^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT effectively contribute to early diagnosis of infection of arteriovenous graft for hemodialysis

Monika Medricka^a, Jana Janeckova^a, Pavel Koranda^b, Eva Buriankova^b, Petr Bachleda^a

Objective. An arteriovenous graft (AVG) is indicated in hemodialysis patients with failed arteriovenous access. Early treatment of AVG infection is important because an advanced prosthetic infection leads to the removal of the prosthesis. The aim of this study was to evaluate the benefits of ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT in early detection of AVG infections.

Subjects and Methods. Fifty-one AVGs were evaluated. ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT studies were performed at intervals of 10, 20–30, and 40–50 weeks after AVG insertion. Agreement between the imaging methods and reference parameters (i.e. clinical presentation, C-reactive protein and microbiological findings on the hemodialysis cannula extracted after hemodialysis from AVG) was evaluated.

Results. The study results showed that focal accumulation of the radiopharmaceuticals can be considered a sign of AVG infection. At 10 weeks after AVG implantation, the focal ^{18}F -FDG findings showed the best agreement with the reference parameters (agreement coefficients AC1 - clinical status: 0.693, CRP: 0.605, cannula microbiology: 0.518, respectively). At 20 to 30 weeks after AVG implantation, the diagnostic value of focal $^{99\text{m}}\text{Tc}$ -HMPAO-WBC accumulation increased (AC1 coefficients: 0.658, 0.658, 0.408) and was similar to that of focal ^{18}F -FDG uptake (AC1s: 0.656, 0.570, 0.409). Between 40 and 50 weeks since AVG implantation, the diagnostic significance of focal $^{99\text{m}}\text{Tc}$ -HMPAO-WBC accumulation (AC1 coefficients: 0.771, 0.811, 0.611) slightly exceeded the diagnostic value of focal ^{18}F -FDG accumulation (AC1 coefficients: 0.524, 0.456, 0.569).

Conclusion. ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT can both serve as important tools contributing to early diagnosis of AVG infection.

Key words: ^{18}F -FDG PET/CT, $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT, infection, arteriovenous graft, hemodialysis

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^aDepartment of Vascular and Transplantation Surgery, University Hospital Olomouc, Czech Republic

^bDepartment of Nuclear Medicine, University Hospital Olomouc and Palacky University, Olomouc, Czech Republic

Corresponding author: Jana Janeckova, e-mail: jana.fialova@email.cz

INTRODUCTION

For patients on chronic hemodialysis treatment, vascular access is required. A native arteriovenous fistula is preferred as the most favorable. An arteriovenous graft (AVG) is indicated in patients with a failed arteriovenous fistula, exhausted superficial venous bed, or unsuitable vessels. Most commonly, expanded polytetrafluorethylene (ePTFE) prostheses are used. AVG is often a last option to ensure high-quality access for hemodialysis.

Infection of the AVG is a serious and life-threatening complication. It is associated with high morbidity and is the second leading cause of vascular access failure¹. AVG infection rate ranges from 9.5% to 35% in the literature²⁻⁵. If a full-blown prosthetic infection occurs, the treatment options are quite limited and it mostly leads to the removal of the prosthesis; thus, access for hemodialysis is lost.

Our aim was to evaluate the benefits of fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT) and technetium-99-hexamethylpropyleneamine oxime labeled white

blood cells ($^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT) in the detection of AVG infection and to compare these methods in situation when AVGs were altered by repeated punctures. We attempted to ascertain the suitability of these procedures for the early detection of AVG infection in hemodialysis programs – whether their additional use could bring desirable benefits, such as a more rapid and more precise diagnosis of AVG infection with a conservative treatment option, a reduced risk of advanced infection, and salvage of vascular access. The current graft infection rate in our group of patients was compared to a similar group of hemodialysis patients from a previous similar period before the introduction of radionuclide methods.

SUBJECTS AND METHODS

Patients

A prospective, open-label study included all patients in whom ePTFE prostheses for hemodialysis were implanted during a period of 3.5 years in total. The study

was approved by the Ethics Committee of the University Hospital Olomouc and Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic and each patient signed an informed consent form. Patient data were handled anonymously.

The group was comprised of 56 patients in whom 62 AVGs for hemodialysis were created. There were 22 women and 34 men, with a mean age of 62.7 years (range 29–89 years). Eleven patients had no radionuclide examinations at all for the following reasons: death (4 cases), non-compliance (5), thrombosis (1), and early infection of AVG (1). 51 AVGs were evaluated by using both radionuclide methods.

During the first year since AVG implantation, patients with an AVG for hemodialysis were monitored by follow-up protocol for 50 weeks in total. The monitoring period was shortened in case of infected graft removal or due to non-compliance of some patients - one-year monitoring was completed in 30 AVGs. ^{18}F -FDG PET/CT was done 108 times and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC scintigraphy 101 times.

The follow-up protocol

Once a week, clinical evaluation of the patients was performed, blood samples were taken and the C-reactive protein (CRP) level was investigated as a marker of inflammation.

Microbiological testing was performed in each patient every week. A swab was sampled from the hemodialysis cannula (inserted in AVG during hemodialysis) immediately after the hemodialysis procedure, i.e. directly after its contact with the vascular prosthesis. In the case of suspected infection, the swab was taken directly from the most probable location of infection.

$^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT and ^{18}F -FDG PET/CT were performed at intervals of 10, 20–30, and 40–50 weeks after AVG insertion. The interval between both examinations was 1 day in 88% cases, maximum delay was 16 days (due to health issues). The radiopharmaceuticals were injected intravenously into the contralateral arm.

^{18}F -FDG PET/CT images were acquired on the PET/CT scanner (Biograph 16 Hi-Rez, Siemens Erlangen, Germany) allowing 3D-only PET acquisition. All patients were advised to fast for six hours prior to the PET/CT examination. 5.7 MBq/kg (0.154 mCi/kg) of ^{18}F -FDG was injected intravenously; thereafter, patients rested for a period of 60 minutes. PET scans of the upper extremities (ranging from the neck to the hand) were acquired for 2–3 min per bed position, with a longer acquisition time in patients with a body weight above 100 kg. PET data were reconstructed into transaxial slices with a 168×168 matrix (pixel size 4 mm) and slice thickness of 2 mm using iterative 3D OSEM reconstruction (4 iterations, 8 subsets, 5 mm Gaussian post-reconstruction filtration). Multislice, diagnostic quality CT with intravenous contrast medium (80 ml of Ultravist® 370 mg/mL) was acquired, the CT settings were as follows: quality reference 130 mAs (CareDose4D on), 120 kV, beam width 16×1.5 mm,

$^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT scintigraphy was performed using the double detector SPECT/CT gamma

camera (Infinia Hawkeye 4, GE Healthcare, Milwaukee, USA). Planar and SPECT/CT images were obtained 4 h after administration of 550 MBq (14.9 mCi) of $^{99\text{m}}\text{Tc}$ -HMPAO-WBC; second planar scintigrams were acquired 24 h post injection. A pathologically increased uptake of radioactivity and its increase in time were evaluated as a criterion of inflammatory changes.

Data evaluation

All scintigraphic images were evaluated independently by two experienced nuclear medicine physicians aware of the patients' clinical history and results of all the other examinations.

PET/CT and SPECT/CT studies were assessed on the basis of qualitative analysis of FDG and WBC uptake patterns. Increased accumulation of FDG and WBC in the prosthesis was classified as intense focal, diffuse, and simultaneous focal and diffuse. The finding was considered as a diffuse uptake if the majority of the graft was affected. The group of findings with any increase in the accumulation of FDG or WBC, i.e. with focal or diffuse accumulation, was also evaluated as part of the statistical analysis.

Statistics

Agreement between the methods was evaluated using the Gwet's agreement coefficient AC1 and percentage of the overall agreement. The strength of agreement between the methods was characterized using Gwet's coefficient AC1 – strength of agreement: < 0.0 Poor, 0.0 to 0.20 Slight, 0.21 to 0.40 Fair, 0.41 to 0.60 Moderate, 0.61 to 0.80 Substantial (Good), 0.81 to 1.00 Almost Perfect (Very Good). The McNemar test for symmetry was used to detect bias; in the case of statistically significant bias between the methods compared, these combinations of methods were excluded from further evaluation of agreement.

RESULTS

Clinical manifestations of advanced infection developed in 7 out of 62 AVGs (11.3%), graft infection was also ascertained by radionuclide examinations as well as by increased CRP levels. All grafts had to be removed and access for hemodialysis was lost. The diagnosis of infection was verified by microbiological assays obtained at surgery.

In another 7 AVGs (11.3%), infection was suspected on the basis of positive ^{18}F -FDG PET/CT and a positive microbiological swab from the cannula. In these grafts, the clinical signs of graft infection were missing or very subtle. All these patients had a nonspecifically increased marker of inflammation – the CRP levels were slightly elevated (values 35–62). These patients were treated as potentially infectious using targeted antibiotic therapy. In all 7 cases, the suspicious infection was treated successfully, the possible development of clinically apparent infection was prevented, and access for hemodialysis could be rescued; the AVGs were fully functional and without signs of infection during the follow-up. Thus, no microbio-

Table 1. Evaluation of agreement between the clinical signs, microbiological test result of the hemodialysis cannula swab and CRP at 10, 21–30, and 41–50 weeks after AVG insertion.

	AC1	Overall agreement (%)	Method 1 positive, Method 2 negative	Method 1 negative, Method 2 positive	McNemar
Week 10					
Clinical vs. Micro	0.626	76.2	11.9%	11.9%	1
Clinical vs. CRP	0.670	78.6	11.9%	9.5%	1
Micro vs. CRP	0.524	69.0	16.7%	14.3%	1
Weeks 21–30					
Clinical vs. Micro	0.486	70.4	6.8%	22.7%	0.092
Clinical vs. CRP	0.860	90.9	4.5%	4.5%	1
Micro vs. CRP	0.565	75.0	20.5%	4.5%	0.065
Weeks 41–50					
Clinical vs. Micro	0.692	79.3	0.0%	20.7%	0.031
Clinical vs. CRP	0.781	82.7	6.9%	10.3%	1
Micro vs. CRP	0.524	69.0	24.1%	6.9%	0.180

AC1 – Gwet's agreement coefficient, Method 1 – the first method in the comparison line, Method 2 – the second method in the comparison line, McNemar – McNemar test for symmetry, Clinical – clinical signs, Micro – microbiological test result of the hemodialysis cannula swab, CRP – C-reactive protein.

Table 2a. Evaluation of agreement between reference parameters and diffuse or focal ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT findings at 10 weeks after surgery.

	AC1	Overall Agreement (%)	McNemar
Week 10			
Clinical vs. F FDG	0.693	81.6	0.453
Clinical vs. F WBC	0.378	58.3	1
Clinical vs. D FDG	0.079	47.5	0.189
Clinical vs. D WBC	0.111	52.8	0.002
Clinical vs. (F FDG and D FDG)	0.617	71.8	0.065
Clinical vs. (F WBC and D WBC)	0.487	63.9	1
Clinical vs. (F FDG or D FDG)	0.137	56.4	< 0.0001
Clinical vs. (F WBC or D WBC)	0.017	47.2	0.001
CRP vs. F FDG	0.605	76.3	0.508
CRP vs. F WBC	0.491	66.7	1
CRP vs. D FDG	0.167	52.5	0.167
CRP vs. D WBC	0.047	50.0	0.008
CRP vs. (F FDG and D FDG)	0.695	77.0	0.039
CRP vs. (F WBC and D WBC)	0.596	72.3	0.754
CRP vs. (F FDG or D FDG)	0.036	51.3	0.0001
CRP vs. (F WBC or D WBC)	0.081	44.5	0.003
Micro vs. F FDG	0.518	71.1	0.549
Micro vs. F WBC	0.378	58.3	1
Micro vs. D FDG	0.255	57.5	0.143
Micro vs. D WBC	0.007	47.2	0.004
Micro vs. (F FDG and D FDG)	0.628	71.8	0.065
Micro vs. (F WBC and D WBC)	0.487	63.9	1
Micro vs. (F FDG or D FDG)	0.137	56.4	< 0.0001
Micro vs. (F WBC or D WBC)	0.124	41.7	0.001

AC1 – Gwet's agreement coefficient, McNemar – McNemar test for symmetry, Clinical – clinical signs, CRP – C-reactive protein, Micro – microbiological test result of the hemodialysis cannula swab, F – focal, D – diffuse, FDG – ^{18}F -FDG PET/CT, WBC – $^{99\text{m}}\text{Tc}$ -HMPAO-WBC.

logical findings directly from a removed prosthesis were available.

Due to these facts, it was not possible to use a uniform “gold standard parameter” to demonstrate AVG infection in the study. Therefore, to assess the diagnostic

significance of different findings of ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT at three time periods, an evaluation of agreement between the imaging methods and reference parameters observed (clinical presentation, CRP, and microbiological test result of the hemodialysis

Table 2b. Evaluation of agreement between reference parameters and diffuse or focal ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT findings at 20 to 30 weeks after surgery.

Week 20-30	AC1	Overall Agreement (%)	McNemar
Clinical vs. F FDG	0.656	79.0	0.070
Clinical vs. F WBC	0.658	75.7	1
Clinical vs. D FDG	0.073	47.4	0.041
Clinical vs. D WBC	0.084	43.2	< 0.0001
Clinical vs. (F FDG and D FDG)	0.596	71.0	1
Clinical vs. (F WBC and D WBC)	0.674	75.7	1
Clinical vs. (F FDG or D FDG)	0.135	55.2	< 0.0001
Clinical vs. (F WBC or D WBC)	0.106	43.2	< 0.0001
CRP vs. F FDG	0.570	73.7	0.109
CRP vs. F WBC	0.658	75.7	1
CRP vs. D FDG	0.166	52.6	0.031
CRP vs. D WBC	0.084	43.2	< 0.0001
CRP vs. (F FDG and D FDG)	0.669	76.4	1.000
CRP vs. (F WBC and D WBC)	0.674	75.7	1
CRP vs. (F FDG or D FDG)	0.033	50.0	0.0001
CRP vs. (F WBC or D WBC)	0.106	43.2	< 0.0001
Micro vs. F FDG	0.409	68.5	0.774
Micro vs. F WBC	0.408	64.9	0.092
Micro vs. D FDG	0.076	52.6	0.815
Micro vs. D WBC	0.135	43.2	0.078
Micro vs. (F FDG and D FDG)	0.518	71.1	0.012
Micro vs. (F WBC and D WBC)	0.344	59.5	0.035
Micro vs. (F FDG or D FDG)	0.001	50.0	0.064
Micro vs. (F WBC or D WBC)	0.024	48.6	0.019

AC1 - Gwet's agreement coefficient, McNemar - McNemar test for symmetry, Clinical - clinical signs, CRP - C-reactive protein, Micro - microbiological test result of the hemodialysis cannula swab, F - focal, D - diffuse, FDG - ^{18}F -FDG PET/CT, WBC - $^{99\text{m}}\text{Tc}$ -HMPAO-WBC.

Table 2c. Evaluation of agreement between reference parameters and diffuse or focal ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT findings at 40 to 50 weeks after surgery.

Week 40-50	AC1	Overall Agreement (%)	McNemar
Clinical vs. F FDG	0.524	69.0	0.039
Clinical vs. F WBC	0.771	82.2	1
Clinical vs. D FDG	0.347	58.6	0.039
Clinical vs. D WBC	0.314	57.2	0.039
Clinical vs. (F FDG and D FDG)	0.673	75.8	0.453
Clinical vs. (F WBC and D WBC)	0.771	82.2	1
Clinical vs. (F FDG or D FDG)	0.156	51.7	0.002
Clinical vs. (F WBC or D WBC)	0.314	57.2	0.039
CRP vs. F FDG	0.456	65.5	0.109
CRP vs. F WBC	0.811	85.7	1
CRP vs. D FDG	0.385	62.1	0.065
CRP vs. D WBC	0.471	67.8	0.039
CRP vs. (F FDG and D FDG)	0.710	79.3	0.687
CRP vs. (F WBC and D WBC)	0.811	85.7	1
CRP vs. (F FDG or D FDG)	0.075	48.3	0.007
CRP vs. (F WBC or D WBC)	0.471	67.8	0.039
Micro vs. F FDG	0.569	75.9	1
Micro vs. F WBC	0.611	75.0	0.125
Micro vs. D FDG	0.371	65.5	0.754
Micro vs. D WBC	0.208	57.2	0.774
Micro vs. (F FDG and D FDG)	0.720	82.7	0.375
Micro vs. (F WBC and D WBC)	0.611	75.0	0.125
Micro vs. (F FDG or D FDG)	0.196	58.6	0.146
Micro vs. (F WBC or D WBC)	0.208	57.2	0.774

AC1 - Gwet's agreement coefficient, McNemar - McNemar test for symmetry, Clinical - clinical signs, CRP - C-reactive protein, Micro - microbiological test result of the hemodialysis cannula swab, F - focal, D - diffuse, FDG - ^{18}F -FDG PET/CT, WBC - $^{99\text{m}}\text{Tc}$ -HMPAO-WBC.

Fig. 1. Imaging of arteriovenous graft infection - subsequent fistula formation despite an antibiotic therapy initiation. Increased focal ^{99m}Tc -HMPAO-WBC uptake - (A) anterior scans acquired 4 and 24 hours post injection, (B) MIP SPET, (C) SPECT/CT, (D) CT. Increased focal ^{18}F -FDG uptake (E) MIP, (F) PET/CT, (G) CT.

cannula swab) was used, while excluding combinations shown to have a significant bias between the two compared methods (McNemar test).

It is obvious from Table 1 that the best agreement between the different reference parameters is the one between the clinical presentation and CRP. Furthermore, it is evident that, particularly in a longer time interval since AVG implantation, the positivity of the microbiological examination of the hemodialysis cannula outnumbered that of the clinical finding or the CRP in a substantial proportion of the results. In the setting of a higher positivity rate of this microbiological testing than would correspond to the clinical presentation and the CRP elevation, it is necessary to seriously consider a high probability of false positivity due to contamination of the samples taken. It could be supposed that a microbial smear from the cannula could be falsely positive due to long-lasting partially cutaneous insertion of the cannula.

At 10 weeks after AVG creation (Table 2a), the best agreement between the clinical presentation and imaging was found for a focal ^{18}F -FDG PET/CT finding, while the McNemar test did not suggest a significantly higher rate of positive results in either of the methods. The worst agreement with the clinical presentation was shown for the finding of diffusely increased ^{18}F -FDG accumulation or diffusely increased ^{99m}Tc -HMPAO-WBC accumulation.

The greatest agreement between the CRP and the imaging method was found for a simultaneous focal and diffuse ^{18}F -FDG PET/CT finding; however, the McNemar test (0.039) demonstrated significant bias in the results – imaging with ^{18}F -FDG PET/CT yielded a positive result more often than the CRP – it could indicate an increased risk of false positive results. A good agreement between the CRP and the imaging method was also shown for a focal ^{18}F -FDG PET/CT finding alone; moreover, the McNemar test (0.508) showed that in this case, there was no significant bias in the results. A focal ^{18}F -FDG PET/CT finding alone can thus be considered to be the best parameter in diagnosing infection when compared with the CRP. The worst agreement with the CRP was shown for diffuse ^{99m}Tc -HMPAO-WBC hyperaccumulation.

The best agreement between a microbiological test result of the hemodialysis cannula swab and the imaging method was found for a simultaneous focal and diffuse ^{18}F -FDG PET/CT finding; however, the McNemar test (0.065) suggested that microbiological testing yielded a positive result insignificantly more often than ^{18}F -FDG PET/CT. The worst agreement with a microbiological finding was shown for diffuse ^{99m}Tc -HMPAO-WBC hyperaccumulation.

The results show that at 10 weeks since AVG implantation, the findings with ^{18}F -FDG PET/CT demonstrate a better agreement with the reference parameters than ^{99m}Tc -HMPAO-WBC SPECT/CT. Diffuse hyperaccumula-

tion of ^{99m}Tc -HMPAO-WBC is a particularly nonspecific finding.

At 20 to 30 weeks after AVG creation (Table 2b), the best agreement between the clinical presentation and imaging was found for simultaneous diffuse and focal finding with ^{99m}Tc -HMPAO-WBC SPECT/CT while the McNemar test (1.0) did not suggest a systematically higher rate of positive results in either method. A similarly good agreement with the clinical presentation and no bias (McNemar test 1.0) was shown for a focal ^{99m}Tc -HMPAO-WBC SPECT/CT finding. A focal ^{18}F -FDG PET/CT finding alone also showed a good agreement; however, the McNemar test (0.070) suggested an insignificantly higher rate of positive results with PET/CT.

The best agreement between the CRP and the imaging method was shown for a simultaneous focal and diffuse ^{99m}Tc -HMPAO-WBC SPECT/CT finding, simultaneous focal and diffuse ^{18}F -FDG PET/CT finding, as well as focal ^{99m}Tc -HMPAO-WBC SPECT/CT finding alone. McNemar test excluded asymmetric distribution of results in these cases.

The best agreement between a microbiological test result of the hemodialysis cannula swab and the imaging method with no significant bias in the results according to the McNemar test was shown for a focal ^{18}F -FDG PET/CT finding. The worst agreement with a microbiological finding was shown for tests with diffuse hyperaccumulation of the radiopharmaceuticals (^{99m}Tc -HMPAO-WBC and ^{18}F -FDG).

The results imply that at 20 to 30 weeks after AVG implantation, the diagnostic value of focal ^{99m}Tc -HMPAO-WBC hyperaccumulation increases and is similar to that of focal ^{18}F -FDG PET/CT hyperaccumulation.

At 40 to 50 weeks after AVG creation (Table 2c), the greatest agreement between the clinical presentation and the imaging was found for a focal ^{99m}Tc -HMPAO-WBC SPECT/CT finding. An identically good agreement with the clinical presentation was shown for a simultaneous focal and diffuse ^{99m}Tc -HMPAO-WBC SPECT/CT finding. McNemar test excluded asymmetric distribution of results in both cases. The worst agreement with a clinical finding was shown for a diffuse increase in the accumulation of both radiopharmaceuticals.

The best agreement between the CRP and the imaging method without asymmetric distribution of results was shown for focal or focal and diffuse accumulation with ^{99m}Tc -HMPAO-WBC. The worst agreement with the CRP was shown for the findings with a diffuse increase in radiopharmaceutical accumulation with ^{18}F -FDG PET/CT and ^{99m}Tc -HMPAO-WBC SPECT/CT.

The best agreement between microbiological test result of the hemodialysis cannula swab and the imaging method was shown for a focal and diffuse ^{18}F -FDG PET/CT finding (without significant asymmetry of results - McNemar 0.375). A lower agreement with a microscopy finding was shown for a diffuse increase in radiopharmaceutical accumulation with ^{18}F -FDG PET/CT and ^{99m}Tc -HMPAO-WBC SPECT/CT.

The results show that between 40 and 50 weeks since AVG implantation, the diagnostic significance of focal ^{99m}Tc -HMPAO-WBC hyperaccumulation increased - this finding slightly exceeds the diagnostic value of focal ^{18}F -FDG accumulation.

When comparing the maximum values (Gwet's agreement coefficient) in the individual periods (Table 2a-c), it is clear that the greatest diagnostic benefit is provided by imaging methods with a time distance of no less than six months since AVG creation. In this period, healing of the AVG had already occurred.

DISCUSSION

The clinical manifestation in the early stages of infection is usually minimal and if some symptoms do appear, they are nonspecific. This is sometimes referred to as subclinical infection, when clinical signs are mild, laboratory findings may show increased markers of acute inflammation, and blood cultures are negative⁶. Common signs of inflammation are late only and carry a poor prognosis for the fate of the AVG. A lack of signs and symptoms does not exclude the possibility of a clinically silent graft infection⁷.

Only a few studies have addressed the question of early detection of infection with the rescue of hemodialysis vascular access^{8,9}. Early detection and early diagnosis of AVG infection in a phase of subclinical infection is essential for the correct choice of treatment; a reliable diagnostic method is necessary in order to provide adequate treatment before the development of obvious clinical signs as well as to avoid further complications.

^{18}F -FDG PET/CT is emerging as a promising tool in detecting prosthetic infection in vascular surgery, with a number of studies with excellent results having been published¹⁰⁻¹⁴. According to the literature, ^{99m}Tc -HMPAO-WBC continues to be successfully used in the diagnosis of bacterial infections of vascular prosthesis¹⁵.

Currently, there are no published studies or case reports of using radiopharmaceutical methods in a patent AVG that is both functional and utilized for hemodialysis. It can be assumed that the reason for the existing underuse of radionuclide imaging techniques is the fear of false positivity of the findings due to the accumulation of radiopharmaceuticals at the venipuncture sites¹⁶. We tried to minimize this risk by using the longest possible time between hemodialysis and radionuclide examination and dual-time acquisition of ^{99m}Tc -HMPAO-WBC SPECT.

It is obvious from our results that both imaging methods, i.e. ^{18}F -FDG PET/CT and ^{99m}Tc -HMPAO-WBC SPECT/CT, exhibit significant agreement with the results of our reference methods used to detect early AVG infection (clinical presentation, microbiological test result of the hemodialysis cannula swab, and CRP). For these comparisons, the values of Gwet's agreement coef-

ficient (AC1) reach the levels of “Substantial (Good)” to “Perfect (Very Good)”.

These values were ascertained only if focal (or focal and diffuse) accumulation of radiopharmaceuticals was considered a sign of AVG inflammation (Fig. 1). This fact is consistent with the results of previous ^{18}F -FDG PET/CT studies as well as $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT studies evaluating the importance of scintigraphy in detecting infection of vascular prostheses^{11,12,15}. The non-specific character of a diffusely increased accumulation of ^{18}F -FDG was described by Keidar et al. who found that this finding was observed in up to 92% of noninfected vascular prostheses¹⁰.

Moreover, our results are consistent with the previous publications that evaluated each method on its own and demonstrated a major benefit of both methods in detecting infection of vascular prostheses^{11,12,15}. Of great importance is the fact that the diagnostic accuracy of $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPET is increased significantly with the use of SPECT/CT, in which a more precise locating of increased leukocyte accumulation using CT improves the interpretation of the SPET findings^{13,14}.

Our study deals with the early detection of infection of vascular prostheses using ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT. It is of particular importance that both methods were compared directly as part of a single study.

In early phases after AVG implantation (10 weeks), a higher level of agreement with our reference parameters of infection was achieved with ^{18}F -FDG PET/CT than with $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT imaging. In the following period of 20 to 30 weeks, the benefit of imaging with $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPET/CT reached the level of that with ^{18}F -FDG PET/CT imaging, and in the period of 40 to 50 weeks since surgery, a focal $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT finding was the most significant one. The reason for the above-described trend cannot be clearly elicited from our cohort. Nevertheless, it can be assumed that the healing of the AVG continues with increasing time since surgery and the conditions for detecting infection using $^{99\text{m}}\text{Tc}$ -HMPAO-WBC are improved.

In a comparable time period between the years 2006 and 2009, the rate of AVG infections in our department was 28.3%; all of them resulted in AVG removal and loss of access for hemodialysis⁵. The monitoring of a group of hemodialysis patients with AVG, using the above-described protocol, led to an early detection of AVG infection and allowed for a timely commencement of targeted antibiotic treatment, which resulted in an overall substantial decrease in advanced AVG infections to 11.3%.

The most significant effect of careful patient monitoring using ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT was the possibility to commence antibiotic treatment already in early stages of infection and to prevent it from developing fully. A positive effect of this active therapeutic approach was a reduction in the number of AVGs removed due to advanced infection. It is therefore obvious that in accordance with Husmann et al's conclusion that ^{18}F -FDG PET/CT represents a useful tool in

therapy monitoring of prosthetic vascular graft infection and has an impact on patient management¹⁵.

CONCLUSION

The study results show that focal hyperaccumulation of both ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC can be considered a sign of AVG infection. ^{18}F -FDG PET/CT and $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT can both serve as important tools contributing to early diagnosis of AVG infection. By direct comparison of both hybrid methods, we have found that examination with ^{18}F -FDG PET/CT appears to be more effective in the first months after AVG creation. Both methods have the similar efficiency approximately half a year after AVG implantation, while $^{99\text{m}}\text{Tc}$ -HMPAO-WBC SPECT/CT is slightly more beneficial in the later period.

Only timely administration of antibiotics is capable of preventing the development of advanced AVG infection. If the results of all individual tests are evaluated comprehensively, i.e. in collaboration of a vascular surgeon, microbiologist, nephrologist, and nuclear medicine physician, AVG infection can be detected in time and with appropriate treatment, the number of AVGs removed due to infection can be reduced significantly.

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