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Original article

# Impact of thoracoabdominal imaging on diagnosis and management in patients with suspected infective endocarditis

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ARTICLE INFO	A B S T R A C T
Keywords: Infective endocarditis CT scan <sup>18</sup> F-FDG PET/CT Embolization Acute kidney injury	<ul> <li>Background: Embolic events (EEs) are a common complication of infective endocarditis (IE) and their presence can impact diagnosis and modify the therapeutic plan. The present study aimed to describe the role of thoracoabdominal imaging, either thoracoabdominal-pelvic Computed Tomography or <sup>18</sup>F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography, on diagnosis and management of patients with suspected IE.</li> <li>Methods: This study was conducted at a university hospital, from January 2014 to June 2022. EEs and IE were defined according to modified Duke criteria.</li> <li>Results: Among 966 episodes with suspected IE and thoracoabdominal imaging, 528 (55%) patients were asymptomatic. At least one EE was found in 205 (21%) episodes. Based on thoracoabdominal imaging findings, the diagnosis was reclassified from rejected to possible or from possible to definite IE in 6 (1%) and 10 (1%) episodes, respectively. Among the 413 patients with IE, at least one EE was found on thoracoabdominal imaging in 143 (35%) episodes. Together with the presence of left-side valvular vegetation &gt;10 mm, the results of thoracoabdominal imaging established a surgical indication (prevention of embolism) in 15 (4%) episodes, 7 of which were asymptomatic.</li> <li>Conclusions: Thoracoabdominal imaging performed in asymptomatic patients with suspected IE improved the diagnosis in only a small proportion of patients. Thoracoabdominal imaging led to a new surgical indication (in association with left-side valvular vegetation &gt;10 mm) in only a small percentage of patients.</li> </ul>

# 1. Introduction

A common feature of infective endocarditis (IE) is the risk of organ embolization with approximately 30% of IE patients presenting at least one embolic event (EE), with the most common site of embolization being the central nervous system. [1–4] Since the majority of EEs are asymptomatic, the reported rate depends on the imaging practices. [3,5, 6] In the European Endocarditis Registry, EURO-ENDO, 53% of patients had a multislice Computed Tomography (CT). [7] In a previous study, systematically performed cerebral MRI found cerebral EEs in 82% of patients (79% among asymptomatic patients), leading to modification of management in 22% of patients. [1]

Abdominal organs are the second most common localization of embolization after the central nervous system. [8–10] Even though the benefit of performing systematic cerebral magnetic resonance imaging (MRI) in patients with IE has been established, [11] the role of systematic thoracoabdominal imaging (TA-Im), including thoracoabdominal-pelvic CT scan and <sup>18</sup>F-Fluorodeoxyglucose Positron Emission Tomography/CT (<sup>18</sup>F-FDG PET/CT), remains unclear. The benefit of <sup>18</sup>F-FDG PET/CT, apart from detection of cardiac lesions, is

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the discovery of peripheral EEs as shown in previous studies. [12,13] The European Society of Cardiology (ESC) guidelines recommend considering TA-Im to detect EEs in patients whose IE diagnosis is not yet proven, despite a high clinical suspicion. [14] The presence of EEs by TA-Im can facilitate IE diagnosis, since they are part of the vascular minor criterion in the Duke classification. Furthermore, the presence of organ EE in a patient with a vegetation >10 mm establishes a surgical indication for further embolism prevention. [14] In addition, TA-Im may reveal lesions other than EEs, which could affect management, such as metastatic infection needing drainage, or pulmonary embolism requiring anticoagulation treatment. However, the routine use of TA-Im evaluating patients with infective endocarditis remains controversial. In a study of IE patients, abdominal MRI detected an abdominal EE in 34% of IE patients, but had no effect on diagnosis since no patient was reclassified from possible to definite due to the establishment of the vascular criterion. [10] In a previous study in patients with IE, anatomical thoracoabdominal-pelvic CT scan, showed limited potential for improving the diagnosis of IE and infrequently lead to a change in clinical management. [6] Furthermore, contrast-enhanced CT scan is associated to several adverse events such as acute kidney injury (AKI) or immediate hypersensitivity reactions. [6] Apart from iodinated contrast toxicity, there are many predisposing factors of AKI among IE patients, such as the presence of EEs, acute cardiac failure and use of diuretics, nephrotoxic or vasopressor drugs. [15,16]

Even though previous studies included TA-Im findings in the description of IE patients, only a limited number of them assessed the impact of TA-Im findings on clinical decisions. [5,6] Furthermore, to the best of our knowledge no study evaluated the diagnostic impact of TA-Im in patients with IE and those with clinical suspicion of IE without IE diagnosis. Therefore, we aimed to describe the prevalence of symptomatic and asymptomatic EEs, as well as other thoracoabdominal lesions, detected by TA-Im in patients with suspected or confirmed IE, and to determine the impact of such findings on diagnosis and clinical management.

# 2. Materials and methods

# 2.1. Study design

This study was conducted at the Lausanne University Hospital, Switzerland, a 1100-bed primary and tertiary care hospital from January 2014 to June 2022 (2014–17: retrospective cohort; 2018 onwards: prospective cohort). The study was approved by the ethics committee of the Canton of Vaud (CER-VD 2017-02137).

# 2.2. Patients

For the prospective cohort, inclusion criteria were adult patients (>18 years old) with clinical suspicion of IE, TA-Im realization [thoracoabdominal-pelvic CT, <sup>18</sup>F-FDG PET/CT or <sup>18</sup>F-FDG PET/CT angiography (<sup>18</sup>F-FDG PET/CTA)] and written consent. For the retrospective cohort, inclusion criteria were adult patients (≥18 years old) with possible or definite IE, TA-Im realization and absence of refusal to use their data. A subsequent episode was excluded if it occurred within two months from the initial one. Clinical suspicion of IE was established if blood cultures were drawn and echocardiography was performed specifically for IE. Data regarding demographics (age, sex), comorbidities, cardiac predisposing factors, [14] cardiac implantable electronic devices, microbiologic etiology, systemic symptoms, fever, acute heart failure, sepsis or septic shock, heart murmur, immunological phenomena, [14] site of cardiac involvement and type of lesion, including vegetation size (according to cardiac imaging modalities, macroscopic lesions on surgery or autopsy), cardiac surgery (timing), results of thoracoabdominal and cerebral imaging studies (timing, results, use of contrast media), embolic events (type, timing, symptoms), acute kidney injury within 5 days from thoracoabdominal imaging study were retrieved from patients' electronic health records.

# 2.3. Definitions

IE was defined according to modified Duke criteria. [14] EEs were defined as septic lung emboli, renal or splenic emboli, mycotic aneurysm, intracranial ischemia or bleeding, cerebral abscess, conjunctival bleeding, retinal emboli, chorioretinitis, Janeway lesions or nail bed bleeding and peripheral major vascular emboli.

# 2.4. Thoracoabdominal imaging

All patients with local symptoms underwent TA-Im, while its use in asymptomatic patients was at the discretion of the treating physician and infectious diseases consultant. A patient was considered symptomatic in the presence of thoracic symptoms (dyspnea, cough, thoracic pain), abdominal symptoms (nausea/vomiting, diarrhea, abdominal pain), spinal or articular pain (limited to articulations visualized in the TA-Im); absence of all aforementioned symptoms categorized the patient as asymptomatic.

EEs detected by TA-Im included septic lung emboli, hepatic, renal or splenic emboli, mycotic aneurysm or major vascular emboli. An EE detected by TA-Im was considered new, only if no previous EE was detected by clinical examination or studies other than TA-Im (*e.g.* cerebral EE by cerebral imaging studies).

Other lesions (non-EEs) detected by TA-Im included septic arthritis, prosthetic joint infection, osteomyelitis (vertebral or non-vertebral, native or related to prosthetic material), other infections, and non-infectious findings (pulmonary embolism, venous thrombosis, new malignant lesions, signs of acute cardiac insufficiency, other).

# 2.5. Impact of embolic event detection by thoracoabdominal imaging

IE was classified according to modified Duke criteria at day 60 based on clinical, microbiological, imaging, surgical data or autopsy results (final diagnosis). A second IE probability was calculated according to the ESC-modified Duke criteria blinded to TA-Im results. Then, changes in classification (reclassification from rejected to possible or from possible to definite) were calculated.

The changes in management due to TA-Im, were calculated among patients with possible or definite IE. The impact on management was defined as the presence of a new surgical indication for embolic prevention.

# 2.6. Adverse events related to thoracoabdominal imaging

After excluding patients on hemodialysis, AKI and its grading were defined according to international guidelines [17] within 5 days after the realization of contrast-enhanced TA-Im (contrast-enhanced CT scan or <sup>18</sup>F-FDG PET/CTA) or non-contrast-enhanced TA-Im (non-contrast-enhanced CT scan or <sup>18</sup>F-FDG PET/CT). Immediate hypersensitivity reactions to contrast media were also reported.

# 2.7. Analysis

SPSS version 26.0 (SPSS, Chicago, IL, USA) software was used for data analysis. Categorical variables were analyzed using the *chi*-square or Fisher exact test and continuous variables with Mann–Whitney *U* test. Multivariable logistic regression analyses were performed with the dependent variable being EE found on TA-Im in patients suspected of IE and those with definite or possible IE. Variables with *P*<0.1 in the bivariate analyses that did not contribute to multicollinearity were used in multivariable analyses. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association. All statistic tests were 2-tailed and *P* <0.05 was considered statistically significant.

#### 3. Results

# 3.1. Study population

Among the 1259 episodes of the prospective cohort, 816 had a TA-Im and thus included (Fig. 1). From the 190 episodes in the retrospective cohort, 150 had a TA-Im and thus were included. In total, 966 episodes (in 893 patients) with suspected IE were included, of which 413 (43%) had IE (definite IE: 326; 79%, possible: 87; 21%). For the remaining 553 episodes, the final diagnosis was another type of infection (445; 80%), auto-immune disease (17; 3%), malignancy (15; 3%), non-infective endocarditis (9; 1%) and other diagnoses (67; 12%). The majority of included patients were bacteraemic (717; 74%), with *S. aureus* being the most prominent isolated pathogen (309; 43%).

# 3.2. Thoracoabdominal imaging in patients with suspected infective endocarditis

TA-Im included 740 (77%) contrast-enhanced thoracoabdominalpelvic CT scans, 145 (15%) <sup>18</sup>F-FDG PET/CT, 68 (7%) non-contrastenhanced thoracoabdominal-pelvic CT scans and 13 (1%) <sup>18</sup>F-FDG PET/CTA. Median time from IE suspicion to Ta-Im was 4 days (2 days for CT and 7 days for  $^{18}\mbox{F-FDG}$  PET/CT or PET/CTA). In total, 495 (51%) patients had the TA-Im before the first cardiac imaging study. Most of the episodes with TA-Im were asymptomatic (528; 55%). Among symptomatic episodes (438; 45%), the most prominent symptoms were dyspnea (210; 48%) and abdominal pain (118; 27%). At least one EE was found on TA-Im in 205 (21%) episodes (Table 1). Pulmonary septic emboli were most commonly identified (88: 43%), followed by splenic emboli (82: 40%). In 63 (7%) episodes, the vascular criterion was already fulfilled prior to the realization of the TA-Im. Thus, only 142 (5%) initially met the vascular criterion due to the TA-Im findings; 6 (1%) episodes were reclassified from rejected to possible IE and 10 (1%) from possible to definite IE according to modified Duke criteria.

The vascular criterion was fulfilled by the TA-Im in asymptomatic episodes in 60 (11%) episodes (Fig. 2), leading to the reclassification of the episode from rejected to possible and from possible to definite IE in 2 (<0.5%) and 5 (1%) episodes, respectively.

Following the result of the TA-Im, 20 (2%) episodes had a source control intervention (endovascular, surgical, or CT-guided drainage) directed towards the detected EEs [six (1%) among asymptomatic episodes]. Source control intervention (surgery, or CT-guided drainage) for other infectious findings (non-EEs) on TA-Im was performed in 18 (2%) episodes [2 (1%) among asymptomatic episodes] (Supplementary Table 1).

The comparison of patients' characteristics with and without EE on TA-Im is shown in Table 2. In the multivariable analysis (Supplementary

Table 2), the detection of EEs on TA-Im was associated among other factors with final IE diagnosis (P < 0.001; OR 3.35, CI 1.85-6.07) and thoracoabdominal symptoms (P 0.003; OR 1.71, CI 1.20–2.44), while presence of EE prior to TA-Im (P 0.188; OR 1.33, CI 0.87-2.04) and positive imaging Duke criterion (P 0.452; OR 1.23, CI 0.72–2.08) had no impact.

# 3.3. Mycotic aneurysms

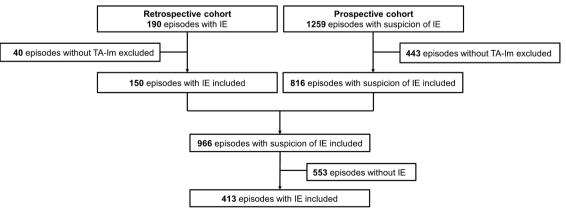
In total, 17 patients presented with a mycotic aneurysm detected by TA-Im (13 by CT and 4 by <sup>18</sup>F-FDG PET/CT). The most frequent localization was the femoral or common iliac artery (n = 5), followed by thoracic (n = 4) or abdominal aorta (n = 3), pulmonary (n = 2), splenic (n = 1), hepatic (n = 1) or renal arteries (n = 1). Surgical or endovascular treatment of the mycotic aneurysm was employed in 10 (59%) patients.

#### 3.4. Thoracoabdominal imaging in patients with infective endocarditis

Among the 413 episodes with IE, TA-Im included 329 (80%) contrast-enhanced thoracoabdominal-pelvic CT scans, 52 (14%) <sup>18</sup>F-FDG PET/CT, 27 (7%) non-contrast-enhanced thoracoabdominal-pelvic CT scans and 5 (1%) <sup>18</sup>F-FDG PET/CTA. Most of the episodes with TA-Im were asymptomatic (223; 54%). At least one EE was found on TA-Im in 143 (35%) episodes (Table 3). Splenic emboli (71; 50%) were the most commonly identified, followed by pulmonary septic emboli (52; 36%). For 58 (14%) episodes, the vascular criterion was fulfilled prior to the realization of the TA-Im. Thus, 85 (21%) met the vascular criterion due to the TA-Im; 6 (2%) patients were reclassified from rejected to possible IE and 10 (2%) from possible to definite IE according to modified Duke criteria. The vascular criterion was fulfilled by the TA-Im in asymptomatic episodes in 35 (16%) episodes, leading to the reclassification of the episode from rejected to possible and from possible to definite IE in 2 (1%) and 5 (2%) patients, respectively.

A surgical indication (prevention of embolism) was established by the results of the TA-Im in association with left-side vegetation >10 mm in 15 (4%) episodes (all subsequently benefiting from a valvular operation), 7 of which were asymptomatic. Among the subgroup of episodes (n = 127) with left-side vegetation >10 mm, TA-Im established a surgical indication in 12% of episodes (15 patients), 10% among asymptomatic episodes (7 out of 73).

Nine (2%) episodes had a source control intervention (endovascular or surgical) directed towards the EEs found on TA-Im, four (2%) among asymptomatic episodes. Source control intervention (surgical, or CT-guided drainage) for other infectious findings on TA-Im was performed in 10 (2%) episodes; 2 (<0.5%) among asymptomatic episodes (Supplementary Table 3).



The comparison of patients' characteristics with and without EE on

Fig. 1. Study flowchart. TA-Im: thoracoabdominal imaging, IE: Infective endocarditis.

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#### Table 1

Type of embolic events and their impact on diagnosis in episodes with suspected infective endocarditis.

	Total ( $n = 966$ ) Asymptomatic ( $n = 528$ )		somatic ( $n = 528$ )	Symptomatic ( <i>n</i> = 438)		Р	
No embolic event	761	79%	433	82%	328	75%	
Embolic events	205	21%	95	18%	110	25%	0.007
Pulmonary septic emboli	88	9%	33	6%	55	13%	0.001
Intrabdominal organs							
Spleen	82	8%	43	8%	39	9%	0.536
Kidneys	45	5%	23	4%	22	5%	0.446
Liver	16	2%	7	1%	9	2%	0.451
Drainage of hepatic lesion	7	1%	1	<0.5%	6	1%	0.051
Major artery emboli	11	1%	6	1%	5	1%	1.000
Treatment (surgical or endovascular) of major artery emboli	3	<0.5%	2	<0.5%	1	<0.5%	1.000
Mycotic aneurysm	17	2%	3	1%	14	3%	0.012
Treatment (surgical or endovascular) of mycotic aneurysm	10	1%	3	1%	7	2%	0.199
Vascular criterion initially fulfilled by TA-Im findings <sup>a</sup>	142	15%	60	11%	82	19%	0.001
Upgrade from rejected to possible infective endocarditis <sup>b</sup>	6	1%	2	<0.5%	4	1%	0.489
Upgrade from possible to definite infective endocarditis <sup>b</sup>	10	1%	5	1%	5	1%	1.000

TA-Im: thoracoabdominal imaging studies.

<sup>a</sup> No prior cutaneous, ocular or cerebral embolic events detected by clinical examination or imaging studies other than TA-Im.

<sup>b</sup> Among patients with final infective endocarditis diagnosis.

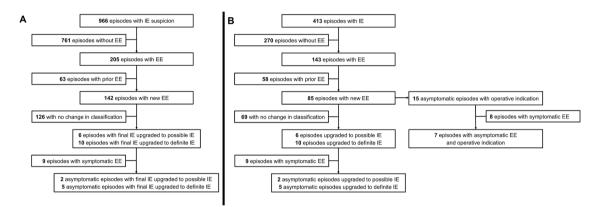


Fig. 2. Changes in diagnostic classification and management due to thoracoabdominal imaging results in patients suspected (A) and those with infective endocarditis (B).

EE: embolic event, TA-Im: thoracoabdominal imaging, IE: Infective endocarditis.

TA-Im are shown in Table 4. In the multivariable analysis (Supplementary Table 4), the detection of EEs on TA-Im was associated among other factors with a vegetation size  $\geq 10$  mm (*P* 0.003; OR 2.18, CI 1.32–3.61), while presence of EE prior to TA-Im (*P* 0.174; OR 1.43, CI 0.85–2.41) and presence of thoracic symptoms (*P* 0.524; OR 1.19, CI 0.70–2.20) had no impact.

# 3.5. Adverse events related to thoracoabdominal imaging

Among episodes with suspected IE, who were not on hemodialysis and underwent contrast-enhanced TA-Im (n = 721), 7% (50 episodes; grade I: 27; II: 11; III: 12) developed AKI within 5 days from TA-Im. The rate of AKI among episodes that had non-contrast-enhanced TA-Im (n =198) was 5% (10 episodes; grade I: 7; II: 2; III: 1). Four patients (0.6%) developed immediate hypersensitivity reaction following contrastenhanced TA-Im.

Among episodes with IE, who were not on hemodialysis and underwent contrast-enhanced TA-Im (n = 321), 12% (39 episodes; grade I: 20; II: 8; III: 11) developed AKI within 5 days from TA-Im. The rate of AKI among episodes that had non-contrast-enhanced TA-Im (n = 75) was8% (6; grade I: 4; II: 1; III: 1).

# 4. Discussion

In the present study, among patients with suspected IE, who underwent TA-Im, EEs were common (21%), but their identification had limited impact on diagnosis (only 2% classified as IE due to TA-Im findings). However, detection of EE by TA-Im frequently influenced subsequent surgical management, with 12% of IE patients with left-side vegetation >10 mm meeting a new surgical indication. To the best of our knowledge this is the first study to investigate the role of TA-Im in patients with IE suspicion, and not only patients with IE diagnosis.

Among IE patients, splenic emboli were detected in 17%, being second to cerebral (24%); this finding was in line with other studies. [5, 8-10] EEs detection rate in patients with IE was similar to studies that included patients that benefited from TA-Im, [6] or abdominal MRI. [10] In the present study, the prevalence of EEs in asymptomatic and symptomatic patients was similar (31% *versus* 39%; *P* 0.097).

In the 2015 ESC guidelines, imaging for embolic events (cerebral MRI, whole body CT scan and/or <sup>18</sup>F-FDG PET/CT) was recommended in patients with possible IE with a high clinical suspicion of IE. [14] The role of cerebral imaging, and especially MRI, has been established in previous studies, after demonstrating that cerebral MRI allowed a combined reclassification of patients (reclassification from rejected to possible or possible to definite IE) in 5–32% [1,2,11] and led to changes in clinical management (new indication for valvular surgery, management of cerebral EEs) in 14%. [11]

On the other hand, the role of TA-Im in IE patients remains controversial, with a scarcity of studies evaluating their role in diagnosis or management. In a previous study including IE patients, only 2% were reclassified according to TA-Im findings, a proportion similar to the present study (4%). [6] In a study including 58 patients with IE, who

#### Table 2

Predictors of embolic events detected by thoracoabdominal imaging episodes with suspected infective endocarditis.

	Without embolic events ( <i>n</i> = 761)		With embolic events ( <i>n</i> = 205)		Р
Demographics					
Male sex	536	70%	158	77%	0.066
Age (years)	65	16	57	16	< 0.001
Age >60 years	507	67%	100	49%	< 0.001
Co-morbidities					
Congestive heart failure	81	11%	18	9%	0.517
Chronic obstructive pulmonary	109	14%	20	10%	0.105
disease	67	00/	10	60/	0.217
Cirrhosis Diabetes mellitus	67 190	9% 25%	13 45	6% 22%	0.317 0.410
Chronic kidney disease (moderate or	153	20%	36	18%	0.410
severe)	100	2070	50	1070	0.107
Malignancy (solid organ or	167	22%	36	18%	0.178
haematologic)					
Obesity	193	25%	33	16%	0.005
Immunosuppression	143	19%	33	16%	0.415
Cardiac predisposing factors	213	28%	76	37%	0.013
Cardiac implantable electronic devices	107	14%	27	13%	0.820
Bacteraemia	553	73%	164	80%	0.038
S. aureus	222	29%	87	42%	< 0.001
Coagulase negative staphylococci	41	5%	8	4%	0.475
Streptococci	128	17%	33	16%	0.916
Enterococci Other Gram-positive	84 22	11% 3%	21 1	10% 1%	0.802 0.066
HACEK	12	3% 2%	4	2%	0.000
Other Gram-negative	67	270 9%	8	4%	0.018
Fungi	24	3%	8	4%	0.659
Polymicrobial bacteraemia	43	6%	5	2%	0.069
Manifestations			-		
Systemic symptoms	673	88%	190	93%	0.097
Fever	623	82%	164	80%	0.544
Heart murmur	288	38%	100	49%	0.005
New heart murmur	191	25%	70	34%	0.013
Immunologic phenomena	30	4%	19	9%	0.004
Sepsis	264	35%	107	52%	< 0.001
Septic shock	84	11%	39	19%	0.004
TA-Im performed due to symptoms	328	43%	110	54%	0.007
Thoracic symptoms	176	23% 19%	71 62	35%	0.001
Dyspnea Cough	148 27	19% 4%	62 15	30% 7%	0.001 0.031
Thoracic pain	27	4%	15	7%	0.031
Abdominal symptoms	107	14%	35	17%	0.317
Nausea/vomiting	18	2%	5	2%	1.000
Diarrhea	19	2%	3	1%	0.597
Abdominal pain	86	11%	32	16%	0.117
Spinal pain	41	5%	9	4%	0.722
Pain of articulations	30	4%	4	2%	0.204
Embolic events prior to TA-Im	118	16%	63	31%	< 0.001
Cutaneous	28	4%	25	12%	< 0.001
Ocular	15	2%	9	4%	0.072
Cerebral	88	12%	49	24%	< 0.001
Days to TA-Im	4	5	3	4	0.010
Findings of TA-Im (other than embolic events)					
Infectious findings	187	25%	24	12%	< 0.001
Septic arthritis	22	3%	5	2%	1.000
Prosthetic joint infection	7	1%	0	0%	0.356
Osteomyelitis	8	1%	1	0%	0.693
Spondylodiscitis	23	3%	6	3%	1.000
Other sites of infection	132	17%	14	7%	< 0.001
Noninfectious findings	42	5%	8	4%	0.477
Venous thrombosis/pulmonary	13	2%	7	3%	0.162
embolism					
Malignancy	11	1%	1	0%	0.478
Acute cardiac insufficiency	4	1%	0	0%	0.584
Other non-infectious findings	15	2%	0	0%	0.051
Infective endocarditis (final diagnosis)	270 233	36% 31%	143 120	70% 59%	$< 0.001 \\ < 0.001$
Positive imaging Duke criterion	200	31%		59%	<0.001

Data are depicted as number/percentage or mean/standard deviation.

HACEK: Haemophilus spp, Aggregatibacter spp, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae; TA-Im: thoracoabdominal imaging studies.

# Table 3

Type of embolic events and imp	ct on diagnosis and	management in infective
endocarditis episodes.		

endocarditis episodes.							
	Total ( 413)	(n =	Asymptomatic $(n = 223)$		Symptomatic $(n = 190)$		Р
No embolic event	270	65%	154	69%	116	61%	
Embolic events	143	35%	69	31%	74	39%	0.097
Pulmonary septic	52	13%	15	7%	37	20%	< 0.001
emboli							
Intrabdominal							
organs							
Spleen	71	17%	38	17%	33	17%	1.000
Kidneys	40	10%	20	9%	20	11%	0.620
Liver	7	2%	6	3%	1	1%	0.130
Drainage of	0	0%	0	0%	0	0%	-
hepatic lesion							
Major artery	9	2%	5	2%	4	2%	1.000
emboli							
Treatment	3	1%	2	1%	1	1%	1.000
(surgical or							
endovascular) of							
major artery							
emboli							
Mycotic	11	3%	2	1%	9	5%	0.027
aneurysm							
Treatment	6	2%	2	1%	4	2%	0.420
(surgical or							
endovascular) of							
mycotic							
aneurysm							
Vascular criterion	85	21%	35	16%	50	26%	0.010
initially fulfilled							
by TA-Im							
findings <sup>a</sup>							
Upgrade from	6	2%	2	1%	4	2%	0.420
rejected to							
possible							
endocarditis							
Upgrade from	10	2%	5	2%	5	2%	1.000
possible to							
definite							
endocarditis							
Operative	15	4%	7	3%	8	4%	0.606
indication			_		_		
Surgery	15	4%	7	3%	8	4%	0.606
performed							

TA-Im: thoracoabdominal imaging studies.

<sup>a</sup> No prior cutaneous, ocular or cerebral embolic events detected by clinical examination or imaging studies other than TA-Im.

benefited from both abdominal and cerebral MRI, 34% had an abdominal EE, none of which led to reclassification of diagnosis. [10] According to our results, among patients with suspected IE, a reclassification to definite or possible IE according to TA-Im results occurred in only 2% (1% among asymptomatic patients). Therefore, a policy of systematic TA-Im in asymptomatic patients with suspected IE does not seem warranted to improve diagnosis.

Even though TA-Im only had little incremental impact on IE diagnosis, it could establish in association with left-side vegetation >10 mm a new indication for valvular surgery (embolism prevention) in 4% of patients with IE (3% among asymptomatic episodes). The proportion was 12% in the subgroup of patients with left-side valvular vegetation >10 mm (10% among asymptomatic episodes) detected on cardiac imaging. The presence of EEs in TA-Im among patients with IE was independently associated with vegetation  $\geq$ 10 mm. [4] In the first randomized clinical trial of patients with large vegetations without heart failure, but at high-risk for EEs, early surgery resulted in significantly lower rate of EEs, as compared to conventional treatment (0% versus 21%; P 0.005). [18] On the other hand, in a previous study of 58 patients, abdominal MRI findings (embolic events in 20 patients; 34%) had no effect on valvular surgical management. [10] In addition, the detection of EEs by TA-Im did not alter therapeutic management

#### Table 4

Predictors of embolic events detected by thoracoabdominal imaging among infective endocarditis episodes.

	Without embolic events ( <i>n</i> =		With embolic events ( <i>n</i> =		Р
	270)		143)		
Demographics					
Male sex	204	76%	113	79%	0.464
Age (years)	66	16	58	17	< 0.001
Age >60 years old Co-morbidities	192	71%	68	48%	< 0.001
Congestive heart failure	30	11%	14	10%	0.740
Chronic obstructive pulmonary	35	13%	15	10%	0.528
disease					
Cirrhosis	21	8%	8	6%	0.544
Diabetes mellitus	75	28%	33	23%	0.347
Chronic kidney disease (moderate or	49	18%	23	16%	0.683
severe)	07	1.00/	15	1.00/	0.044
Malignancy (solid organ or	27	10%	15	10%	0.866
haematologic) Obesity	76	28%	21	15%	0.002
Immunosuppression	29	28% 11%	10	7%	0.002
Setting of infection onset	2)	1170	10	770	0.200
Community or non-nosocomial	233	86%	133	93%	
healthcare-associated					
Nosocomial	37	14%	10	7%	0.050
Cardiac predisposing factors	139	51%	70	49%	0.679
Cardiac implantable electronic devices	52	19%	23	16%	0.503
Timing of infective endocarditis					
2015–2017 (retrospective cohort)	90	33%	60	42%	0.007
2018–2022 (prospective cohort)	180	68%	83	58%	0.087
Microbiological identification	93	34%	74	52%	0.001
S. aureus Coagulase negative staphylococci	93 18	34% 7%	74 7	52% 5%	0.001 0.524
Streptococci	76	28%	, 32	22%	0.239
Enterococci	39	14%	19	13%	0.882
Other Gram-positive	10	4%	0	0%	0.017
HACEK	12	4%	5	3%	0.797
Other Gram-negative	10	4%	1	1%	0.106
Intracellular pathogens	4	1%	1	1%	0.663
Fungi	3	1%	3	2%	0.421
Polymicrobial infection	9	3%	4	3%	1.000
No identification Manifestations	14	5%	5	3%	0.622
Systemic symptoms	250	93%	137	96%	0.287
Fever	227	84%	115	80%	0.411
Heart murmur	163	60%	86	60%	1.000
New heart murmur	115	43%	63	44%	0.835
Immunologic phenomena	20	7%	18	13%	0.106
Sepsis	112	41%	81	57%	0.004
Septic shock	45	17%	34	24%	0.088
TA-Im performed due to symptoms	116	43%	74	52%	0.097
Thoracic symptoms Dyspnea	77 65	29% 24%	55 50	39% 35%	0.046 0.021
Cough	8	3%	13	9%	0.009
Thoracic pain	11	4%	10	7%	0.240
Abdominal symptoms	22	8%	15	10%	0.470
Nausea/vomiting	4	1%	1	1%	0.663
Diarrhea	3	1%	1	1%	1.000
Abdominal pain	17	6%	15	10%	0.174
Spinal pain	16	6%	8	6%	1.000
Pain of articulations	14	5%	3	2%	0.193
Embolic events prior to TA-Im Cutaneous	73 25	27% 9%	58 25	41% 17%	0.006
Ocular	25 7	3%	23 7	17% 5%	0.018 0.256
Cerebral	, 54	20%	, 46	32%	0.230
Days to TA-Im	5	6	3	4	0.018
Findings of TA-Im (other than embolic	64	24%	18	13%	0.007
events)					
Infectious findings	47	17%	13	9%	0.027
Septic arthritis	12	4%	5	3%	0.797
Prosthetic joint infection	2	1%	0	0%	0.546
Osteomyelitis	6	2%	1	1%	0.430
Spondylodiscitis	9	3%	4	3%	1.000
Other sites of infection	21 18	8% 7%	4	3% 4%	0.051
Noninfectious findings	18	7%	6	4%	0.380

Table 4 (continued)

	embol	Without embolic events ( <i>n</i> = 270)		ic 5 (n =	Р
Venous thrombosis/pulmonary embolism	6	2%	5	3%	0.524
Malignancy	4	1%	1	1%	0.663
Acute cardiac insufficiency	3	1%	0	0%	0.554
Other non-infectious findings	5	2%	0	0%	0.169
Site of infection					
Aortic valve	140	52%	69	48%	0.535
Mitral valve	115	43%	57	40%	0.602
Other left-side site of infection	3	1%	1	1%	1.000
Tricuspid valve	7	3%	33	23%	< 0.001
Pulmonary valve	6	2%	4	3%	0.743
Multivalvular	19	7%	26	18%	0.001
CIED-IE	25	9%	14	10%	0.861
Type of valve					
Native	175	65%	111	78%	0.007
Prosthetic	75	28%	28	20%	0.074
Positive imaging Duke criterion	209	77%	115	80%	0.530
Vegetation	170	63%	111	78%	0.003
Vegetation $\geq 10$ mm	83	31%	79	55%	< 0.001
Abscess	50	19%	35	24%	0.161
Other lesions <sup>a</sup>	44	16%	21	15%	0.777

Data are depicted as number/percentage or mean/standard deviation.

CIED: Cardiac implantable electronic device; HACEK: *Haemophilus* spp, *Aggregatibacter* spp, *Cardiobacterium hominis, Eikenella corrodens, Kingella kingae*; TA-Im: thoracoabdominal imaging.

<sup>a</sup> Perforation, dehiscence of prosthetic valve, fistula, pseudoaneurysm, aneurysm.

(medical or surgical) among 147 IE patients, nor influenced survival. [5] More studies are needed to elucidate the role of valve surgery in preventing further EEs in patients with asymptomatic intraabdominal EEs.

Another potential impact of TA-Im on patients with IE suspicion, was the specific treatment of EEs or other sites of infection such as source control interventions (endovascular, surgical, or CT-guided drainage). The rate in the present study was comparable to previously reported. [6, 10,19] In the present study, most cases necessitating specific management occurred in symptomatic patients.

AKI among IE patients who underwent contrast-enhanced TA-Im occurred in 12%, comparable to the rate previously reported (12%). [6] No significant difference in the incidence of AKI was observed among patients receiving or not contrast-media, illustrating the role of other factors in AKI development among IE patients (hemodynamic instability due to septic or cardiac shock, nephrotoxic medication). [20]

The study has several limitations. First, the study is noninterventional, and the realization of TA-Im was at the discretion of the treating physician and infectious diseases specialist. Concerning the indication for valvular surgery during the prospective cohort, all IE patients were discussed during the weekly Endocarditis Team meetings. Second, the long-term impact of changes in diagnostic classifications and therapeutic plans on outcome was not evaluated. Third, the performance of Duke criteria for the diagnosis of IE is moderate (sensitivity ~80%) and should not replace clinical judgment. [21] Accordingly, the final IE diagnosis was made only after 2 months of follow-up, incorporating the Endocarditis Team appreciation. Lastly, performing <sup>18</sup>F-FDG PET/CT or PET/CTA on a latter course (median of 7 days of antibiotic treatment) of the disease could affect their performance, since this imaging method relies on the presence of inflammatory cells, which can be reduced after a longer course of antibiotic treatment.

In conclusion, the present study confirmed that performing systematic TA-Im in asymptomatic patients with suspected IE improved the detection of EEs, but with a limited impact on IE diagnosis. A policy of systematic TA-Im is, therefore, not warranted for diagnostic purposes only. The role of systematic TA-Im in the clinical management of asymptomatic IE patients remains unclear, since it identified a new indication for valvular surgery in only a small proportion of patients. The scenario, where TA-Im could be beneficial on management is when a patient has a vegetation >10 mm but no EE detected clinically or by brain imaging; in such cases, systematic TA-Im may lead to a new surgical indication in 10% of cases. More studies are needed to evaluate whether a subset of asymptomatic IE patients may nevertheless benefit from systematic TA-Im.

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# Author contributions

M.P.O., P.M. and B.G. conceived the idea. M.P.O., P.M., D.C.R., C.H. K., G.F., J.O.P., N.I., Y.M., P.T., and M.K. collected the patients' data. B. G. supervised the project. M.P.O. performed the analysis and interpreted the results. M.P.O. wrote the manuscript. All authors contributed to manuscript revision and read and approved the submitted version.

### **Declaration of Competing Interest**

The authors declare there is no conflict of interests.

# Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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# Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2023.06.007.

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