The value of ^{18}F-FDG-PET/CT in diagnosis and during follow-up in 273 patients with chronic Q fever

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ABSTRACT

In 1-5% of all acute Q fever infections, chronic Q fever develops, mostly manifesting as endocarditis, infected aneurysms, or infected vascular prostheses. In this study, we investigated the diagnostic value of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) in chronic Q fever at diagnosis and during follow-up.

Methods: All Dutch adult patients suspected of chronic Q fever who were diagnosed since 2007 were retrospectively included until March 2015 when at least one ^{18}F-FDG-PET/CT was performed. Clinical data and results from ^{18}F-FDG-PET/CT at diagnosis and during follow-up were collected. ^{18}F-FDG-PET/CT scans were prospectively reevaluated by three nuclear medicine physicians using a structured scoring system.

Results: In total, 273 patients with possible, probable, and proven chronic Q fever were included. Of all ^{18}F-FDG-PET/CT scans performed at diagnosis, 13.5% led to a change in diagnosis. Q fever-related mortality rate in patients with and without vascular infection based on ^{18}F-FDG-PET/CT was 23.8% and 2.1%, respectively (p= 0.001). When adding ^{18}F-FDG-PET/CT as a major criterion to the modified Duke criteria, 17 patients (1.9-fold increase) had definite endocarditis. At diagnosis, 19.6% of ^{18}F-FDG-PET/CT led to treatment modification. During follow-up, 57.3% of ^{18}F-FDG-PET/CT resulted in treatment modification.

Conclusions: ^{18}F-FDG-PET/CT is a valuable diagnostic technique in diagnosis of chronic Q fever and during follow-up often leading to a change in diagnosis and/or treatment modification, also providing important prognostic information on patient survival.

Key-words

Q-fever; ^{18}F-FDG-PET/CT; vascular infection; endocarditis

INTRODUCTION

Q fever is a zoonosis with a worldwide distribution caused by the intracellular bacterium *Coxiella burnetii*. In the Netherlands, a large Q fever outbreak occurred between 2007 and 2010 with over 4,000 notified cases of acute Q fever and more than 40,000 infected patients (*1*). In 1-5% of infections with *C. burnetii*, chronic Q fever infection develops (*2,3*). In most patients, manifestations of chronic Q fever are endocarditis, infected aneurysms, or infected vascular prostheses. Even if adequate treatment is started, chronic Q fever causes high morbidity and mortality. Many patients with chronic Q fever present when severe complications develop, such as a ruptured aneurysm, with an associated high mortality (*4*). Therefore, it is important to diagnose chronic Q fever in an early stage and start adequate treatment as soon as possible. However, diagnosing chronic Q fever is often difficult.

^{18}F-FDG-PET/CT is very effective in localizing metastatic infection in case of bacteremia (*5,6*). In endocarditis, diagnosis is made using the modified Duke criteria with evidence of endocardial involvement on echocardiography as one of the major criteria (*7*). The value of ^{18}F-FDG-PET/CT for diagnosing native valve endocarditis has been investigated, but sensitivity is not optimal (*8,9*). For prosthetic valve endocarditis, ^{18}F-FDG-PET/CT has shown promising results and recently ^{18}F-FDG-PET/CT was added to the European Society of Cardiology criteria as a major criterion for diagnosing prosthetic valve endocarditis (*10*). In diagnosing vascular infection, ^{18}F-FDG-PET/CT has proven its effectiveness (*11,12*), also in chronic Q fever vascular infection (*13,14*).

In this study, we investigated the diagnostic value of ^{18}F-FDG-PET/CT in patients with chronic Q fever at the time of diagnosis and during follow-up, and also the effect on treatment modification. We also studied whether addition of ^{18}F-FDG-PET/CT to the modified Duke criteria can improve diagnosis of chronic Q fever endocarditis.

MATERIALS AND METHODS

Patients and study design

All Dutch patients ≥18 years with possible, probable, or proven chronic Q fever according to the Dutch consensus guideline (Table 1) (*15*) were included when one or more ^{18}F-FDG-PET/CT-scans were performed. All Dutch hospitals treating chronic Q fever patients were actively approached to include all chronic Q fever patients who were detected since the start of the Dutch Q fever epidemic in 2007. Patients were included in this study until March 2015. Data on patient characteristics, signs and symptoms, microbiological results, ^{18}F-FDG-PET/CT results and their consequences, echocardiography, type and duration of antibiotic therapy, and outcome were collected from patient records. The institutional review board approved this retrospective study and the requirement to obtain informed consent was waived.

Diagnostic work-up

Patients included in this study underwent ^{18}F-FDG-PET/CT in the hospital where they were evaluated and/or treated for their chronic Q fever. For this study, Siemens Biograph (16, 20, mCT40) and Philips Gemini (GXL16, TF16, TF64) PET/CT-scanners were used. Before ^{18}F-FDG injection, all patients fasted and any glucose- or insulin-containing infusions were discontinued for at least 6 hours. In 22.5% of patients, a low carbohydrate fat allowed diet was followed 24 hours before ^{18}F-FDG-PET/CT. One hour after injection of ^{18}F-FDG, a low dose CT scan of the area between proximal femora and skull base was acquired for anatomical correlation and attenuation correction of the PET data. To avoid interpretation bias, the retrospectively acquired ^{18}F-FDG-PET/CT images were prospectively reevaluated by 3 nuclear medicine physicians (CH, LFdG, WJGO) without knowledge of prior clinical evaluation and blinded for any clinical information or patient history. For evaluation, specific criteria for assessment of vascular infection and endocarditis were used (Table 2). ^{18}F-FDG-PET/CT assessed by this structured scoring system was compared to the final clinical diagnoses, which were based on medical history, physical examination, laboratory and microbiological results, and imaging.

Microbiological analysis for the diagnosis of chronic Q fever consisted of serology and polymerase chain reaction (PCR) for *C. burnetii* DNA on plasma, serum, and tissue. An indirect fluorescent-antibody assay (IFA; Focus Diagnostics, Inc., Cypress, CA, USA) was used for serologic analysis in all patients. The modified Duke criteria were used for diagnosing infective endocarditis (*7*). Whether sensitivity of these criteria could be improved by adding the result of the ^{18}F-FDG-PET/CT was studied in an attempt to improve the diagnostic

criteria for chronic Q fever endocarditis. The impact of ^{18}F-FDG-PET/CT on treatment modification was determined by two study co-authors (IJEK and CBR) for all cases based on all available clinical information as registered in the patient records and classified as follows: 1) initiation of antibiotic treatment, 2) discontinuation of antibiotic treatment, 3) changing type of antibiotic treatment, 4) continuation of antibiotic treatment, and 5) surgical intervention. If the result of ^{18}F-FDG-PET/CT did not result in any modification, this was also reported.

Statistical methods

All data were analyzed using SPSS version 20 (SPSS, Inc., Chicago, IL). Two-tailed chi-square test or Wilcoxon tests were used to compare qualitative data. Mean values were analyzed by Student's t-tests.

RESULTS

In total, 379 patients had a diagnosis of proven, probable, or possible chronic Q fever according to the Dutch consensus guideline (*15*). In 273 patients, ^{18}F-FDG-PET/CT was performed and in 230 of these patients, ^{18}F-FDG-PET/CT scans were performed at diagnosis of chronic Q fever. During follow-up, 218 ^{18}F-FDG-PET/CT scans were performed in 143 patients. Reasons for follow-up ^{18}F-FDG-PET/CT were suspected new complications (175, 80.3%) or end of treatment evaluation (43, 19.7%). Suspected new complications in chronic Q fever patients, such as new abscesses or spondylodiscitis or progression of the primary infection during treatment, were suspected in case of new positive serum PCR, no change in antibody titer after one year of treatment, or increasing titers, and/or new or increasing complaints. In 43 patients, only follow-up ^{18}F-FDG-PET/CT scans were performed without a baseline ^{18}F-FDG-PET/CT at diagnosis. In these patients, diagnosis of chronic Q fever was based on a combination of serology, PCR, and/or CT imaging. Of all 273 patients, 147 patients were eventually diagnosed with proven chronic Q fever, 60 patients with probable chronic Q fever, and 66 patients with possible chronic Q fever. Of all patients, 199 (72.9%) were male and the mean age at diagnosis was 65.0 years. A known history of acute Q fever was identified in 105 patients (38.5%). Risk factors and outcome for all patients are shown in Table 3. Overall, in 93 patients (63.3%) with proven chronic Q fever, infectious foci were seen on ^{18}F-FDG-PET/CT. Of all 448 ^{18}F-FDG-PET/CT scans performed in this study, 438 scans could be reevaluated as 10 scans were not available for reevaluation.

Vascular infection

Of all 142 ^{18}F-FDG-PET/CT scans performed at diagnosis of chronic Q fever with grade 1 and grade 2 vascular patterns (Table 2), 3 patients (2.1%) had a clinical diagnosis of vascular infection. Of these patients, reevaluated follow-up ^{18}F-FDG-PET/CT confirmed this diagnosis of vascular infection in 2 patients and in one patient follow-up ^{18}F-FDG-PET/CT was missing but diagnosis was confirmed by positive PCR on tissue of the aneurysm. Results of all reevaluated ^{18}F-FDG-PET/CT scans performed at diagnosis of chronic Q fever for vascular infection (Fig. 1.) and Q-fever related mortality are shown in Table 4. Of 29 scans with homogeneous FDG uptake pattern, 16 scans (55.2%) were considered as inflammation without infection and 13 scans (44.8%) as vascular infection due to peri-graft soft tissue involvement of which 9 cases had positive PCR on vascular tissue. Q fever-related mortality rates in patients with and without vascular infection based on this scoring system were 23.8% and 2.1%, respectively (p= 0.001).

Endocarditis

Of all chronic Q fever patients, 9 patients (3.3%) had definite endocarditis according to the modified Duke criteria and 59 patients (21.6%) had possible endocarditis. In 36 of all patients, no echocardiography was performed. By reevaluating ^{18}F-FDG-PET/CT, the heart showed diffuse ^{18}F-FDG-uptake (grade 2) on 300 ^{18}F-FDG-PET/CT-scans in 193 patients making a reliable assessment of the heart impossible. In 92.3% of these scans, no prior low carbohydrate fat allowed diet was followed. Of all 80 patients in whom ^{18}F-FDG-PET/CT were assessable for the heart region, 10 ^{18}F-FDG-PET/CT scans (12.5%) showed focal ^{18}F-FDG-uptake indicating endocarditis (grade 3) (Fig. 2). Of these 10 patients, 2 (20.0%) had a diagnosis of definite endocarditis according to the modified Duke criteria. Of all 70 patients without relevant ^{18}F-FDG-uptake of the heart valve (grade 1), 2 patients (2.9%) had definite endocarditis according to the modified Duke criteria. Of all 237 patients who underwent echocardiography, 9 had valve vegetations on echocardiography. Of these 9 patients, evaluation of ^{18}F-FDG-PET/CT showed grade 1 ^{18}F-FDG-uptake in 2 patients, grade 2 in 4 patients, and grade 3 in 3 patients.

When adding ^{18}F-FDG-PET/CT as a major criterion to the Duke criteria, 17 patients (7.2%) had a definite endocarditis. In Table 5, the modified Duke criteria were compared with the Duke criteria including ^{18}F-FDG-PET/CT as a major criterion by a two-tailed Wilcoxon test, which showed a significant difference in the number of patients with proven endocarditis (p = 0.008). Of the 8 patients who had the diagnosis definite endocarditis based on the ^{18}F-FDG-PET/CT result, 5 patients had a positive PCR on blood, 2 had a valve prosthesis, and 6 had no other infectious foci. Of these 8 patients, 2 patients were originally diagnosed with possible endocarditis and 6 patients with rejected endocarditis according to the modified Duke criteria.

^{18}F-FDG-PET/CT and treatment modification

At diagnosis, after a negative PCR result on blood and/or tissue was obtained, ^{18}F-FDG-PET/CT contributed to a change in diagnosis in 31 patients (13.5%). In all these patients, the diagnosis probable chronic Q fever changed to proven chronic Q fever. At diagnosis, ^{18}F-FDG-PET/CT contributed to treatment modification in 45 patients (19.6%). In 37 patients (16.1%), ^{18}F-FDG-PET/CT led to a start of antibiotic treatment and in 2 patients (0.9%) antibiotic treatment was changed. In 6 patients (2.6%) the ^{18}F-FDG-PET/CT result led to surgical intervention.

At follow-up, ^{18}F-FDG-PET/CT performed to make a decision on stopping antibiotic treatment was

negative in 31 cases (72.1%) and showed suspicion of ongoing infectious foci in 12 cases (27.9%). Of the 175 follow-up ^{18}F-FDG-PET/CT scans performed because of suspected new complications, 84 scans (48.0%) were negative. Of all follow-up ^{18}F-FDG-PET/CT scans, 125 scans (57.3%) led to treatment modification, 21 scans (9.6%) led to discontinuation of antibiotic treatment, 7 scans (3.2%) led to a change in antibiotic treatment, and in 97 scans (44.5%) the result of ^{18}F-FDG-PET/CT contributed to the decision to continue antibiotic treatment (Fig. 3). In 6 patients (3.4%), ^{18}F-FDG-PET/CT led also to surgical intervention.

DISCUSSION

In this study, we investigated the value of ^{18}F-FDG-PET/CT in diagnosis and during follow-up in patients with chronic Q fever. Specific guidelines when to perform ^{18}F-FDG-PET/CT are lacking. Because of the largest Q fever outbreak ever reported in the Netherlands between 2007 and 2010, it was possible to analyze the value of ^{18}F-FDG-PET/CT in a large cohort of 273 patients with chronic Q fever.

The results of our study show that ^{18}F-FDG-PET/CT is a valuable diagnostic technique, with a contribution to the diagnosis of chronic Q fever in 13.5% of patients after serology and PCR has already been performed. In follow-up of chronic Q fever, ^{18}F-FDG-PET/CT performed for decision making in stopping antibiotic treatment showed persisting focal infection in 27.9%, although patients had low serological titers and were asymptomatic. This emphasizes the important value of ^{18}F-FDG-PET/CT in follow-up of chronic Q fever. ^{18}F-FDG-PET/CT is also valuable for decision making in treatment of chronic Q fever patients with 19.6% of treatment modification at diagnosis and in 57.3% during follow-up of chronic Q fever. Moreover, ^{18}F-FDG-PET/CT provided important prognostic information on patient survival.

Several case reports indicated that ^{18}F-FDG-PET/CT could be valuable in diagnosing chronic Q fever (*16-18*). One study on a screening program in patients with chronic Q fever reported that ^{18}F-FDG-PET/CT showed vascular infection in 5 out of 10 patients (*19*). In a retrospective study in 52 patients with chronic Q fever, ^{18}F-FDG-PET/CT was performed in 13 out of 18 patients with proven chronic Q fever and was helpful in 77% showing 7 infected vascular prostheses and 3 infected aneurysms (*13*). Recently, a Dutch study reported that ^{18}F-FDG-PET/CT showed a vascular infection in 6 out of 13 patients with proven chronic Q fever based on positive PCR for *C. burnetii* and known aneurysm or vascular prosthesis (*14*).

Very recently, Eldin et al. (*20*) reported on a case series of 99 patients with abnormalities seen on ^{18}F-FDG-PET/CT performed after diagnosis of both acute and chronic Q fever. ^{18}F-FDG-PET/CT contributed to a change in diagnosis in 62.6% of patients. Limitations of the study of Eldin et al. are the fact that only ^{18}F-FDG-PET/CT-scans showing signs of infection were included and that no central reevaluation of ^{18}F-FDG-PET/CT scans was performed. Also, because both acute and chronic Q fever patients were included in the study of Eldin et al., a comparison with our study is difficult. Furthermore, the 62.6% of change in diagnosis was only based on a new abnormality seen on ^{18}F-FDG-PET/CT, but it is not clear whether these abnormalities were Q fever foci because the exact clinical context of the patients was not mentioned.

In vascular chronic Q fever infection, a structured protocol for assessment of ^{18}F-FDG-PET/CT is

lacking. Also, non-infected vascular prostheses may show increased ^{18}F-FDG uptake due to postsurgical inflammation (*21*,*22*). In our study, we used a structured grading score for prospectively reevaluation of the ^{18}F-FDG-PET/CT scans, which is a modified adaptation of scoring systems used in other studies on vascular infection (*12*,*22*). The value of this score as shown in Table 2 was endorsed by the fact that patients with grade 1 or 2 had no vascular infection in 97.9% and a significantly lower Q fever-related mortality rate. Our score shows that a homogeneous uptake pattern does not exclude vascular infection, especially in case of involvement of surrounding tissue and also considering the high amount of positive PCR on vascular tissue in this group. It is important that interpretation of ^{18}F-FDG-PET/CT is done multidisciplinary based on the individual clinical context.

In prosthetic valve endocarditis (not caused by Q fever), the diagnostic value of ^{18}F-FDG-PET/CT has been investigated and has shown promising results (*23*). Recently, ^{18}F-FDG-PET/CT was added to the European Society of Cardiology modified diagnostic criteria as a major criterion for prosthetic valve endocarditis (*10*). Sensitivity of ^{18}F-FDG-PET/CT in diagnosing native valve endocarditis is not optimal (*8*,*9*). In chronic Q fever endocarditis, vegetations are small and often not seen on echocardiography (*24*). As endocardial involvement seen on echocardiography is a major criterion of the modified Duke criteria, many patients with chronic Q fever endocarditis are missed using these criteria. Therefore, a high anti-phase I IgG titer was added earlier to the modified Duke criteria as a major criterion (*24*). Our study shows that adding increased ^{18}F-FDG valve uptake as a major criterion to the modified Duke criteria, led to a 1.9 fold increase in diagnoses of proven endocarditis. Thus, adding ^{18}F-FDG-PET/CT to the modified Duke criteria for diagnosing chronic Q fever endocarditis could be a valuable improvement since missed diagnoses have always been expected in this disease.

Potential limitations of our study are the fact that only chronic Q fever patients who underwent ^{18}F-FDG-PET/CT were included. This could lead to selection bias, as patients with i.e. early death were not included in this study. Also, the lack of additional clinical context in reevaluation of ^{18}F-FDG-PET/CT could have led to less sensitive reading.

CONCLUSION

^{18}F-FDG-PET/CT is a valuable imaging technique in chronic Q fever and should be performed at diagnosis and should be considered during follow-up when new complications are suspected or before end of treatment when the first ^{18}F-FDG-PET/CT scan was abnormal. Scans should be interpreted using a structured protocol. Addition of the ^{18}F-FDG-PET/CT to the modified Duke criteria in patients with chronic Q fever could be valuable.

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FIGURE LEGENDS

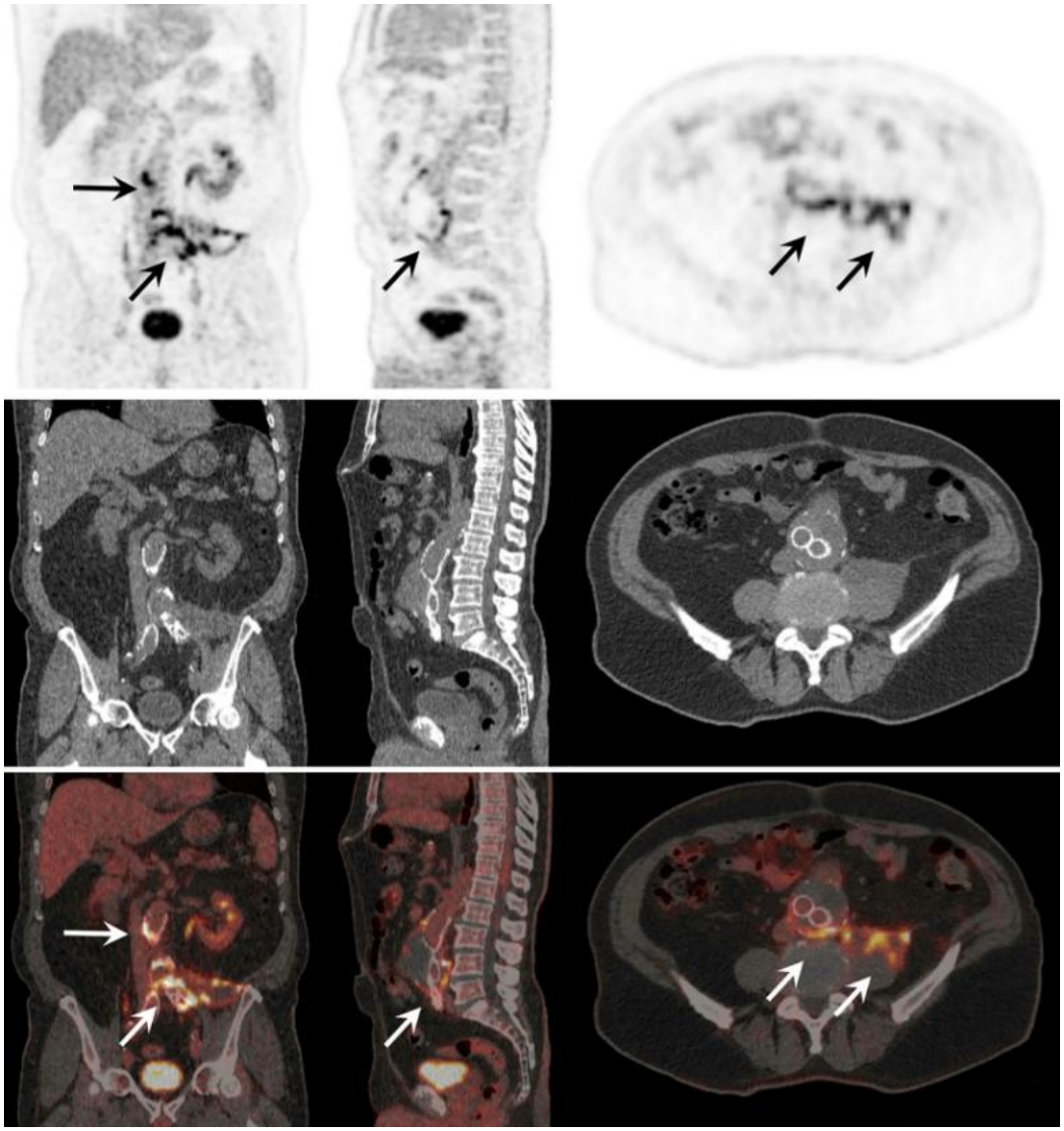

FIGURE 1.

^{18}F-FDG-PET/CT-scan of a 72-year-old man with proven chronic Q fever with an infected endovascular aortic graft and psoas abscess. This patient had vascular surgery six months after initiation of antibiotic therapy with doxycyclin and hydroxychloroquin because of the severity of infection. Four years later, this patients is still on antibiotic treatment because of persisting chronic Q fever infection.

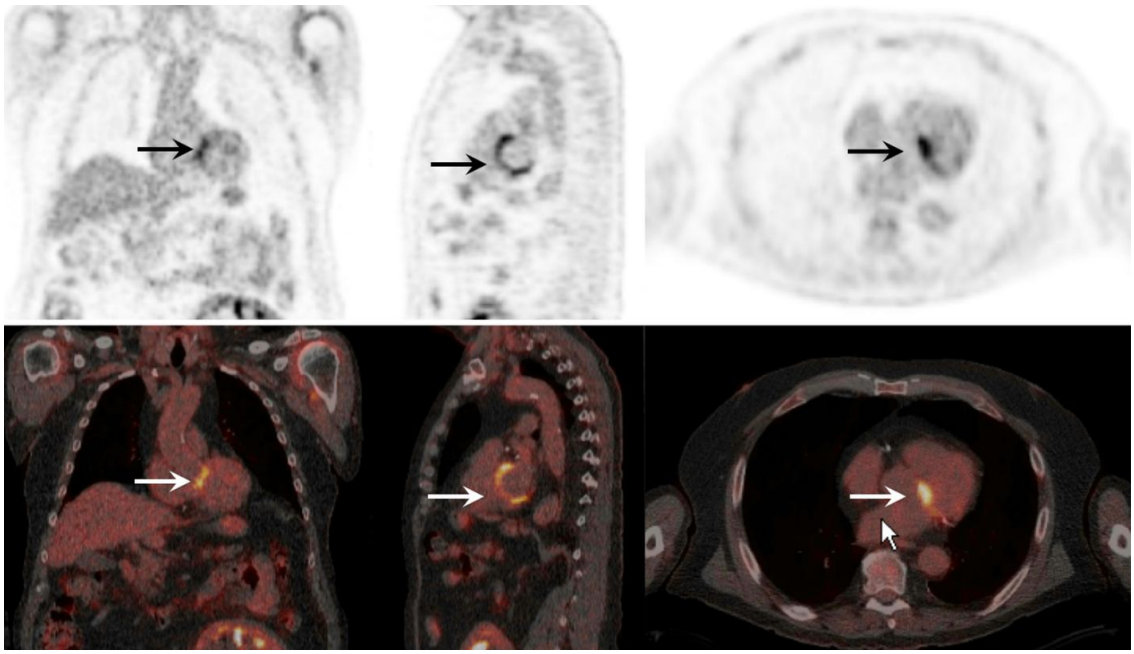

FIGURE 2.

^{18}F-FDG-PET/CT-scan of a 67-year-old man with a history of acute Q fever and analysis because of severe fatigue. Serology for *C. burnetii* showed increased antiphase 1 IgG, PCR on blood was negative. Transesophageal echocardiography was negative for endocarditis, but ^{18}F-FDG-PET/CT showed highly increased ^{18}F-FDG uptake of his native mitral valve. This patient was treated for almost 2 years with antibiotic therapy because of chronic Q fever endocarditis.

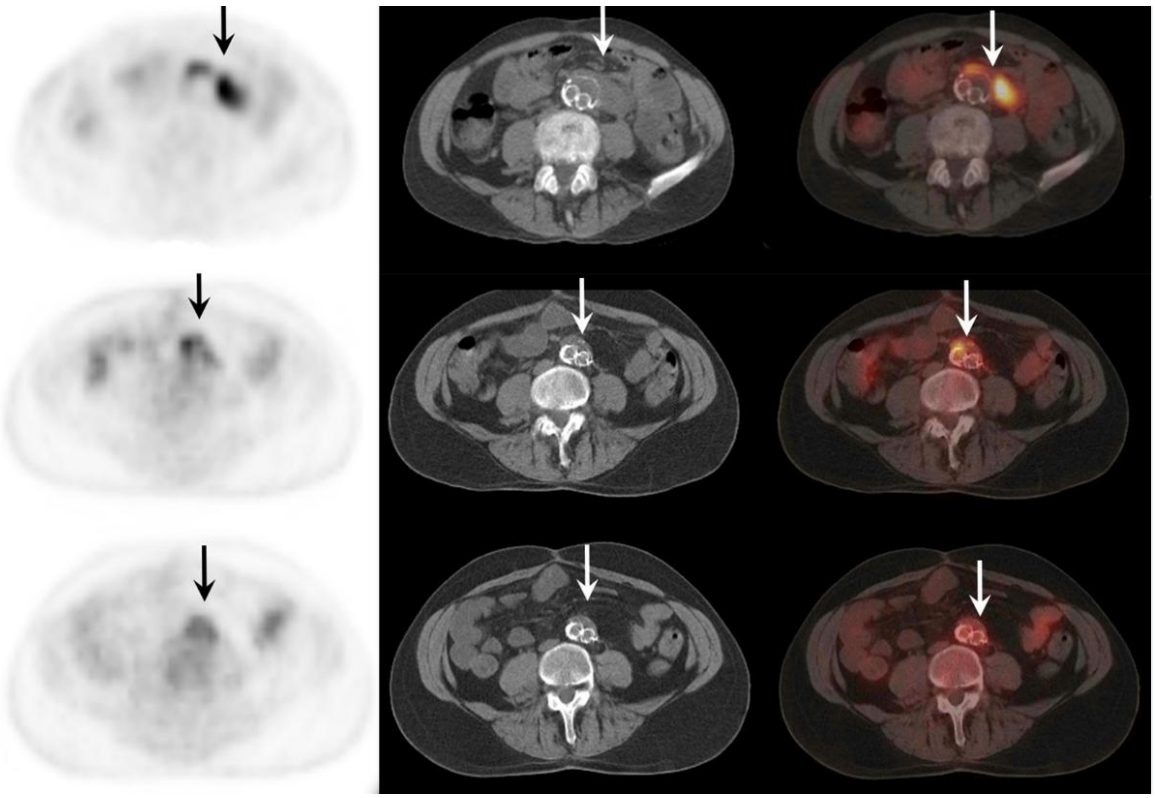

FIGURE 3.

^{18}F-FDG-PET/CT-scan of a 64-year-old man with proven chronic Q fever with an infected aneurysm and infected vascular graft in the aorta. The upper ^{18}F-FDG-PET/CT-scan shows the vascular infection before initiation of antibiotic treatment with doxycyclin and hydroxychloroquin. The middle ^{18}F-FDG-PET/CT-scan shows the same area after one year of treatment. The lower ^{18}F-FDG-PET/CT-scan was performed two years after start of treatment and did no longer show vascular infection and therefore antibiotic treatment was discontinued. Four years later this patients died due to a septic cholangitis. Autopsy did not show any Q fever foci and PCR for *C. burnetii* on several tissues including the aorta was negative.

TABLES

TABLE 1. Dutch consensus guidelines on chronic Q fever diagnosis (*15*)

Diagnosis	Characteristics
Proven chronic Q fever	Positive *Coxiella burnetii* PCR in blood or tissue OR IFA of ≥ 1024 for *C. burnetii* phase I IgG with either definite endocarditis according to the modified Duke criteria or proven large vessel or prosthetic infection by imaging techniques (^{18}F-FDG-PET/CT, MRI, CT, US).
Probable chronic Q fever	IFA of ≥ 1024 for *C. burnetii* phase I IgG AND valvulopathy not meeting the modified Duke criteria OR known aneurysm and/or vascular or cardiac valve prosthesis without signs of infection by imaging techniques (TTE/TEE, ^{18}F-FDG-PET/CT, MRI, CT, US) OR suspected osteomyelitis, hepatitis, or pericarditis as manifestations of chronic Q fever OR pregnancy OR symptoms and signs of chronic infection such as fever, weight loss, night sweats, hepatosplenomegaly, and persistant ESR or CRP OR granulomatous tissue inflammation as proven by histological examination OR immunocompromised state.
Possible chronic Q fever	IFA of ≥ 1024 for *C. burnetii* phase I IgG without manifestations meeting the criteria for proven or probable chronic Q fever.

PCR= polymerase chain reaction. IFA= immunofluorescense assay. IgG= immunoglobulin G. ^{18}F-FDG= ^{18}F-fluorodeoxyglucose. PET/CT= positron emission tomography/computed tomography. MRI: magnetic resonance imaging. CT= computed tomography. US= ultrasound. TTE= transthoracic echocardiography. TEE= transesophageal echocardiography. ESR= erythrocyte sedimentation rate. CRP= C-reactive protein.

TABLE 2. Interpretation of ^{18}F-FDG-PET/CT combining a visual grading score and uptake pattern

Vascular infection	
Grade 1	^{18}F-FDG-uptake similar to background
Grade 2*	Low ^{18}F-FDG-uptake comparable to uptake by inactive muscles and fat, and above background but below liver
Grade 3*	Moderate ^{18}F-FDG-uptake clearly visible and higher than the uptake by inactive muscles and fat, and similar to liver uptake
Grade 4*	Strong ^{18}F-FDG-uptake clearly above liver uptake
Interpretation	
No vascular infection	Grade 1 and 2
Inflammation	Grade 3 and 4 and homogeneous uptake pattern without peri-graft soft tissue involvement
Vascular infection	Grade 3 and 4 and inhomogeneous uptake pattern with or without peri-graft soft tissue involvement

Endocarditis	
Grade 1	No relevant ^{18}F-FDG-uptake of the heart
Grade 2†	Diffuse ^{18}F-FDG-uptake in the heart (reflecting normal uptake in myocardium)
Grade 3	Focal ^{18}F-FDG-uptake in the heart with or without diffuse low-level uptake in the myocardium
Interpretation	
No endocarditis	Grade 1
Evaluation not possible	Grade 2
Endocarditis	Grade 3

* An additional ‘a’ for homogeneous ^{18}F-FDG-uptake and ‘b’ for inhomogeneous ^{18}F-FDG uptake was registered.

† Evaluation of the heart valves for endocarditis was not possible due to diffuse myocardial ^{18}F-FDG-uptake.

TABLE 3. Risk factors and outcome of all patients with proven, probable, and possible chronic Q fever

	Proven chronic Q fever number of patients	Probable chronic Q fever number of patients	Possible chronic Q fever number of patients
Number of patients	147	60	66
Diagnostics			
Positive PCR blood + tissue (%)	25 (17.0)	0	0
Positive PCR blood only (%)	58 (39.5)	0	0
Positive PCR tissue only (%)	27 (18.4)	0	0
Anti-phase I IgG at diagnosis (range)	4096 (256-131071)	4096 (512-65536)	2048 (1024-32768)
Vascular prosthesis (%)	76 (51.7)	17 (28.3)	0
Infected vascular prosthesis (%)	63 (82.9)	0	0
Known aneurysm (%)	44 (29.9)	8 (13.3)	0
Infected aneurysm (%)	34 (77.3)	0	0
Cardiac valve prosthesis (%)	26 (17.7)	10 (16.7)	0
Modified Duke criteria			
- Definite endocarditis (%)	9 (6.1)	0	0
- Possible endocarditis (%)	37 (25.2)	19 (31.7)	3 (4.5)
- Rejected endocarditis* (%)	77 (52.4)	37 (61.7)	55 (83.3)
Other preexisting valvular disease (%)	13 (8.9)	10 (16.7)	1 (1.5)
Pacemaker (%)	5 (3.4)	1 (1.7)	0
Intra-cardiac defibrillator (%)	2 (1.4)	2 (3.3)	0
Other infection			
Other vascular infection (%)	3 (2.0)	0	0
Other metastatic infection † (%)	24 (16.3)	0	0
Mortality			
Q fever related	18 (12.2)	1 (1.7)	0
Overall mortality	33 (22.4)	8 (13.3)	8 (12.1)

* In 36 patients with chronic Q fever no echocardiography was performed.

† Other metastatic foci were pulmonary foci (n = 4), cutaneous foci (n = 2), spinal infection (n = 3), psoas abscesses (n = 11), and both a psoas abscess and spondylodiscitis (n = 4).

PCR= polymerase chain reaction. IgG= immunoglobulin G. PTA= percutaneous transluminal angiography.

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Reevaluation of ^{18}F-FDG-PET/CT at diagnosis n = 221	Q-fever related mortality n = 18 (%)
No infection: grade 1 and 2 n = 142	3 (2.1)
Inflammation: grade 3a and 4a without peri-graft soft tissue involvement n = 16	0
Infection: grade 3b and 4b with or without peri-graft soft tissue involvement n = 63	15 (23.8)

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TABLE 5. Comparison of ^{18}F-FDG-PET/CT to the modified Duke criteria for diagnosing endocarditis

	Modified Duke criteria (%)	Duke criteria including ^{18}F-FDG-PET/CT as major criterion (%)	Significance*
Definite endocarditis	9 (3.8)	17 (7.2)	0.008
Possible endocarditis	59 (24.9)	57 (24.1)	0.063
Rejected endocarditis	169 (71.3)	163 (68.8)	0.008
Total	237†	237†	

* Wilcoxin test, 2-tailed.

† In 36 patients, no echocardiography was performed.