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Diagnostic Accuracy of PET/CT and Contrast Enhanced CT in Patients With Suspected Infected Aortic Aneurysms

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WHAT THIS PAPER ADDS

The study analyses the diagnostic accuracy of two imaging modalities in the detection of infected aortic aneurysms. The accuracy of positron emission tomography/computed tomography (PET/CT) is higher than contrast enhanced CT. The high metabolic activity of infected aortic aneurysms, measurable and quantifiable only by PET/CT by means of maximum standardised uptake values (SUV_{max}), may account for the excellent sensitivity of PET/CT. However, its specificity is hampered, owing to false positive findings in inflammatory aneurysms and in arteritis. Findings may influence future clinical practice, as PET/CT may become the imaging modality of choice in infected aortic aneurysms.

Objective: Infected aortic aneurysms are highly lethal, and management is very demanding, requiring an early diagnosis. The aim of this study was to evaluate the diagnostic accuracy of positron emission tomography/computed tomography with ^{18}F-fluorodeoxyglucose (PET/CT) and contrast enhanced CT (CE-CT) in patients with suspected infected aortic aneurysms.

Methods: PET/CT was performed in patients with clinically suspected infected aortic aneurysms, and additional CE-CT was performed if feasible. Diagnostic accuracy was assessed by two independent readers using a four point grading score for both imaging modalities. Maximum standardised uptake values (SUV_{max}) were calculated for quantitative measurements of metabolic activity in PET/CT. The reference standard was a combination of clinical presentation, laboratory findings, and imaging.

Results: Ten patients were included prospectively in the study, 24 retrospectively; 16 patients (47%) prior to the start of antimicrobial treatment and all 34 patients prior to any vascular intervention. Thirteen of the 34 patients had an infected aortic aneurysm (38%). Proven infected aortic aneurysms were all metabolically active on PET/CT with a median SUV_{max} of 6.6 (interquartile range 4.7—21.8). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of PET/CT for the diagnosis of infected aortic aneurysm was 100%, 71%, 68%, 100%, and 82%, for reader 1 and 85%, 71%, 65%, 88%, and 77%, for reader 2. Respective values for CE-CT, performed in 20 patients (59%), were 63%, 75%, 63%, 75%, and 70%, for reader 1 and 88%, 50%, 54%, 86%, and 65%, for reader 2.

Conclusion: The diagnostic accuracy of PET/CT in the detection of infected aortic aneurysms ($n = 13$) is high, and higher than CE-CT. While PET/CT demonstrates an excellent sensitivity, its specificity is hampered because of false positive findings.

Keywords: PET-CT, 18F-FDG, Computed tomography angiography, Infected aneurysm, Infection, Data accuracy
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INTRODUCTION

Infected (mycotic) aneurysms are infected arterial aneurysms which can develop at any level within the circulatory system.[1] The prevalence of thoracic (≈30%) and abdominal (≈70%) infected aortic aneurysms accounts for 0.7%—4.5% of all aortic aneurysms.[2] Infected aortic aneurysms are rare,

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thus complicating statistical evaluation. The management of infected aortic aneurysms is very demanding, and these aneurysms are highly lethal.[3,4]

Early diagnosis is the cornerstone of effective treatment,[5] based on physical findings, laboratory (including blood cultures), and imaging. Imaging is particularly important, since clinical findings are often non-specific. Contrast enhanced computed tomography (CE-CT) is the imaging modality of choice, as it is readily available and enables surgeons to define the vessel anatomy for surgery.[6] However, as ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT has been shown to have higher sensitivity and diagnostic accuracy in other infectious diseases such as pyrexia of unknown origin, chronic osteomyelitis, or vascular graft infections,[3,7,8] it is hypothesised that PET/CT might be superior to CE-CT in the initial imaging diagnosis of infected aortic aneurysms.

Thus, the aim of the present study was to (i) assess the use of PET/CT in the diagnosis of infected aortic aneurysms, and (ii) to compare the accuracy of PET/CT and CE-CT.

MATERIALS AND METHODS

Study design

Participants in the Vascular Graft Cohort Study (VASGRA) with suspected infected aortic aneurysms were prospectively included in this analysis. VASGRA is an open, prospective, observational cohort study located at the University Hospital Zurich, Zurich, Switzerland, with continued enrolment of patients aged 18 years or more with vascular graft surgery, vascular graft infection, or secondary vascular graft infection due to infected aortic aneurysm since March 2013. A retrospective chart review was performed in all patients with suspected infected aortic aneurysms who had been examined with PET/CT between the years 2005 and 2018 if the term “mycotic” or “infected aneurysm” was mentioned in the written PET/CT report, and was found to refer to an aneurysm of the thoracic, abdominal, or pelvic arteries.

The institutional review board approved the study (BASEC-Nr. 2018−01904), and written informed consent was obtained from all participants who were either enrolled prospectively or examined between the years 2016 and 2018. For patients scanned between the years 2005 and 2015, written informed consent was waived due to retrospective inclusion. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Definitions

Diagnostic criteria for infected aortic aneurysms as suggested by Soerelius *et al.*[9] were used. The gold standard was the combination of clinical presentation (pain, fever, sepsis), laboratory positive microbiological culture of aortic/aneurysmal wall; presence of bacteria in thrombus or blood culture; elevation of inflammatory markers such as C reactive protein and white blood cells; and imaging (i.e. rapid expansion of aneurysm, saccular aneurysm, multi lobular aneurysm, eccentric aneurysm, peri-aortic gas, and peri-aortic soft tissue mass). All patients were followed up until the clinical diagnosis was confirmed or excluded. If cases remained equivocal (e.g. due to insufficient clinical follow up), they were excluded retrospectively from the analyses.

Inflammatory aortic aneurysm was defined as a non-infected subset of aortic aneurysm, thought to be caused by a pathogenic immuno-inflammatory process, occasionally immunoglobulin G4 related, in which corticosteroid and/or immunosuppressive therapies may be effective.[10]

PET/CT and CT data acquisition

Between the years 2005 and 2018, five different types of PET/CT scanners were used in the department. Initially, a Discovery ST16 and a Discovery VCT (both GE Healthcare, Waukesha, WI, USA) were used. Both systems were replaced in 2016 by two Discovery MI scanners (GE Healthcare). In 2010 and in 2015 a Discovery 690 and a Discovery 710 (both GE Healthcare) scanners respectively, were also installed.

All PET/CT systems used non-enhanced CT scans for attenuation correction, and scans were acquired from the vertex of the skull to the mid of the thigh, or to the foot (depending on clinical request). CT data for attenuation correction and anatomic reference were reconstructed with a slice thickness of 3.75 mm and an increment of 3.0 mm.

All patients fasted for at least four hours and had no insulin injections within four hours prior to the FDG administration. Body weight, height, and blood glucose level were recorded prior to injection of FDG. Patients who did not have diabetes and a blood glucose level $<$8 mmol/L and patients with diabetes and a blood glucose level $<$12 mmol/L were accepted for imaging. After intravenous injection of FDG (i.e. 343 MBq (interquartile range (IQR) 288−420)), patients rested for a standardised uptake time of 60 min. Whenever possible, data were acquired with the patient in the supine position with arms overhead.

In the prospectively enrolled study population, CE-CT of the chest and/or abdomen was performed, depending on the location of the aneurysm. After intravenous injection of 80 mL of iodinated contrast medium (Visipaque® 320, GE Healthcare), CE-CT was timed for arterial phase imaging (threshold based initiation using a region of interest in the aorta) and portal venous phase (50 s after the arterial phase) with a tube voltage of 120 kV and a tube current−time product of 100−320 mAs. If CE-CT with a comparable imaging protocol and diagnostic image quality had been performed at the institution within seven days prior to the PET/CT, no separate CE-CT was acquired as part of the PET/CT. In the retrospectively enrolled study population, all CE-CT examinations performed at the institution within seven days of the PET/CT examination were accepted for further

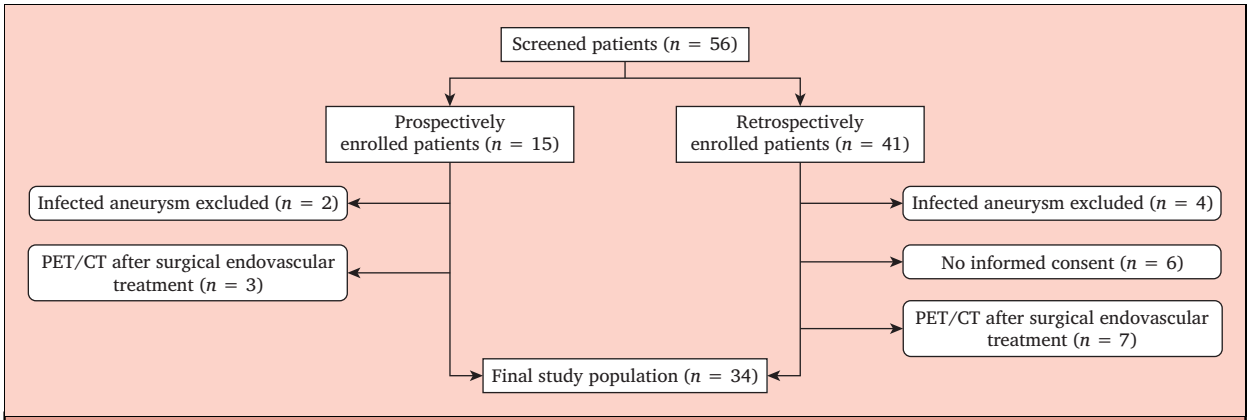

Figure 1. Flow diagram showing the numbers of patients enrolled, excluded and finally included in the study of suspected infected aortic aneurysms. PET/CT = positron emission tomography/computed tomography.

evaluation, including those acquired as part of the PET/CT scan.

Image analysis

All data sets (PET/CT and CE-CT) were analysed retrospectively and independently by two experienced and double board certified radiologists and nuclear medicine physicians on an Advantage Workstation (AW) version 4.7 (GE Healthcare Biosciences, Pittsburgh, PA, USA). Readers were blinded to all clinical patient data. All data sets were analysed for additional findings (e.g. infected foci not in the vicinity of the aorta or other relevant findings such as malignancies) and documented if found relevant for diagnosis by the readers.

PET/CT

Readers determined the FDG uptake in the aneurysm by measuring the maximum standardised uptake value (SUV_{max}) in the aneurysm as well as in the liver and mediastinal blood pool (the last two for reference) using in built software. SUV_{max}) was calculated as a proxy of the activity of the tracer. The correct placement of the volume of interest in the aneurysm was confirmed using axial, coronal, and sagittal reformatted images in order to avoid partial volume effects or signal spill over from neighbouring organs such as the kidney. For negative imaging for infected aortic aneurysm SUV_{max} was measured in the abdominal aorta for reference.

CE-CT

The readers determined whether an infected aortic aneurysm was present or not. Additionally, CE-CT readers were asked to document the presence or absence of the following imaging findings: fat stranding, peri-aortic fluid collection or mass, contrast enhancement, lymphadenopathy, and gas formation. Differences between -readers were analysed, but no consensus reading was performed.

For both imaging modalities, readers scored their confidence in their diagnosis, using a four point score. Score 1 (no signs for infected aortic aneurysm) and score 2 (most likely a non-infected aneurysm) were considered negative for infected aortic aneurysm, while score 3 (suspicion of infected aortic aneurysm) and score 4 (clear signs of infected aortic aneurysm) were considered positive for infection. The rate of "confident" and "non-confident" findings (score 1 and 4 *vs.* score 2 and 3) was calculated for each reader and each imaging modality. Six months after the initial reading, both readers repeated their scoring for the calculation of intra-reader variability.

Patient follow up

Patient data were recorded at the time of imaging, including patient demographics, laboratory data (e.g. level of C-reactive protein and leucocyte count), microbiological results, results of other diagnostic procedures (e.g. results from colonoscopy, if performed to confirm an incidental PET/CT finding), treatment information (e.g. type of vascular graft, type, and duration of antibiotic treatment), and patient's general health status (e.g. clinical signs of infection, pain, etc.). Clinical follow up of all patients was performed by reviewing the electronic patient charts to confirm the diagnosis or the exclusion of infected aortic aneurysm.

Statistical analyses

Statistical analysis was performed using commercially available software (Stata, Version 15, StataCorp, College Station, TX, USA).

Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy were determined for the diagnosis of infected aortic aneurysm for both readers of both imaging modalities (PET/CT and CE-CT), and receiver operating characteristic (ROC) areas under the curve (AUC) were calculated. The intra- and inter-reader agreement regarding presence of absence of infected aortic aneurysms as well as for the four point score for PET/CT and CE-CT were analysed by kappa statistics, respectively. According to Landis and Koch, kappa values of 0.61—0.80 were interpreted as substantial, and 0.81—1.00

Table 1. Patient demographics of the final study population with suspected infected aortic aneurysms

Patient characteristics	Patients (n = 34)
Age − years	64 (57–85)
Female gender	8 (24)
Diabetes mellitus	7 (21)
Renal insufficiency	17 (50)
Smoking/history of smoking	19 (56)
Antimicrobial treatment at time of imaging	18 (53)
C reactive protein at time of imaging − mg/L	79 (16–253)
WBC − g/L	9.0 (6.9–19.5)
Confirmed infected aneurysms	13 (38)

Data are given as median (interquartile range [IQR]) or n (%). PET/CT = positron emission tomography/computed tomography; CE = contrast enhanced CT = computed tomography; WBC = white blood cell count.

as high agreement. Variables were expressed as median and IQR (25th, 75th percentiles) or percentages.

RESULTS

Patient population

Fifteen of 56 patients (27%) were prospectively enrolled (part of the VASGRA cohort as described in the methods sections). Forty-one patients (73%) were evaluated for retrospective inclusion in the study, as the term "mycotic" or "infected" (related to an aneurysm of the thoracic, abdominal, or pelvic arteries) was found either in the reason for referral or in the findings of the written PET/CT report in the data bank search. Six patients were excluded because no written informed consent was given. The reasons for referral of the remaining 50 patients were (multiple reasons for referral possible): signs of infected aortic aneurysm (n = 38), vascular graft infection (n = 8), aortitis (n = 4), infected foci in general (n = 16), or other indications unrelated to infected aortic aneurysm. (i.e. question of lymphoma (n = 4), other tumour staging or restaging (n = 3)).

Six patients were excluded retrospectively, since no definitive diagnosis could be confirmed by clinical follow up. Furthermore, the PET/CT examinations of another 10 patients (20%) were excluded, as they were performed after vascular intervention (i.e. graft placement), and the aim was to avoid potential bias caused by possible post-interventional inflammatory changes, foreign body reactions, or secondary graft infections.

Hence, the final patient population consisted of 34 patients (10 prospectively enrolled, 24 retrospectively, Fig. 1). Patients' demographics data are displayed in Tables 1 and 2. In 20 (59%) patients, CE-CT was performed as part of the PET/CT or as a separate scan within seven days of the PET/CT scan.

Table 2. Patient demographics of the final study population with suspected infected aortic aneurysms

ID	Age	Male	Diabetes	Smoking	Renal insufficiency
01	62	y	n	y	n
02	64	y	n	n	n
03	70	y	y	n	y
04	64	y	n	n	n
05	62	y	n	y	y
06	48	y	n	y	y
07	58	y	y	y	y
08	46	n	n	n	y
09	61	y	y	y	y
10	65	y	n	y	n
11	71	y	n	y	n
12	64	n	n	y	n
13	80	y	n	y	n
14	64	y	y	y	y
15	48	y	n	y	n
16	81	n	n	y	y
17	75	n	n	n	y
18	71	y	y	n	n
19	55	y	n	n	n
20	70	n	n	y	n
21	57	y	n	n	y
22	69	n	n	n	n
23	71	n	n	n	y
24	69	y	n	n	n
25	52	y	y	n	n
26	41	y	n	y	n
27	76	y	n	y	y
28	66	y	y	n	y
29	61	y	n	y	y
30	73	y	n	y	n
31	54	n	n	y	y
32	85	y	n	n	y
33	47	y	n	n	n
34	68	y	n	y	y

ID = patient identification; y = yes; n = no.

Prevalence of infected aortic aneurysms and incidental findings

Thirteen patients (38%) had an infected aortic aneurysm, while in 21 patients (62%) infected aortic aneurysm was ruled out using the diagnostic criteria for infected aortic aneurysms as outlined in the methods section. Aortic aneurysms but no infected foci were diagnosed in 10 patients, while one patient had an aneurysm of the coeliac trunk without infecting focus. Twelve patients (35%) had different or additional diagnoses (partly incidental, partly explaining the reason for patient referral; multiple diagnoses possible).

The numbers of specific findings are displayed in brackets (identified by PET/CT; identified by CE-CT): Inflammatory aneurysms (n = 3; 0; 0), pneumonia (n = 2; 2; 2), liver failure (n = 1; 0; 0), arteritis (n = 2; 1; 0), metastasis of urinary bladder cancer (n = 1; 0; 0), lymphoma (n = 1; 1; 1), colonic adenoma (n = 1; 1; 0), colitis (n = 1; 1, 0), diverticulitis (n = 1; 1; 0), endocarditis (n = 1; 0; 0), dental infection (n = 1; 1; 0), psoas muscle abscess (n = 1; 1; 1), and spondylodiscitis (n = 1; 1; 1). Hence; whole body PET/

CT correctly identified 10 of these 17 findings (59%), while CE-CT correctly identified five (29%).

Diagnostic performance of PET/CT

Proven infected aortic aneurysms ($n = 13$) were all metabolically active on PET/CT with a median SUV_{max} of 6.6 (IQR 4.7—21.8) (Fig. 2); median background activity was 2.6 (IQR 2.3—4.1) in the mediastinal blood pool and 3.4 (IQR 2.9—6.1) in the liver (see Table 3).

Inter-reader variability of diagnostic accuracy was comparably high for PET/CT and CE-CT (Table 4). Readers' confidence in their diagnosis was higher for PET/CT (62% reader 1, 82% reader 2) than for CE-CT (35% reader 1, 70% reader 2).

In PET/CT, false positive findings occurred in inflammatory aneurysms ($n = 3$; both readers; Fig. 3), arteritis ($n = 1$; both readers), and in non-infected aneurysms ($n = 2$ for both readers; one was a suspected non-ruptured abdominal aortic aneurysm in a haemodynamically unstable patient (previously called "pre-rupture")[11] (Fig. 4).

False negative PET/CT findings only occurred with reader 2 ($n = 2$), despite the fact that all infected aortic aneurysms showed metabolic activity above background activity in the liver (see also 100% sensitivity for PET/CT when using a SUV_{max} cut off larger than liver background activity in Table 4). However, metabolic activity in these two aneurysms was lower (SUV_{max} 4.5 and 4.0) than the median of all infected aortic aneurysms (see above), and antimicrobial treatment was not started in these two patients. When using a SUV_{max} cut off higher than background activity in the liver in order to determine the presence of an infected aortic aneurysm, no false negative findings occurred (Table 4). However, nine false positive findings were detected in inflammatory aneurysms ($n = 3$, Fig. 3), arteritis ($n = 1$), and in non-infected aneurysms ($n = 5$; one was considered to be a non-ruptured abdominal aortic aneurysm in a haemodynamically unstable patient (previously called "pre-rupture") Fig. 4).

Diagnostic performance of CE-CT

In CE-CT, false positive findings occurred in inflammatory aneurysms ($n = 2$ for both readers; Fig. 3), and in non-infected aneurysms ($n = 1$ for reader 1, $n = 4$ for reader 2; one was considered a non-ruptured abdominal aortic

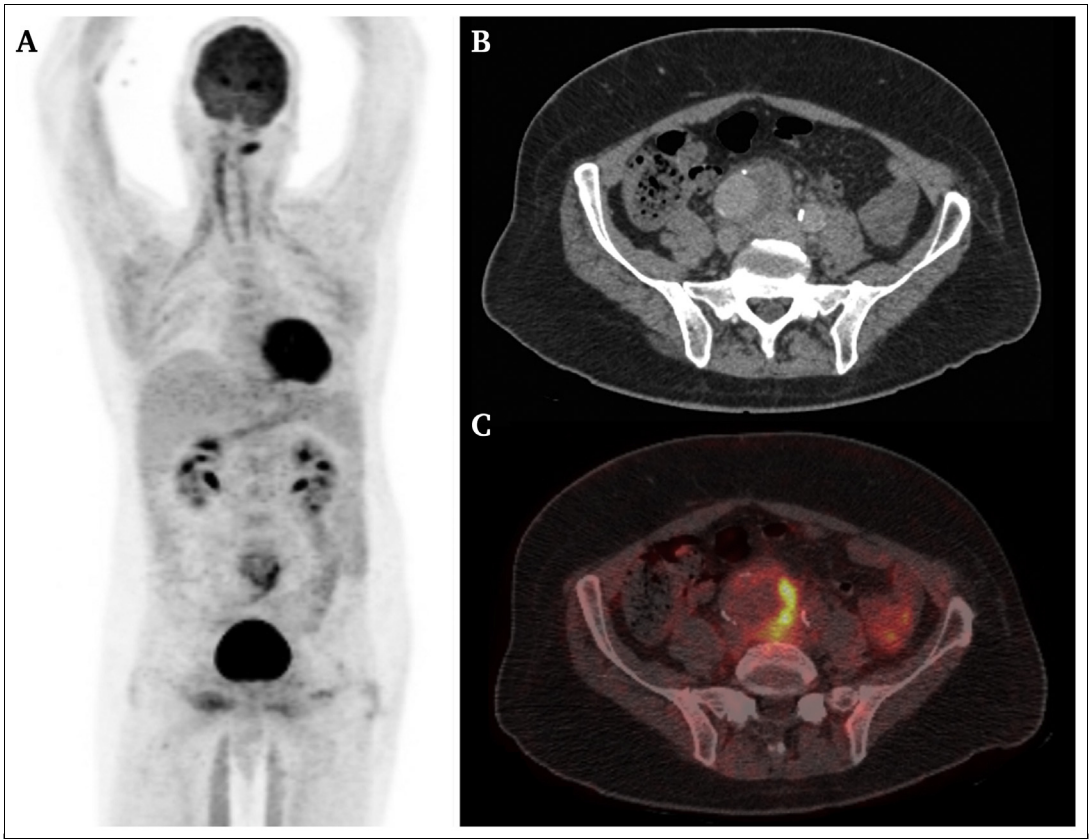

Figure 2. A 48 year old male patient presented with fever and abdominal pain, and was diagnosed with an infected aortic aneurysm caused by *Staphylococcus aureus*. Maximum intensity reconstructions of positron emission tomography (PET) (A) and fused PET/computed tomography (CT) images (C) showed strongly increased, focal ^{18}F-fluorodeoxyglucose (FDG) uptake in the abdominal aortic aneurysm wall, while contrast enhanced CT (B) showed mild thickening and mild contrast enhancement in the wall of the aneurysm. Both PET readers rated the examination true positive for an infected aneurysm, and both stated they were confident about their diagnosis. Only one reader of contrast enhanced CT rated the examination true positive, the other false negative; however, the latter was not confident about his findings.

Table 3. Patient and aneurysm characteristics of the final study population with suspected infected aortic aneurysms

ID	IA	Aneurysm	Clinical presentation	Time to PET − d	CRP − mg/L	WBC − g/L	Follow up days	Microbiology (location of isolation)
01	y	AA	Abdominal pain, fever	3	199	19.5	785	*Escherichia coli* (BC)
02	y	TA	Fever	11	27	8.9	817	*Candida albicans* (BC)
03	y	TA	Chest pain	6	122	9.1	298	*Streptococcus agalactiae* (BC)
04	n	AA	Abdominal pain, weakness	n.a.	47	3.8	572	n.a.
05	n	AA	Abdominal pain	n.a.	9	5.9	387	n.a.
06	y	AA	Abdominal pain, fever	3	145	10.7	594	*Staphylococcus aureus* (BC)
07	n	AA	Back pain, fever	n.a.	44	7.4	1 022	n.a.
08	n	n.a.	Sepsis, liver failure	n.a.	79	14.5	45	n.a.
09	n	n.a.	Fever	n.a.	154	15.9	826	n.a.
10	n	AA	Fever	n.a.	212	5.6	1 338	n.a.
11	n	AA	Abdominal pain	n.a.	11	9.3	1 141	n.a.
12	n	AA	None	n.a.	n.a.	6.3	1 688	n.a.
13	n	TAA	Fever, cough, shortness of breath	n.a.	137	8.8	81	n.a.
14	n	TAA	None	n.a.	14	7.6	1 622	n.a.
15	n	AA	None	n.a.	12	10.3	1 579	n.a.
16	y	TAA	Abdominal pain	n.a.	140	10.7	40	Negative during antimicrobial treatment
17	n	TAA	None	n.a.	16	8.2	n.a.	n.a.
18	y	TAA	Fever	14	n.a.	n.a.	61	*Salmonella enteritidis* (BC)
19	n	AA	Abdominal pain	n.a.	121	18.8	1 468	n.a.
20	n	TA	Chest pain	n.a.	96	8.7	591	n.a.
21	n	AA	Fever	n.a.	10	6.6	2 689	n.a.
22	y	TAA	Abdominal pain	33	34	11.9	384	*Streptococcus pneumoniae* (BC)
23	y	TAA	Abdominal pain	0	31	9.5	1 077	*Coxiella burnetii* (tissue)
24	n	TAA	None	n.a.	n.a.	n.a.	156	n.a.
25	y	TAA	None	n.a.	100	10.5	271	Diplococci (BC)
26	n	AA	Ruptured cerebral infected aneurysm	n.a.	19	9.8	3 017	n.a.
27	n	n.a.	Septic emboli in lower limb	n.a.	n.a.	n.a.	n.a.	n.a.
28	y	TAA	Abdominal pain	n.a.	93	10.7	12	*Listeria monocytogenes* (tissue)
29	y	AA	Chest pain	n.a.	10	6.7	1 954	*Coxiella burnetii* (tissue)
30	n	AA	Abdominal pain	n.a.	13	5.4	2 126	n.a.
31	n	n.a.	Enteritis	n.a.	n.a.	n.a.	4 105	n.a.
32	y	AA	Fever	n.a.	126	5.2	1 967	*Porphyromonas gingivalis* (BC)
33	n	TA	Chest pain	n.a.	253	10.4	1 168	n.a.
34	y	TAA	Abdominal pain	n.a.	234	8.2	1 821	*Mycobacterium bovis* (tissue)

ID = patient identification; IA = infected aneurysm; AA = abdominal aorta; TA = thoracic aorta; TAA = thoraco-abdominal aorta; PET = positron emission tomography/computed tomography; Time to PET = days between initial diagnosis and PET; CRP = C reactive protein; WBC = white blood cell count; Follow up = days of clinical follow up; BC = blood culture; d = days; y = yes; n = no; n.a. = not applicable.

aneurysm in a haemodynamically unstable patient (previously called "pre-rupture") Fig. 4)). False negative findings in CE-CT only occurred in three patients with reader 1 and in one patient for reader 2, antimicrobial treatment had already been started in all of these cases. Reader 1 detected the following CE-CT imaging findings in patients with proven infected aortic aneurysms ($n = 8$): fat stranding ($n = 8$, 100%), peri-aortic fluid collection or mass ($n = 5$; 63%), contrast enhancement ($n = 7$; 88%), lymphadenopathy ($n = 2$; 25%), and gas formations ($n = 0$; 0%); respective values for reader 2 were $n = 7$ (88%), $n = 4$ (50%), $n = 7$ (88%), $n = 7$ (88%), and ($n = 0$; 0%). In all other patients without infected aortic aneurysm ($n = 12$), reader 1 described the following CE-CT imaging findings): fat stranding ($n = 9$, 75%), peri-aortic fluid collection or mass ($n = 6$; 50%), contrast enhancement ($n = 4$; 33%), lymphadenopathy ($n = 4$; 33%) and gas formation ($n = 0$; 0%); respective values for reader 2 were $n = 11$ (92%), $n = 4$ (33%), $n = 5$ (42%), $n = 11$ (92%), and ($n = 0$; 0%). Reader 1 described at least one imaging CE-CT finding in 18 patients (90%), while no imaging finding was described in two patients (both true negative); reader 1 described imaging findings in 10 of 12 patients (83%) without infected aortic aneurysm. CE-CT reader 2 found at least one imaging finding in 19 patients (95%), one patient without imaging findings had an infected aortic aneurysm (false negative); reader 2 described CE-CT imaging findings in all patients without infected aortic aneurysm. Notably, when using only

Table 4. Diagnostic accuracy of positron emission tomography/computed tomography (PET/CT) and contrast enhanced (CE) computed tomography (CT) in suspected infected aortic aneurysm prior to vascular intervention

	n	Sensitivity (CI) − %	Specificity (CI) − %	NPV (CI) − %	PPV (CI) − %	Accuracy (CI) − %	ROC-AUC(CI)	Intra-rater (kappa)		Inter-rater (kappa)	
								y/n	Score	y/n	Score
PET/CT reader 1 overall	34	100 (75.3–100)	71.4 (47.8–88.7)	100 (78.2–100)	68.4 (43.4–87.4)	82.4 (65.5–93.2)	0.86 (0.76–0.96)	0.94	0.67	0.88	0.50
Prior to any treatment	16	100 (39.8–100)	66.7 (34.9–90.1)	100 (63.1–100)	50.0 (15.7–84.3)	75.0 (47.6–92.7)	0.83 (0.69–0.97)	0.94	0.82	0.75	0.47
Population with CE-CT	20	100 (63.1–100)	66.7 (34.9–90.1)	100 (63.1–100)	66.7 (34.9–90.1)	80.0 (56.3–94.3)	0.83 (0.69–0.97)	0.89	0.64	0.89	0.51
PET/CT reader 2 overall	34	84.6 (54.6–98.1)	71.4 (47.8–88.7)	88.2 (63.6–98.5)	64.7 (38.3–85.8)	76.5 (58.8–89.3)	0.78 (0.64–0.92)	0.88	0.64	n.a.	n.a.
Prior to any treatment	16	50.0 (6.8–93.2)	66.7 (34.9–90.1)	80.0 (44.4–97.5)	33.3 (4.3–77.7)	62.5 (35.4–84.8)	0.58 (0.27–0.90)	0.88	0.50	n.a.	n.a.
Population with CE-CT	20	87.5 (34.9–96.8)	66.7 (34.9–90.1)	88.9 (44.4–97.5)	63.6 (26.2–87.8)	75.0 (45.7–88.1)	0.77 (0.59–0.96)	0.89	0.55	n.a.	n.a.
PET/CT SUV_{max} > blood pool	34	100 (75.3–100)	33.3 (14.6–57.0)	100 (59.0–100)	48.1 (28.7–68.1)	58.8 (40.7–75.4)	0.67 (0.56–0.77)	n.a.	n.a.	n.a.	n.a.
Prior to any treatment	16	100 (39.8–100)	33.3 (9.9–65.1)	100 (39.8–100)	33.3 (9.9–65.1)	50.0 (24.7–75.4)	0.67 (0.53–0.81)	n.a.	n.a.	n.a.	n.a.
PET/CT SUV_{max} > liver	34	100 (75.3–100)	57.1 (34.0–78.2)	100 (73.5–100)	59.1 (36.4–79.3)	73.5 (55.6–87.1)	0.79 (0.68–0.89)	n.a.	n.a.	n.a.	n.a.
Prior to any treatment	16	100 (39.8–100)	50.0 (21.1–78.9)	100 (54.1–100)	40.0 (12.2–73.8)	62.5 (35.4–84.8)	0.75 (0.60–0.90)	n.a.	n.a.	n.a.	n.a.
CE-CT reader 1 overall	20	62.5 (24.5–91.5)	75.0 (42.8–94.5)	75.0 (42.8–94.5)	62.5 (24.5–91.5)	70.0 (45.7–88.1)	0.69 (0.47–0.91)	0.89	0.72	0.53	0.41
Prior to any treatment	10	100 (15.8–100)	62.5 (24.5–91.5)	100 (47.8–100)	40.0 (5.3–85.3)	70.0 (34.8–93.3)	0.81 (0.63–0.99)	1.0	0.74	0.60	0.36
CE-CT reader 2 overall	20	87.5 (47.3–99.7)	50.0 (21.1–78.9)	85.7 (42.1–99.6)	53.8 (25.1–80.8)	65.0 (40.8–84.6)	0.69 (0.50–0.88)	0.79	0.57	n.a.	n.a.
Prior to any treatment	10	100 (15.8–100)	37.5 (8.5–75.5)	100 (29.2–100)	28.6 (3.7–71.0)	50.0 (18.7–81.3)	0.69 (0.51–0.87)	0.78	0.38	n.a.	n.a.

CI = confidence interval; ROC-AUC = receiver operating characteristic area under the curve; intra-rater = intra-rater variability; inter-rater = inter-rater variability; y/n = presence or absence of an infected aneurysm; score = 4 point score for PET/CT and CE-CT for the evaluation of the presence or absence of an infected aneurysm; SUV_{max} = maximum standardised uptake value; NPV = negative predictive value; PPV = positive predictive value; n.a. = not applicable.

previously suggested imaging criteria[6] (i.e. para-aortic soft tissue mass, stranding, and/or fluid formations), detection rates for both CE-CT readers did not differ.

DISCUSSION

This is possibly the first study comparing the diagnostic accuracy of PET/CT and CE-CT in patients with suspected infected aortic aneurysm. The study results show (i) the diagnostic accuracy of PET/CT in the detection of infected aortic aneurysms is high, and higher than CE-CT; (ii) PET/CT adds more relevant additional information than CE-CT in patients without infected aortic aneurysm; (iii) the specificity of both imaging modalities is hampered by false positive findings in inflammatory aneurysms and arteritis.

CE-CT is currently the most commonly used imaging modality to assess aortic infections.[12] In 2004, Macedo *et al.*[6] described para-aortic soft tissue mass, stranding, and/or fluid formations in only 48% of their patients with proven infected aneurysms. At least one of these imaging criteria was found in all of the patients with proven infected aortic aneurysm, but also in the majority of patients without infected aortic aneurysm but other aneurysms (reader dependent between 83 and 100%). The reason for the difference in sensitivity remains unclear. The VASGRA cohort might have introduced a bias towards increased awareness of vascular infections at the institution. Alternatively, the increased sensitivity may be attributed to improvements in CT technology since 2004 with better spatial resolution, possibly resulting in a higher detection rate of morphological imaging criteria. The latter may also account for the fact that the inter-reader variability was rather high in the present study as the known morphological criteria are rather non-specific. Hence, in the study population CE-CT was very sensitive, but not very specific in the detection of infected aortic aneurysms. The overall accuracy of CE-CT, calculated for two experienced readers, was lower than the accuracy of PET/CT.

All infected aortic aneurysms were metabolically active on PET/CT in the present study, quantified with a median SUV_{max} of 6.6, which is in line with a previous report on five

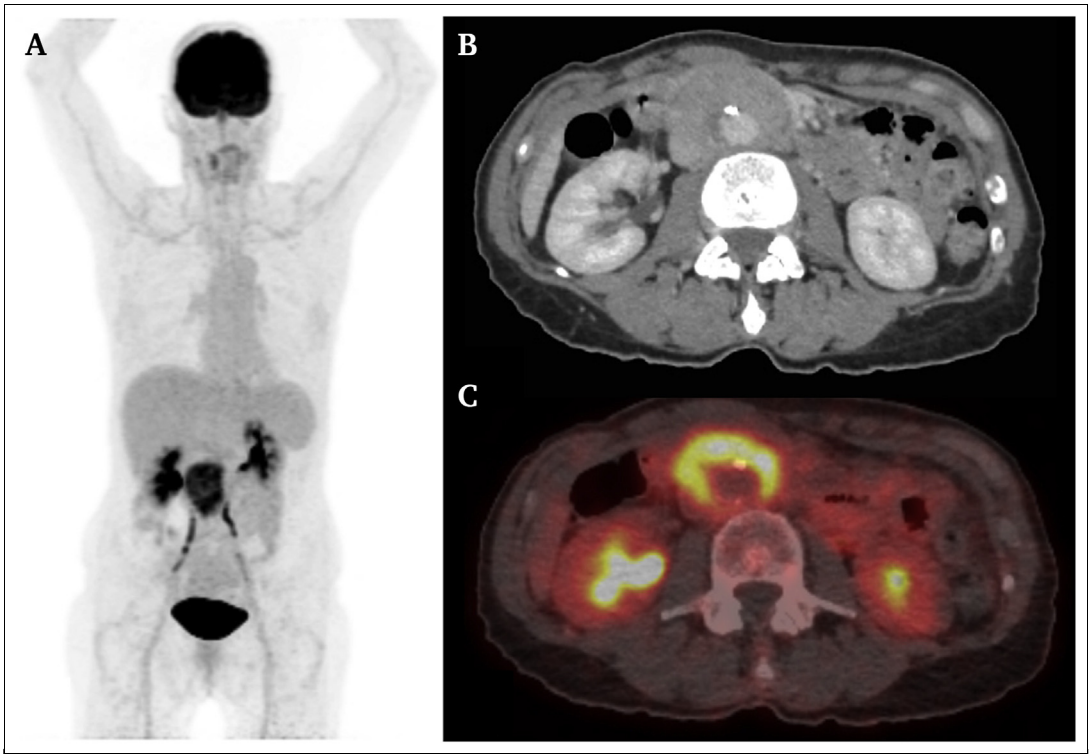

Figure 3. A 65 year old female patient presented with general weakness and abdominal pain. Maximum intensity reconstructions of positron emission tomography (PET) (A) and fused PET/computed tomography (CT) images (C) showed strongly increased ^{18}F-fluorodeoxyglucose (FDG) uptake in the wall of an abdominal aortic aneurysm. Contrast enhanced CT (B) showed profound thickening of the wall of the aneurysm as well as contrast enhancement in the vessel wall. Both readers of PET/CT and contrast enhanced CT rated the examination false positive for an infected aortic aneurysm. However, the final diagnosis was an inflammatory aneurysm caused by Ormond's disease.

patients with infected aneurysms[13] (mean SUV_{max} 6.5), as well as with the findings of Macedo *et al.*, describing increased metabolic activity in six of seven infected aneurysms.[6] The greater diagnostic accuracy of PET/CT in the detection of infected aortic aneurysms as compared with CE-CT may be compared with previous publications on vascular graft infections, in which PET/CT also outperformed CE-CT in the detection a vascular infection.[14–21] In infected aortic aneurysms, a very high sensitivity of PET/CT was also observed; however, the specificity was hampered, as false positive findings occurred for example in inflammatory aneurysms and in arteritis. Notably, all inflammatory aneurysms were also read as false positive in CE-CT. As CT has been described to be highly sensitive and accurate in the detection of inflammatory aneurysms in a retrospective study,[22] it is suspected that the differentiation between infected and inflammatory aneurysms is also non-specific in CE-CT.

In vascular graft infections, previous publications suggested the use of SUV_{max} cut offs for the evaluation of PET/CT,[15,18,19] while others suggested refraining from such cut offs.[17] In the present study, a reasonable diagnostic accuracy of 74% was found when using liver background activity as a cut off value for the detection of infected aortic aneurysms. This method may yield high sensitivity for the detection of infected aortic aneurysms (100% in this study); however, one should be aware of the high likelihood of possible false positive findings (specificity of 57%) when using such a SUV_{max} cut off in PET/CT and infected aortic aneurysms.

Finally, the study demonstrates that PET/CT adds more relevant additional information than CE-CT in patients without infected aortic aneurysm. The latter is in line with a previous publication on vascular graft infections,[17] demonstrating a higher rate of conclusive clinical diagnosis (in a sub-population without graft infection) for PET/CT compared with CE-CT.

Study limitations

Patients were excluded (20%) if PET/CT examinations were performed after vascular intervention (e.g. graft placement), in order to avoid potential bias caused by post-interventional inflammatory changes, foreign body reactions, or secondary graft infections. Still, the present study population remains heterogeneous. Owing to the low incidence of infected aortic aneurysms, it was decided to include patients prospectively and retrospectively, and had

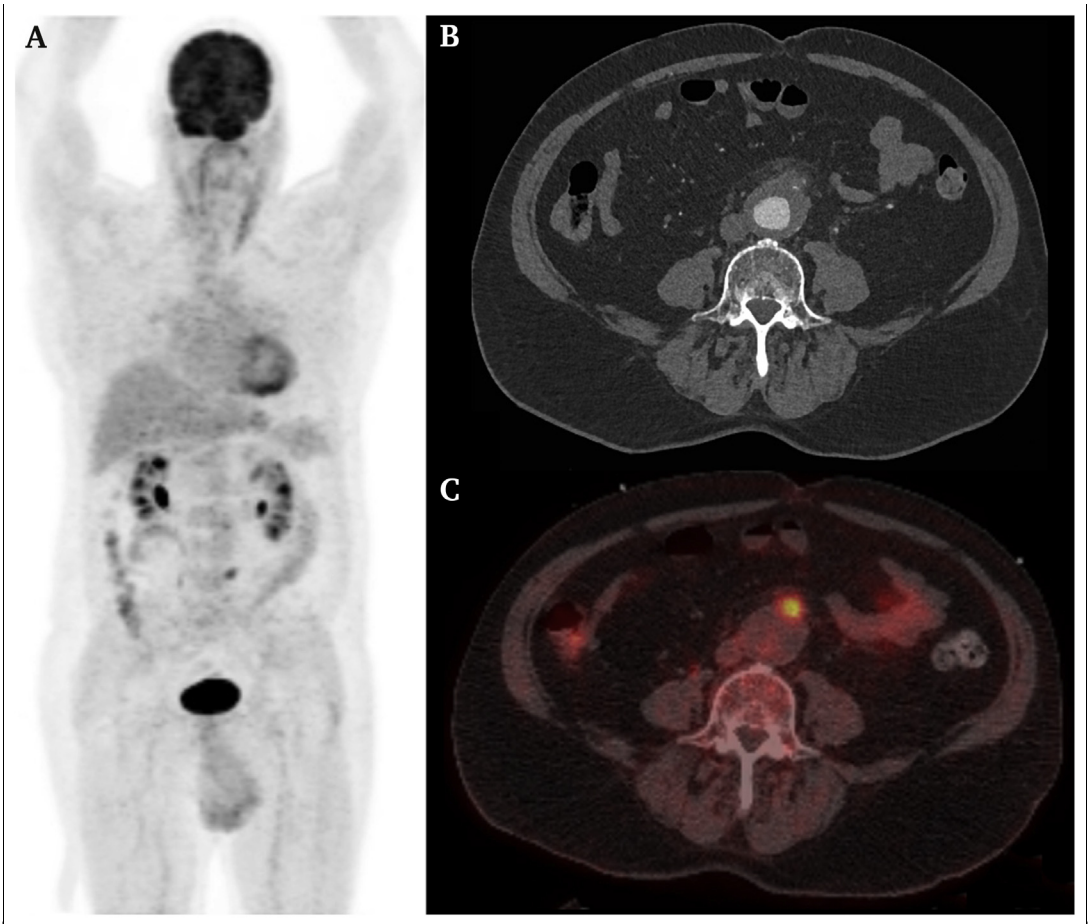

Figure 4. A 71 year old male patient presented with abdominal pain. Maximum intensity reconstructions of positron emission tomography (PET) (A) and fused PET/computed tomography (CT) images (C) showed focally increased FDG uptake in the wall of an abdominal aortic aneurysm. Contrast enhanced CT (B) showed perivascular fat stranding, fluid collection, and contrast enhancement. Both readers of PET/CT and contrast enhanced CT rated the examination false positive for an infected aneurysm. However, the final diagnosis was symptomatic non-ruptured abdominal aortic aneurysm in a haemodynamically unstable patient (previously called "pre-rupture").

to accept the drawback that five different types of PET/CT scanners were used over the study period of 13 years. Furthermore, patients were included before and after the initiation of antimicrobial treatment. This was accepted, as a previous publication stated that antimicrobial treatment does not impair the diagnostic accuracy of PET/CT in the evaluation of known or suspected infectious processes.[23]

CE-CT was not performed in all patients (as it was either not feasible because of renal insufficiency ($n = 7$, 19%), it had already been performed at another institution ($n = 1$, 3%), or because of the partly retrospective study design ($n = 6$, 18%)). This drawback was acknowledged by calculating diagnostic accuracies for the respective subpopulations. However, the presented differences in the detection rate of incidental findings between PET/CT and CE-CT are subtle and should be confirmed in further studies.

CONCLUSION

The diagnostic accuracy of PET/CT in the detection of infected aortic aneurysms is high, and higher than the accuracy of CE-CT. While PET/CT demonstrates an excellent sensitivity, its specificity is hampered owing to false positive findings in inflammatory aneurysms and in arteritis.

CONFLICT OF INTEREST

None

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