Journal of Nuclear Medicine, published on May 14, 2015 as doi:10.2967/jnumed.115.156265

^{18}F-FDG-PET/CT FOR THERAPY CONTROL IN VASCULAR GRAFT INFECTIONS: A FIRST FEASIBILITY STUDY

Short title: THERAPY CONTROL IN GRAFT INFECTIONS

Lars Husmann[1]*, Bert-Ram Sah[1]*, Alexandra Scherrer[2], Irene A. Burger[1], Paul Stolzmann[1], Rainer Weber[2], Zoran Rancic[3], Dieter Mayer[3], Barbara Hasse[3] and the VASGRA Cohort°

* contributed equally

1 Division of Nuclear Medicine, Department of Medical Radiology, University Hospital of Zurich, Raemistrasse 100, CH-8091 Zurich, Switzerland

2 Division of Infectious Diseases and Hospital Epidemiology, University Hospital and University of Zurich, Raemistrasse 100, CH-8091 Zurich, Switzerland

3 Clinic for Cardiovascular Surgery, University Hospital and University of Zurich, Raemistrasse 100, CH-8091 Zurich, Switzerland

° see acknowledgments

Corresponding Author: Lars Husmann, MD

Division of Nuclear Medicine, Department of Medical Radiology

University Hospital of Zurich

Raemistrasse 100

CH-8091 Zurich

Switzerland

phone: +41 44-255 11 11

#

fax: +41 44 255 44 14

e-mail: lars.husmann@usz.ch

Word Count: 4993 words

Financial Support:

This study was financed within the framework of the Vascular graft Cohort Study (VASGRA) supported by the Swiss National Science Foundation grant # 320030_144277/1 (to BH), the Promedica Foundation # 1080/A (to BH), the Vontobel Foundation (to BH) and the Rozalia Foundation (to BH). BH received a "Filling the Gap" grant from the University of Zurich for protected research time. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

#

ABSTRACT

The aim of this study was to evaluate the clinical value of positron emission tomography/computed tomography with ^{18}F-fluorodeoxyglucose (FDG-PET/CT) for therapy control in patients with prosthetic vascular graft infections (PVGI).

Methods: In this single-centre, observational, prospective cohort study, 25 patients with a median age of 66 years (range: 48-81) were included who had a proven PVGI. Follow-up FDG-PET/CT was performed at a median time interval of 170 days (range: 89-249) after baseline examination. Two independent and blinded readers measured maximum standardized uptake values (SUV max.) to quantify metabolic activity and analysed whole body datasets for secondary diagnosis (i.e., infectious foci not within graft vicinity). The metabolic activity of the graft was correlated with clinical information and two laboratory markers (C-reactive protein (CRP) and white blood cell count (WBC)).

Results: FDG-PET/CT had an impact on management in all patients. In 19 of 25 patients (76%) antibiotic treatment was continued due to the results of follow-up FDG-PET/CT. Antibiotic treatment was stopped or changed in 8% and 16% of patients, respectively. In eight patients (32%) additional incidental findings were detected on follow-up FDG-PET/CT which had further impact on patient management. Only in a subgroup of patients with PVGI and no other sites of infection, a significant correlation between the difference in CRP at the time of baseline and follow-up FDG-PET/CT and the difference in SUV max. was found (n = 11; r = 0.84; *P* = 0.001).

Conclusion: FDG-PET/CT represents a useful tool in therapy monitoring of PVGI and impacts on patient management.

Key Words: PET, FDG, prosthetic vascular graft infections, therapy control

#

INTRODUCTION

Morbidity and mortality in prosthetic vascular graft infections (PVGI) are as high as 20-40% (*1, 2*). Outcome data on different treatment modalities are scarce and partly controversial (*2-4*). Routinely performed treatments of PVGI comprise the combination of surgical interventions together with systemic antibiotic medication, since the latter without surgery is associated with an increased mortality rate (*1*). Until now, there are no valid guidelines regarding neither the diagnosis and management, nor the treatment of PVGI. A reliable monitoring tool for therapy control in PVGI is desirable.

FDG-PET/CT is a well-established imaging modality regarding therapy control in many malignant diseases (*5-9*) and FDG-PET/CT has been suggested to be useful in patients with infectious disease (*10*). Initial reports demonstrated a high diagnostic accuracy of FDG-PET/CT in detecting PVGI (between 73 and 94%) (*11-15*) , with a recent article showing an excellent positive predictive value, especially in patients do not receive antibiotics prior to PET (*16*). The known high negative predictive value of the method might allow for determining the end-point of treatment when a known infectious site becomes metabolically inactive on follow-up FDG-PET/CT scan. Treatment duration of a minimum of 3 to 6 month is suggested for PVGI (*4*) and early prediction of response to therapy may offer the potential to identify patients who will benefit from shorter treatment duration in case of graft infection, and hence would allow for more individualized treatment approaches. Furthermore, FDG-PET/CT may also identify non-responders in need of different therapy approaches. There are only limited data regarding imaging guided-therapy control among patients with chronic infections and none with regard to PVGI (*17*). The aim of this feasibility study was to evaluate the FDG-PET/CT for therapy control in patients with PVGI.

MATERIALS AND METHODS

Study design, Patient population and Data Collection

#

The Vascular Graft Cohort Study (VASGRA) is an open, observational cohort with continued enrolment of patients, aged > 18 years receiving any type of vascular graft at the University Hospital of Zurich, Switzerland. The institutional review board approved this study and all subjects signed a written informed consent. Surgical, demographic, clinical and treatment information is prospectively collected every six months.

We used the criteria proposed by FitzGerald *et al* for the diagnosis of PVGI (*18*), and considered positive bacterial cultures of intraoperative specimens or blood samples, clinical, laboratory or radiological signs of infection like perigraft air, fluid persisting for more than 8 weeks postoperatively or abscess formation. Information on PVGI was ascertained and adjudicated by a team of infectious disease specialist and vascular surgeons. Patients receive empiric and later antimicrobial therapy. Operable patients presenting with an infection involving the vascular graft (Szilagyi grade III (*19*)) are treated according to an “in-house” standardized algorithm in a graft-preserving manner (*20*). Surgical debridement of infected tissue is combined with negative pressure wound therapy (NPWT). Tissue obtained during surgical debridement is processed for histopathological and microbiological examinations. A positive microbiological culture of the deep tissue around the vascular graft, obtained by open biopsy, or a positive microbiological culture of an explanted vascular graft represents our gold standard for diagnosis of graft infection. Patients with proven PVGI, are clinically monitored and, at follow-up visits, C-reactive protein (CRP) and white blood cell count (WBC) are obtained.

Since May 2013, patients undergo combined FDG-PET/CT for diagnosis of PVGI diagnosis prior to surgical reintervention (baseline FDG-PET/CT) and three to six months later while being under antimicrobial therapy (follow-up FDG-PET/CT).

PET/CT Data Acquisition

FDG-PET/CT was successfully performed twice with diagnostic image quality in all 25 patients. As per protocol, FDG-PET/CT was performed not less than 60 days after the last vascular

#

surgical intervention. Baseline-PET scan and follow–PET scan were performed after a median time of 439 days (range, 70-5381) and 171 days (range, 75-5491) after the last vascular operation and/or wound closure, respectively. Imaging protocols were identical for baseline and follow-up FDG-PET/CT in all patients. Patients were fasting for at least four hours and had no insulin injections four hours prior to FDG administration. Body weight, height, and blood glucose level were measured prior to injection of FDG. In non-diabetic patients (n = 21) blood glucose level <8 mmol/l and in diabetic patients (n = 4) blood glucose level <12 mmol/l were accepted for imaging (mean glucose 6.2 mmol/l + 1.2 Standard deviation (SD) at baseline; mean glucose 6.3 mmol/l +1.7 (SD) at follow-up). After intravenous injection of body weight-adapted FDG (mean MBq 337 + 58 (SD) at baseline, mean MBq 336 + 56 (SD), at follow-up), patients were resting for a standardized uptake time of 60 minutes. All scans were performed on an integrated PET/CT system (DiscoveryTM VCT; GE Healthcare).

Data were acquired with the patient in supine position with arms overhead. Low-dose CT for attenuation correction was acquired from the mid-thigh to the vertex of the skull with the following scan parameters: tube voltage, 140 kVp; tube current time product, 10-80 mAs/slice; pitch of 1.4; collimation, 64 x 0.625 mm; rotation time, 0.5 ms; and field of view (FOV), 50 cm. Directly after CT data acquisition, PET data was acquired using the 3D mode with a fixed scan duration of 2 minutes per bed position and a FOV of 157 mm. Emission data were corrected for randoms, dead time, scatter, and attenuation. CT data for attenuation correction and anatomical referencing were reconstructed with a slice thickness of 3.75 mm and an increment of 3.0 mm using a filtered back reconstruction algorithm. Attenuation-corrected axial PET images were reconstructed using a standard iterative ordered subset expectation maximization (OSEM) 3D algorithm (matrix size, 256 x 256, Fourier rebinning, 3D OSEM with 8 iterations, 16 subsets).

Image Analysis

#

All FDG-PET/CT images were independently analyzed by two experienced nuclear medicine physicians (LH and BS) on a Advantage Windows Workstation Version 4.4 (AW, GE Healthcare Biosciences). Whole body datasets were analyzed for secondary diagnosis, i.e., infectious foci not in the vicinity of a graft or other relevant or potentially malignant findings. For quantitative measurements of the metabolic activity of the tracer in all grafts at baseline and follow-up FDG-PET/CT we calculated maximum standardized uptake values (SUV max.) using built-in software by placing a volume of interest (VOI) in the wall of the graft at the site of highest uptake. The SUV max. measurements followed the EANM and SNMMI guidelines for use of FDG-PET/CT in inflammation and infection (*21*). Correct VOI placement in the area of highest focal FDG-activity was confirmed on fused FDG-PET/CT images in axial, coronal, and sagittal reformats to avoid partial volume effects or signal spill over from neighbouring organs, such as the kidney. In case of not identical measurements (n = 2) additional measurements were performed by both readers in consensus. As FDG uptake pattern are important for the diagnosis of PVGI (*16, 22*), we used a previously published 5-point visual grading score (*16*) to better describe the PVGI in all patients (Table 1). In follow-up PET/CT scans non-response was defined as equal or increasing SUV max. in the PVGI, partial response as a decrease of SUV max. of more than 20%, and complete response was defined as a complete vanishing of the focal uptake pattern and a decrease of SUV max. below mediastinal blood pool activity. Finally, “Additional metabolically active focus/-i” was defined as any other site of infection or inflammation at baseline and/or follow-up FDG-PET/CT as they may impair clinical presentation or laboratory testing of patients with PVGI.

Statistical Analyses

We used the Wilcoxon matched-pairs signed-rank test to compare baseline and follow-up values. A *P*-value of < 0.05 was considered statistically significant. Linear regressions were performed to compare 1) the difference and 2) the relative change in CRP and SUV max

#

between baseline and follow-up FDG-PET/CT. In additional analyses, the difference and relative change of WBC to SUV max. were compared between baseline and follow-up FDG-PET/CT. We differentiated between patients with a graft infection only and patients with a graft infection plus additional metabolically active foci at follow-up FDG-PET/CT. We performed univariable logistic regression analyses in order to identify potential predictors for the clinical response (absence of clinical signs of infection, negative microbiological cultures and declining or normal inflammatory markers). Statistical analyses were performed with Stata (Version 13, StataCorp).

RESULTS

Index surgical interventions included: total arch or descending aorta replacements (n=6), aorto-biiliac grafts (n=7), femoro-femoral crossover bypass (n=2) and ilio-femoral or femoro-tibial bypass (n=2). Seven patients had an endovascular placement of a stent-graft in the iliac artery (n=3) or they had endovascular aortic repair (abdominal aorta, n=4; thoracic aorta, n=3). Twenty-five patients (2 women, 23 men) with a median age of 66 years (range: 48-81) had a microbiologically proven PVGI at the time of baseline FDG-PET/CT. Patient and FDG PET/ CT characteristics at PVGI diagnosis and at follow up PET/ CT scan is shown in Table 1. Follow-up FDG-PET/CT was performed at a median time interval of 170 days (range: 88-277) after baseline examination.

Metabolic Activity

Graft Infection. The FDG uptake pattern at baseline was focal in all PVGI (*16*) and remained focal in most follow-up scans. Median SUV max. values at the site of highest uptake decreased from baseline (SUV max. 6.7 (range 4.0-17.8)) to follow-up FDG-PET/CT (SUV max: 4.9 (range 3.0-10.5), *P*=0.002) (Figure 1). In four patients (16%) metabolic activity of PVGI increased (Figure 2), while it decreased in 21 patients (84%). None of the 25 patients showed a

#

complete response to therapy on follow-up FDG-PET/CT (the lowest measured SUV max. value on follow-up FDG-PET/CT was 3.0).

Detection of Other Foci with FDG-PET/CT. Fourteen patients had additional metabolically active foci at either one or both time points (baseline and follow-up FDG-PET/CT) (Figure 3). At baseline FDG-PET/CT, ten patients had 11 infectious foci, i.e., sternum (n = 5), gastritis (n = 1), spondylodiscitis (n = 1), septic arthritis (n = 1), colitis (n = 2), and septic embolisms of left thigh (n = 1) (Table 1). At follow-up FDG-PET/CT, twelve patients had 14 metabolically active foci, i.e. rheumatoid arthritis (n = 1), sternum (n = 6), gastritis (n = 1), spondylodiscitis (n = 1), arthritis (n = 1), pneumonia (n = 1), subcutaneous abscess (n = 1) and soft tissue inflammation (n = 2). Only PET/CT findings deemed clinical relevant were proven by further clinical work-up; Table 1 states whether other foci were only “suspected” by PET/CT or also “proven” clinically.

Correlation with Laboratory Markers. Median CRP decreased from the time of baseline to follow-up FDG-PET/CT from 33 mg/l (range 0.80-217) to 6.8 mg/l (0.8-123), $P<0.001$. CRP increased in three patients (12%), was stable in one patient (4%), and decreased in 21 patients (84%). Median WBC also decreased from the time of baseline to follow-up FDG-PET/CT: from 7.51 g/l (2.99-12.4) to 6.54 g/l (3.43-11.42) (Table 1).

The difference in CRP and SUV max between baseline and follow-up FDG-PET/CT correlated in the subgroup of patients with a graft infection only, and no other metabolically active focus (Figure 4A n = 11; R-squared 0.67; $P = 0.002$). There was no correlation in the difference in the subgroup of patients with additional metabolically active foci (n =14; R-squared = 0.17; $P = 0.139$).

Impact of Follow-up PET/CT on Patient Management

In 19 of 25 patients (76%) antibiotic treatment was continued due to follow-up FDG-PET/CT; in two patients (11%) treatment was stopped; in four patients (16%) antibiotic treatment was changed. In eight patients (32%; seven patients with decreasing CRP, one with increasing CRP)

#

findings on follow-up FDG-PET/CT had further impact on patient management: In two patients progression of the graft infection was detected, followed by surgical intervention. In two patients focal FDG-uptake in the colon was noted and subsequent colonoscopy demonstrated one recurrence of rectal carcinoma and one diverticulitis. In one patient, FDG-PET/CT correctly identified acute ischemic stroke which was clinically silent but confirmed by subsequent magnetic resonance imaging of the brain. Finally, in one patient FDG-PET/CT detected a morphologic progression of spondylodiscitis (Figure 5), which was followed by bone biopsy for further evaluation of the infection. We did not find any significant factor associated with the clinical outcome in univariable logistic regression analysis (data not shown).

DISCUSSION

FDG-PET/CT allows for the monitoring of prosthetic vascular graft infection (PVGI) and treatment response. It appears to be superior to blood biomarkers, and can detect alternative metabolically active sites. FDG-PET/CT had an impact on the clinical management in all patients with either continuation or change of antimicrobial therapy. In the subgroup of patients with a vascular graft infection and no other sites of infection, we found a significant correlation between the absolute difference and relative change in CRP and SUV max. between baseline and follow-up FDG-PET/CT.

There are only limited data regarding an imaging guided therapy control in infections (*17*). At present, FDG-PET/CT is not recommended on a routine basis for therapy control in patients with infectious processes in general (*23*) and in PVGI in particular. In vascular graft infection, we would expect a reduction of the SUV max. value after start of antibiotic therapy. Immediately after surgery, we would expect an increased SUV max. value due to hyperperfusion; but if repeated debridements at the infection site are performed over time, we would expect a decrease of SUV max. values in case of response to therapy. Indeed, we could show that median SUV max. values in vascular grafts decreased between baseline and follow

#

up. However, we could not calculate predictors of clinical outcome because only two patients had a complete therapy response within the study period. Hence we used CRP and WBC as an approximation to therapy response. So far, there are no data regarding CRP and monitoring of treatment response in case of PVGI. What we expect is that leucocytes and inflammatory markers may add to the diagnosis of PVGI. Langerhuus et al. evaluated potential biomarkers for aortic graft infections in a pig model, and he found that CRP (sensitivity 86%, specificity 75%) was superior to WBC and TNF-α (*24*). We observed that in patients with PVGI as the only site of infection on baseline FDG-PET/CT, the parameter of CRP seems to represent a valuable indicator for therapy control as we found a significant correlation between the course of CRP and SUV max. changes in this subgroup. The latter is in line with the current body of literature which indicates that a decreasing CRP in patients with vasculitis is correlated with a decrease in metabolic activity (*25*). However, further follow-up and outcome studies are required, as long term antibiotic treatment may hamper the sensitivity of PET/CT in the detection of infection on follow-up scans.

Notably, more a third of our patients with PVGI in our cohort developed additional sites of FDG-uptake at the time of follow-up PET/CT. Thus, we suggest that FDG-PET/CT provides additional information guiding the therapeutic thinking. These newly discovered metabolically active sites impair the routine follow-up parameters such as increasing or stable CRP and WBC, which may be falsely interpreted as a non-success of the vascular graft infection treatment. Regarding patients with PVGI and additional metabolically active foci on baseline and/or follow-up FDG-PET/CT, correlation was not significant between the change in CRP and SUV max. Therapy control with clinical parameters alone seems to be inferior to FDG-PET/CT especially if one of the infectious foci responds well to treatment but the other does not.

The main limitation of this study was that we did not evaluate different types of index operations, graft types, or pathogens as independent predictors because of the small number of

#

patients. However, the results of our study are rather homogenous. Furthermore, we did not compare our findings to other imaging possibilities, such as labelled leukocytes szyntigraphy, which may also be helpful in follow-up of PVGI (*26*).

CONCLUSION

FDG-PET/CT represents a useful tool in therapy monitoring of PVGI and impacts on patient management. By providing quantitative data on the course of the graft infection and whole body imaging data, PET/CT differentiates between response to therapy of the graft infection and other infectious foci. Further long-term studies are needed to determine the exact value and response to therapy of FDG/ PET/CT in PVGI taking into account the costs and limited availability of PET/CT in routine practice.

CLINICALTRIALS.GOV IDENTIFIER

NCT01821664

CONFLICTS OF INTEREST STATEMENT

All authors declare no conflicts of interest.

ACKNOWLEDGMENTS

We are grateful to our patients for their commitment and thank Ruehe B, Rüegg Ch., Wolfensberger A., Matt U., Chaykovska L. and Romero-Toledo M.C. for excellent patient care. We also thank Müller C. and Bürgin S. as our study nurses, and Laich C. and Thoma A. for administrative assistance. The members of the VASGRA Cohort Study are: Bloemberg G, Hasse B, Husmann L, Lachat M, Mayer D, Rancic Z, Scherrer A, Weber R, Zinkernagel A.

AUTHORS' CONTRIBUTIONS STATEMENT

BH and LH designed the study. AS analyzed the data. LH and BS wrote the first draft, and LH, BS, AS and BH wrote the final version of the manuscript. All investigators contributed to data

#

collection and interpretation of the data, reviewed drafts of the manuscript, and approved the final manuscript.

#

REFERENCES

1. Saleem BR, Meerwaldt R, Tielliu IF, Verhoeven EL, van den Dungen JJ, Zeebregts CJ. Conservative treatment of vascular prosthetic graft infection is associated with high mortality. *Am J Surg.* 2010;200:47-52.

2. Calligaro KD, Veith FJ, Yuan JG, Gargiulo NJ, Dougherty MJ. Intra-abdominal aortic graft infection: complete or partial graft preservation in patients at very high risk. *J Vasc Surg.* 2003;38:1199-1205.

3. Ohta T, Hosaka M, Ishibashi H, et al. Treatment for aortic graft infection. *Surg Today.* 2001;31:18-26.

4. Legout L, Sarraz-Bournet B, D'Elia PV, et al. Characteristics and prognosis in patients with prosthetic vascular graft infection: a prospective observational cohort study. *Clin Microbiol Infect.* 2012;18:352-358..

5. Schwarz JK, Grigsby PW, Dehdashti F, Delbeke D. The role of 18F-FDG PET in assessing therapy response in cancer of the cervix and ovaries. *J Nucl Med.* 2009;50 Suppl 1:64S-73S.

6. Goerres GW, Stupp R, Barghouth G, et al. The value of PET, CT and in-line PET/CT in patients with gastrointestinal stromal tumours: long-term outcome of treatment with imatinib mesylate. *Eur J Nucl Med Mol Imaging.* 2005;32:153-162.

7. Brucher BL, Weber W, Bauer M, et al. Neoadjuvant therapy of esophageal squamous cell carcinoma: response evaluation by positron emission tomography. *Ann Surg.* 2001;233:300-309.

#

8. de Wit M, Bohuslavizki KH, Buchert R, Bumann D, Clausen M, Hossfeld DK. 18FDG-PET following treatment as valid predictor for disease-free survival in Hodgkin's lymphoma. *Ann Oncol.* 2001;12:29-37.

9. Barnes JA, LaCasce AS, Zukotynski K, et al. End-of-treatment but not interim PET scan predicts outcome in nonbulky limited-stage Hodgkin's lymphoma. *Ann Oncol.* 2011;22:910-915.

10. Hasse B, Husmann L, Zinkernagel A, Weber R, Lachat M, Mayer D. Vascular graft infections. *Swiss Med Wkly.* 2013;143:w13754.

11. Fukuchi K, Ishida Y, Higashi M, et al. Detection of aortic graft infection by fluorodeoxyglucose positron emission tomography: comparison with computed tomographic findings. *J Vasc Surg.* 2005;42:919-925.

12. Keidar Z, Engel A, Hoffman A, Israel O, Nitecki S. Prosthetic vascular graft infection: the role of 18F-FDG PET/CT. *J Nucl Med.* 2007;48:1230-1236.

13. Spacek M, Belohlavek O, Votrubova J, Sebesta P, Stadler P. Diagnostics of "non-acute" vascular prosthesis infection using 18F-FDG PET/CT: our experience with 96 prostheses. *Eur J Nucl Med Mol Imaging.* 2009;36:850-858.

14. Bruggink JL, Slart RH, Pol JA, Reijnen MM, Zeebregts CJ. Current role of imaging in diagnosing aortic graft infections. *Semin Vasc Surg.* 2011;24:182-190.

15. Saleem BR, Berger P, Vaartjes I, et al. Modest utility of quantitative measures in F-fluorodeoxyglucose positron emission tomography scanning for the diagnosis of aortic prosthetic graft infection. *J Vasc Surg.* December 9, 2014 [Epub ahead of print].

#

16. Sah BR, Husmann L, Mayer D, et al. Diagnostic performance of F-FDG-PET/CT in vascular graft infections. *Eur J Vasc Endovasc Surg.* 2015; 49:455-64

17. Glaudemans AW, de Vries EF, Galli F, Dierckx RA, Slart RH, Signore A. The use of (18)F-FDG-PET/CT for diagnosis and treatment monitoring of inflammatory and infectious diseases. *Clinical & developmental immunology.* 2013;2013:623036.

18. FitzGerald SF, Kelly C, Humphreys H. Diagnosis and treatment of prosthetic aortic graft infections: confusion and inconsistency in the absence of evidence or consensus. *J Antimicrob Chemother.* 2005;56:996-999.

19. Szilagyi DE, Smith RF, Elliott JP, Vrandecic MP. Infection in arterial reconstruction with synthetic grafts. *Ann Surg.* 1972;176:321-333.

20. Mayer D, Hasse B, Koelliker J, et al. Long-term results of vascular graft and artery preserving treatment with negative pressure wound therapy in Szilagyi grade III infections justify a paradigm shift. *Ann Surg.* 2011;254:754-759; discussion 760.

21. Jamar F, Buscombe J, Chiti A, et al. EANM/SNMMI guideline for 18F-FDG use in inflammation and infection. *J Nucl Med.* 2013;54:647-658.

22. Keidar Z, Pirmisashvili N, Leiderman M, Nitecki S, Israel O. 18F-FDG uptake in noninfected prosthetic vascular grafts: incidence, patterns, and changes over time. *J Nucl Med.* 2014;55:392-395.

23. Israel O, Keidar Z. PET/CT imaging in infectious conditions. *Ann N Y Acad Sci.* 2011;1228:150-166.

#

24. Langerhuus SN, Tonnesen EK, Jensen KH, et al. Brief report: biomarkers of aortic vascular prosthetic graft infection in a porcine model with Staphylococcus aureus. *Eur J Clin Microbiol Infect Dis.* 2010;29:1453-1456.

25. Both M, Ahmadi-Simab K, Reuter M, et al. MRI and FDG-PET in the assessment of inflammatory aortic arch syndrome in complicated courses of giant cell arteritis. *Ann Rheum Dis.* 2008;67:1030-1033.

26. Erba PA, Sollini M, Conti U, et al. Radiolabeled WBC scintigraphy in the diagnostic workup of patients with suspected device-related infections. *JACC. Cardiovascular imaging.* 2013;6:1075-1086.

#

#

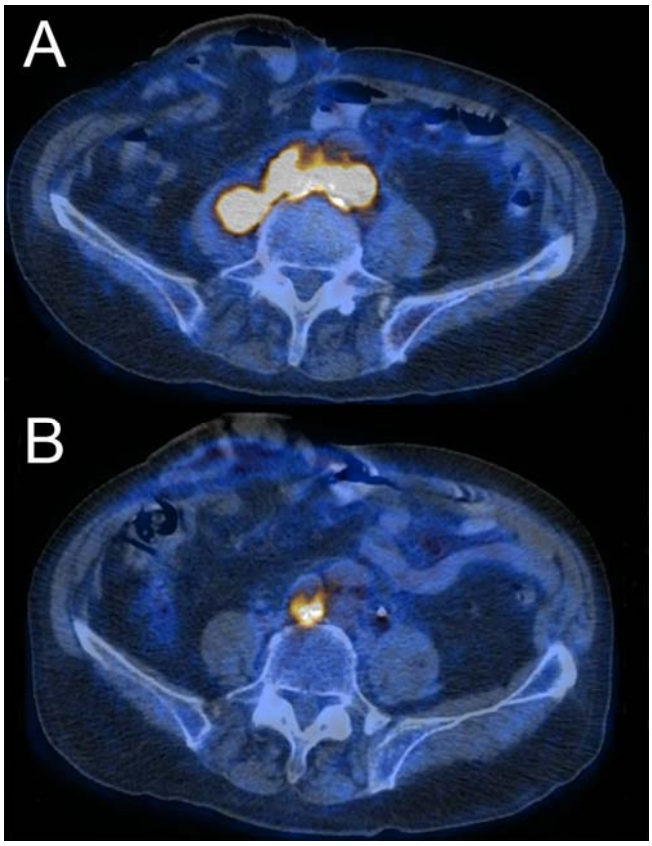

Figure 1:

81year-old male patient with a strongly FDG-avid bifurcated graft-infection (PTFE graft) on baseline FDG-PET/CT in September 2013 (**panel A**). Follow-up FDG-PET/CT in January 2014 (**panel B**) demonstrates partial response to therapy after surgery and antimicrobial therapy. SUV max. decreased from 16.2 to 9.2 while CRP decreased from 85 to 15 mg/l and WBC decreased from 9.2 to 5.3 g/l.

#

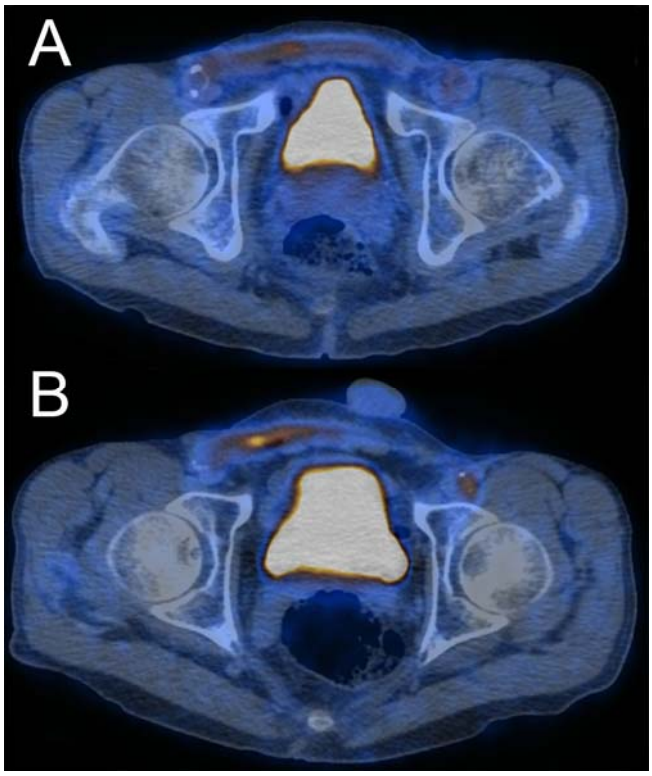

Figure 2:

Seventy-four-year-old male patient with an infection of a femoro-femoral crossover bypass (Dacron graft). Baseline FDG-PET/CT in November 2013 (**panel A**) displays an FDG-avid graft infection with progression of the FDG-activity on follow-up FDG-PET/CT in April 2014 (**panel B**; SUV max. from 4.0 to 5.2). CRP increased from 6 to 10 mg/l while WBC decreased from 9.9 to 9.1 g/l.

#

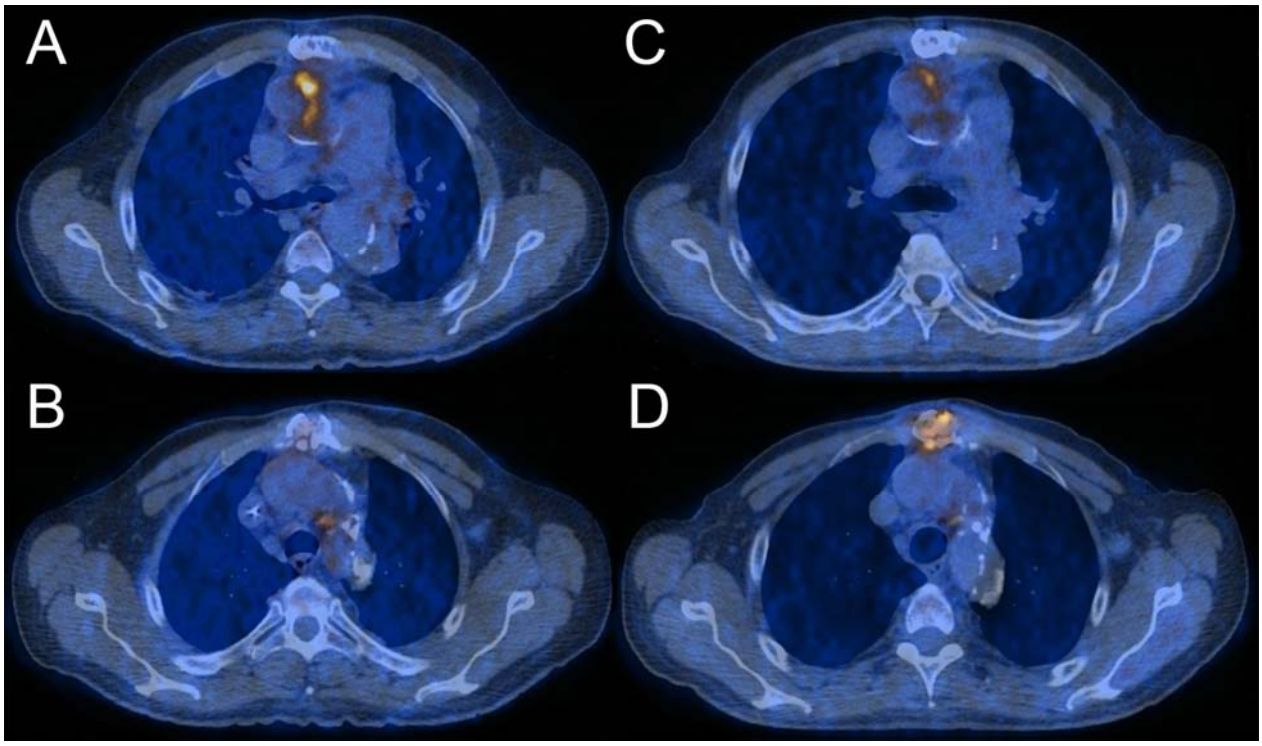

Figure 3:

Sixty-year-old male patient with PVGI after aortic root and total arch replacement (pyrolytic carbon valve; double velour graft and collagen coated polyester graft). Baseline FDG-PET/CT in September 2012 (**panel A and C**) displays an FDG-avid infection of the graft (SUV max. 7.6) and only mild FDG-activity in the sternum (SUV max. 4.0). Follow-up FDG-PET/CT in June 2013 (**panel B and D**) shows partial therapy response at the graft (SUV max. 5.1) but progression in the sternum (SUV max. 5.2). CRP decreased from 33 to 15 mg/l while WBC increased from 2.6 to 4.0 g/l.

#

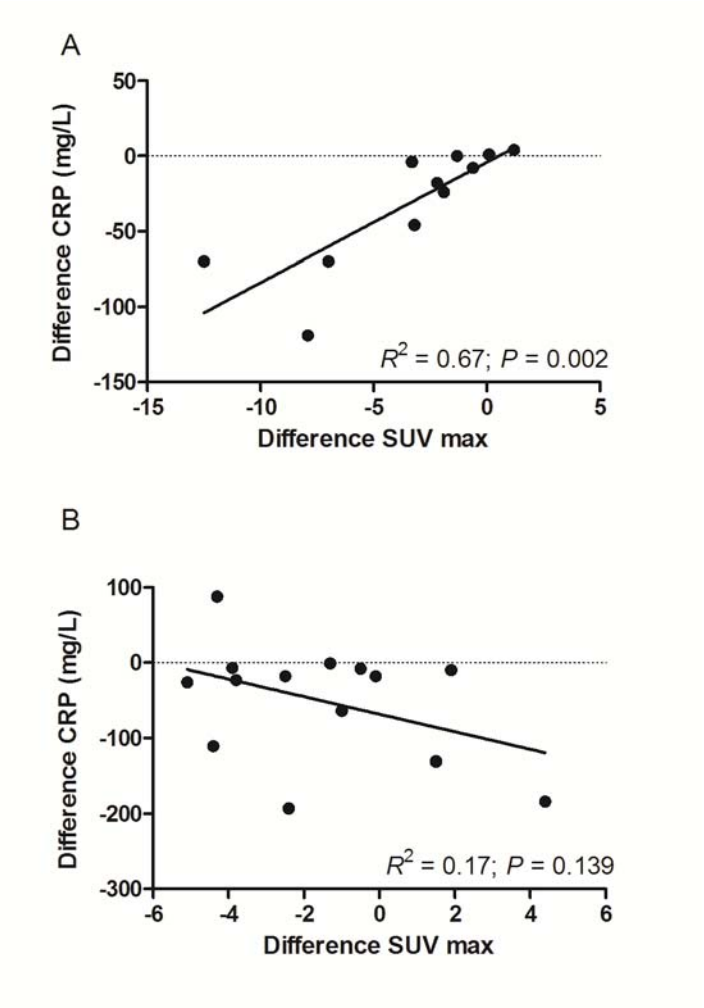

Figure 4

Linear regression plot of the difference and relative change between baseline and follow-up FDG-PET/CT compared to the difference of CRP. **Panel A** show results among patients with PVGI and no other sites of infection (n = 11); **Panel B** among patients with PVGI plus additional metabolically active foci.

#

#

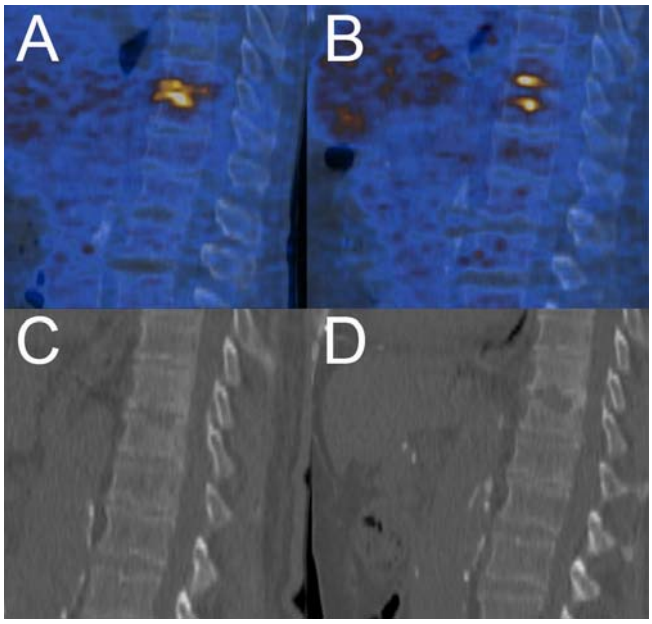

Figure 5:

The same patient as in figure 3 also has a FDG-avid spondylodiscitis (SUV max. 7.0) on baseline FDG-PET/CT in September 2012 (**panel A and C**). FDG-activity is similar (SUV max. 6.9) on follow up FDG-PET/CT in June 2013 (panel B and D), but CT displays progression of osteolysis (**panel B and D**). FDG-PET/CT changed patient treatment as a bone biopsy was performed for further evaluation of the infection.

#

Table 1 Patient Characteristics

Pat	Age	Sex	FDG-PET/CT at PVGI diagnosis						FDG-PET/CT at follow-up						Impact on treatment
			Time OP-PET Scan (days)	SUV max.	FDG-pattern	CRP	WBC	Additional active focus/-i	Time OP-PET scan (days)	SUV max.	FDG-pattern	CRP	WBC	Additional active focus/-i	
1	76	M	96	14.4	5	19	5.8	None	95	10.5	4	12.0	5.3	Proven rheumatoid arthritis	continued
2	48	M	439	4.9	5	136	5.7	Suspected infected sternum	593	6.4	5	5.0	4.5	Suspected Infected sternum (SUV ↓), Suspected gastritis	continued
3	52	M	400	17.8	5	73	8.1	None	173	5.3	5	3.0	4.7	None	continued
4	74	M	110	4.0	4	6	9.9	None	122	5.2	4	10.0	9.1	None	continued
5	63	M	70	8.5	5	26	3.0	Suspected Infected sternum	161	4.7	4	4.0	4.6	Suspected infected sternum (SUV ↓)	continued
6	51	M	610	6.7	5	199	12.4	Suspected Gastritis	162	4.3	5	6.0	7.7	None	continued
7	79	M	1148	4.4	4	17	5.7	None	161	3.1	2	17.0	5.8	None	stopped
8	71	M	644	12.4	5	114	11.9	None	181	4.5	3	1.0	6.7	None	continued
9	71	M	443	10.0	4	30	6.9	Suspected. Infected sternum	97	4.9	4	4.0	5.6	Suspected infected sternum (SUV ↓)	continued
10	62	M	4253	10.2	3	49	11.7	None	171	7.0	3	3.0	8.9	None	continued
11	61	M	464	7.6	5	33	2.6	Suspected infected sternum,	553	5.1	5	15.0	4.0	Suspected infected sternum, (SUV ↑),	changed
12	62	M	111	4.4	3	23	9.7	Proven Spondylodiscitis	224	4.3	3	5.0	9.5	Proven spondylo-discitis (SUV →)	continued
13	62	M	242	7.2	4	42	7.5	None	183	6.6	4	34.0	3.4	None	continued
14	63	M	1925	5.8	4	74	9.7	None	120	4.8	4	10.0	11.4	Suspected soft tissue inflammation Proven diverticulitis	continued
15	70	M	137	5.9	4	1	5.1	None	125	6.0	4	2.0	6.9	None	continued
16	71	M	94	8.2	5	35	4.6	None	261	3.9	3	123	na	Proven pneumonia	changed
17	81	M	5381	16.2	5	85	9.2	None	5491	9.2	4	15.0	5.3	None	continued
18	53	M	624	7.5	4	114	6.7	None	840	3.1	1	3.0	4.8	Proven septic arthritis	stopped
19	81	F	351	7.0	5	2	6.8	Suspected septic arthritis, colitis	173	5.7	5	1.0	6.6	Suspected infected sternum	continued
20	66	M	2150	6.0	5	217	10.1	Suspected septic embolisms left thigh	75	10.4	5	33.0	8.0	Proven soft tissue inflammation	changed
21	80	M	102	6.4	5	5	5.9	None	183	3.1	3	0.8	6.5	None	continued
22	56	M	671	5.4	4	39	9.5	Suspected colitis	185	3.5	3	15.0	8.8	None	continued
23	68	M	97	5.2	3	30	6.7	None	78	3.0	3	12.0	5.3	None	continued
24	77	F	82	4.0	4	24	8.0	Suspected infected sternum	88	3.5	3	16.0	6.6	Suspected infected sternum(SUV→)	continued
25	51	M	983	6.1	5	17	8.7	None	121	8.0	5	6.8	8.1	None	changed

Abbreviations: Pat, patient; M, male; F, female; FDG-PET/CT, positron emission tomography/computed tomography with 18F-fluorodeoxyglucose; time OP-scan, time between initial operation and PET/CT scan; SUV, maximum standardized uptake value; SUV ↑, increasing SUV; SUV→ , stable SUV; SUV ↓, decreasing SUV; CRP, C-reactive protein; WBC, white blood cell count; na, not available; OP, Index vascular operation.

FDG-PATTERN (*16*): GRADE 1, BACKGROUND ACTIVITY; GRADE 2, MILDLY INCREASED, BUT DIFFUSE FDG-UPTAKE ALONG THE GRAFT; GRADE 3, FOCAL, BUT ONLY MILD FDG-UPTAKE OR STRONG DIFFUSE FDG-UPTAKE ALONG THE GRAFT; GRADE 4, FOCAL AND INTENSE FDG-UPTAKE (+/- DIFFUSE FDG-UPTAKE ALONG THE GRAFT); GRADE 5, FOCAL AND INTENSE FDG-UPTAKE PLUS FLUID COLLECTIONS/ABSCESS FORMATION.

#