prosthetic valve ring leads to valve dehiscence and paravalvular leak. Echocardiography depicts leak as paravalvular color Doppler flow, with or without rocking motion of prosthesis (10,30). Cardiac CT depicts leak as thin contrast-filled cavity near prosthetic valve clearly differentiated from sewing ring (**figure 2, images 4a-4b**) (11). Still, TEE is more sensitive in leak detection in comparison to CCT. Koo et al reported lower sensitivity of CCT in leak detection 50% in comparison to TEE 100% (15). Also, two available meta-analysis reported lower sensitivity and specificity of CCT in comparison to TEE; Oliveira et al reported for CCT 72%/ 69% versus TEE 100% / 99%, whereas Jain et al reported for CCT 85.1%/100% versus TEE 100%/95.6% (18,34). With development of software for reduction of metal artefacts, there is improvement in leak detection by CCT, but the reader should keep in mind difference between sewing ring and leak, in order to prevent false positive findings (11).

## Cardiac Computed Tomography Angiography

Initially, CCT was introduced to imaging algorithm of IE in order to assess anatomy and coronary artery disease in aortic IE due to high embolic risk. When cardiac surgery is inevitable therapy of IE, assessment of coronary anatomy is recommended. In 2023 ESC guidelines for the management of endocarditis recommend pre-operative coronary angiography for men > 40 years, post-menopausal women, and in population with one or more risk factors or history of CAD. As an alternative, CCT angiography (CCTA) can be used to rule out significant coronary obstruction (9). Clinical application is supported by high sensitivity and negative predictive value (>95%) of CCTA to rule out CAD, especially in patients with low to intermediate risk of CAD. One of disadvantage of CCTA is overestimation of stenosis severity in heavily calcified plaque, especially in intermediate stenosis, which could be advantage in decision-making process of The Endocarditis Team (35,36). Recent studies questioned necessity of coronary artery bypass grafting of non-critical lesions during surgery of IE as it could have negative impact on peri-operative outcome (9).

## Systemic embolism in infective endocarditis

Embolic events are frequent and potentially life-threatening complications of IE due to migration of cardiac vegetations (9). Whole-body CT is useful imaging method in detection of systemic embolism, but there are no clear recommendations defining the setting in which should be used (10). In 2023 ESC guidelines for the management of endocarditis engaged in predicting the risk of embolism and the use of appropriate imaging method once the complications clinically occurred (9).

## Neurologic complications

Symptomatic neurologic complications occur in 35% patients, whereas in 80% of patients remained clinically silent. They include ischemic stroke, transient ischemic attack, hemorrhage (intracerebral, subarachnoid), meningitis, brain abscess, encephalopathy and infectious aneurysm. Evaluation should include MRI with or without gadolinium, or CT with or without contrast - if MRI is not possible. Catheter angiography should be performed in patients with infective aneurysm, acute brain hemorrhage, with suspicion of aneurysm despite negative non-invasive imaging or if mechanical thrombectomy is considered (9, 10).

## Thoracic complications

There are almost exclusively consequences of right-sided IE and occur in 14% of patients with IE with systemic embolism. They include pulmonary infarction, pulmonary abscess, pleural effusion and empyema (**figure 3, images 1a-1d**) (9,10).

## Vascular complications

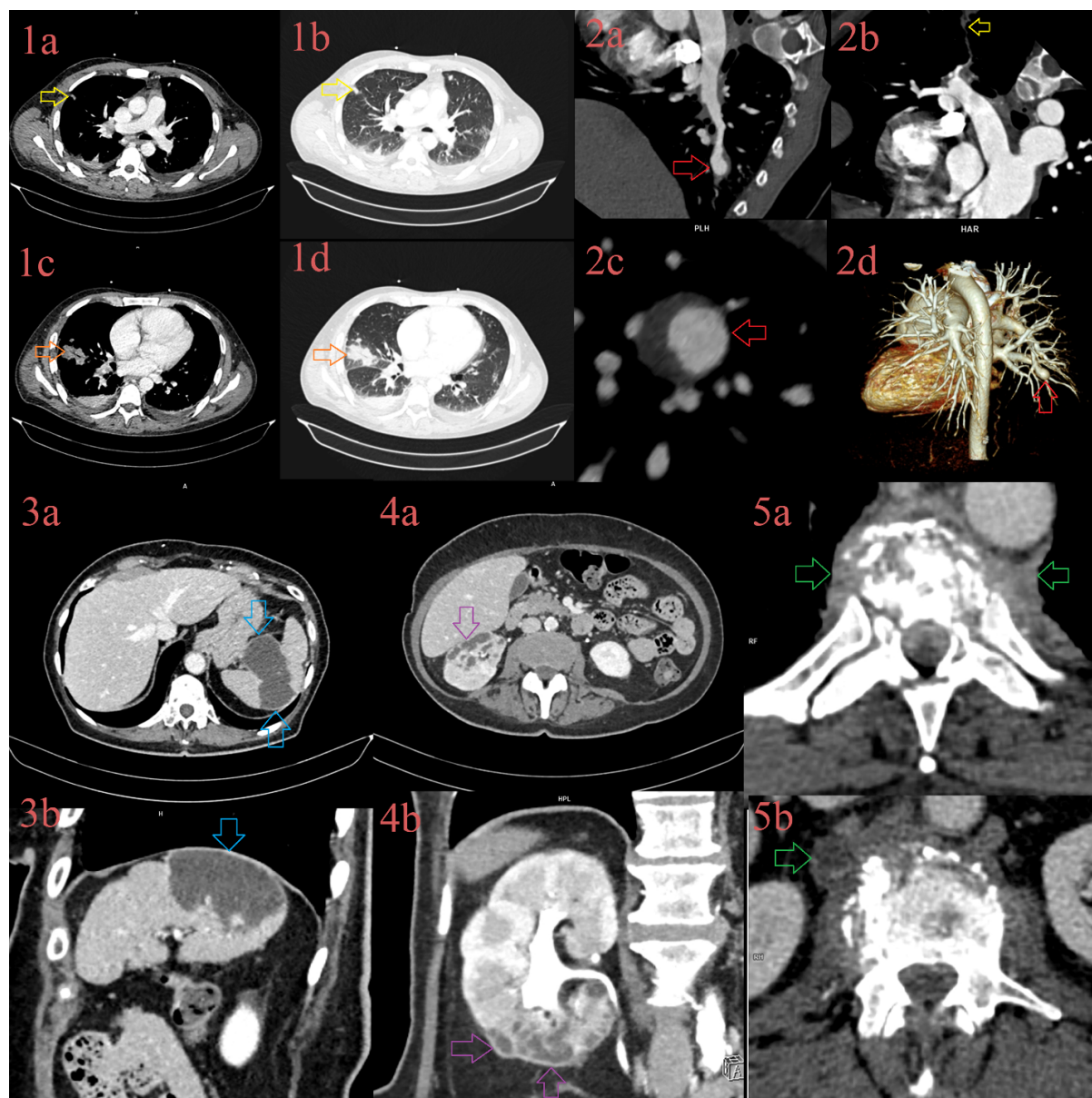
Mycotic aneurysm are rare complications defined as infection of vascular wall. There are more frequent in central nervous system, abdominal aorta and superior mesenteric artery, but in 6% of cases may affect coronary arteries. A CT depicts them as segmental saccular pseudoaneurysms (**figure 3, images 2a-2d**) (10,37).

## Abdominal complications

Associated with left-sided infective endocarditis, with the spleen as the most often affected organ (19-32%), following the kidneys (6-14%), and rarely the liver (3-11%) (37). Splenic involvement includes asymptomatic infarction, with progression to abscess and potential rupture (**figure 3, Images 3a-3b**) (9). Kidney followed the same development pattern as in spleen, infarcts progress to abscess and often multiple, sometimes bilateral (**figure 3, Images 4a-4b**). Liver involvement is manifested by abscess. Also, a CT depicts infarct, independent of affected organ, as triangular hypodense lesion, which with development of contrast-enhanced peripheral rim, develops into abscess, that may strain the organ capsule (10).

## Musculoskeletal complications

Metastatic bone or joint-IE related lesions are relatively frequent, and includes spondylodiscitis (2-10%), osteomyelitis and septic arthritis. The MRI is preferable imaging modality in comparison to CT. In spondylodiscitis, CT detects indirect signs of disease such as loss of disc height, erosion or destruction of end-plates and vertebral bodies, paravertebral soft tissue collections with abscess development (**figure 3, Images 5a-5b**) (9,10).



**Figure 3.** Systemic emboli of infective endocarditis

Thoracic manifestations are depicted as thin fibrous band infarction (Image 1a and 1b, yellow arrows) and abscess in form of consolidation (Image 1c and 1d, orange arrow). Vascular complication presented by mycotic aneurysm of pulmonary artery branch in right-sided IE (Image 2a, 2c and 2d, red arrows) and pulmonary infarct (Image 2b, yellow arrow). Abdominal manifestations are manifested as large splenic abscess (Image 3a and 3b, blue arrow) and multiple small right renal abscesses in lower pole (4a and 4b, purple arrows). There is infective spondylodiscitis (Image 5a, green arrow) complicated by paravertebral abscess (Image 5b, green arrow)

## Conclusion

Cardiac CT is superior imaging method in detection of IE-related lesions due to excellent spatial resolution, but lack of hemodynamic assessment classifies it as inevitable additional imaging method in diagnostic work-up of IE. Consecutive body CT allows prompt detection of systemic manifestation of IE and appliance of appropriate therapy.

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