Modest utility of quantitative measures in 18F-fluorodeoxyglucose positron emission tomography scanning for the diagnosis of aortic prosthetic graft infection

Ben R. Saleem, MD, a Paul Berger, MD, b Ilonca Vaartjes, PhD, c Bart de Keizer, MD, PhD d Evert-Jan P. A. Vonken, MD, e Riemer H. J. A. Slart, MD, PhD, f Gert Jan de Borst, MD, PhD b and Clark J. Zeebregts, MD, PhD, a Groningen and Utrecht, The Netherlands

Background: The clinical dilemma in suspected aortic graft infection (AGI) is how to noninvasively obtain a reliable proof of infection. In addition to confirming the presence of infection, obtaining information regarding the extent of infection to select a proper strategy for reoperation is also necessary. Therefore, developing a more reliable noninvasive physiologic approach to detect infected prostheses is required. 18F-fluorodeoxyglucose positron emission tomography scanning (18F-FDG PET) has been suggested to have a pivotal role in the detection of AGI. In this study, we assessed the contribution of two (semi) quantitative parameters—maximal standardized uptake value (SUVmax) and tissue-to-background ratio (TBR)—and of two visual parameters—fluorodeoxyglucose (FDG) distribution patterns and visual grading scale—in the final confirmation of the diagnosis of AGI.

Methods: Patients with a central aortic prosthetic graft and symptoms clinically suggestive of AGI were gathered from a prospectively maintained database. Included were those who underwent 18F-FDG PET scanning combined with computed tomography angiography and in whom periprosthetic samples were taken at some stage in the diagnostic process. AGI was considered proven in case of a positive culture and compared with a group with negative cultures. Positive predictive values (PPVs) and negative predictive values (NPVs) were calculated. Receiver operating characteristics curves were used to assess the ability of SUVmax and TBR to identify the presence and absence of AGI (ie, accuracy).

Results: In 37 of 77 patients with suspected AGI, 18FDG-PET and perigraft material for culturing was obtained. The tissue culture was positive in 21 of these 37 patients (56.7%). Mean ± standard deviation SUVmax for proven infection was 8.1 ± 3.7 (range, 3.6-18.5) and TBR was 5.9 ± 2.7 (range, 1.7-13.0). The area under the curve for SUVmax was 0.78 (95% confidence interval, 0.63-0.93). A cutoff value of 8 yielded a PPV of 80% and a NPV of 54%. The area under the curve for TBR was 0.70 (95% confidence interval, 0.52-0.87). A cutoff value of 6 yielded a PPV of 73% and NPV of 52%. The PPVs for the visual grading scale and 18F-FDG distribution patterns were 75% and 61%, respectively; the NPVs were 77% and 67%, respectively.

Conclusions: Our study, performed in a small sample of patients suspected of AGI, showed that the diagnostic abilities of quantitative and visual 18F-FDG PET parameters are modest. (J Vasc Surg 2015;61:965-71.)
has been claimed to be a significant predictor for the presence of infection, but the role of the other parameters has not been established. More recently, a semiquantitative method was suggested for the evaluation of thoracic prosthetic graft infections in a small group in which an SUVmax > 8 in the perigraft area was considered the cutoff value for distinguishing between an infected graft and a noninfected graft. Ideally, one would study a large group of patients with symptoms suggestive of AGI in whom the diagnostic procedures of interest and the current gold standard have been performed. The aim of the present study was to assess the performance of the 18F-FDG PET scan-derived SUVmax, TBR, FDG distribution pattern, and VGS in the diagnosis of AGI in patients with suspected AGI.

METHODS

Patients with a central aortic prosthetic graft were identified from a prospectively maintained database at the University Medical Center Utrecht between January 2006 and June 2013. Medical records of all patients in the database were analyzed to identify those with a central aortic prosthetic graft in whom an AGI was clinically suspected. Clinical symptoms suggestive of AGI included undefined fever, a deep wound infection, an incision fistula, persisting high laboratory infection parameters after central prosthetic vascular graft infection to calculate the SUVmax. This was performed in three dimensions (sagittal, coronal, and transaxial). SUVmax was calculated corresponding to the voxels with the highest 18F-FDG uptake. TBR was defined as SUVmax divided by SUVmax of the caval vein (blood pool). The 18F-FDG distribution pattern was classified as focal or diffuse. The VGS was used to classify the probability of AGI on 18F-FDG PET scanning as low (VGS 0, I, or II) or high (VGS III or IV).

The intensity of 18F-FDG uptake was graded on a 5-point scale as:

- Grade 0, 18F-FDG uptake similar to that in the background;
- Grade 1, low 18F-FDG uptake, comparable with that by inactive muscles and fat;
- Grade II moderate 18F-FDG uptake, clearly visible and higher than the uptake by inactive muscles and fat;
- Grade III, strong 18F-FDG uptake, but distinctly less than the physiologic urinary uptake by the bladder; and
- Grade IV, very strong 18F-FDG uptake, comparable with the physiologic urinary uptake by the bladder.

CTA analysis. CTA imaging was performed, after administration of intravenous contrast, by Multidetector CT Siemens Somatom Definition (Siemens AG Medical Solutions, Forchheim, Germany). CTA scans were assessed on a digital workstation by a radiologist who was blinded for clinical and 18F-FDG-PET data. Current literature regards the following items as predictive for vascular prosthetic graft infection on CTA scanning: the presence of aortoenteric fistula, pseudoaneurysm, intergraft thrombus, hydronephrosis, perigraft fluid (Hounsfield units [HU]), perigraft air, perigraft soft tissue attenuation (HU), focal bowel wall thickening (mm), discontinuity of the aneurysmal wrap (mm), maximal diameter of the largest air bubble, maximal diameter of the fluid collection (mm), and visual judgment by a radiologist. Scoring these items was complemented by a visual judgment for the likelihood of AGI. The likelihood of AGI was classified as low or high, based on a visual scale judgement from 10 to 100 points. A low probability was defined from 10 to 54 points and a high probability from 55 to 100 points.
**Statistical analysis.** Baseline characteristics are presented as mean ± standard deviation or percentages. The diagnostic value of 18F-FDG PET for detecting AGI was assessed for the following 18F-FDG PET outcomes: SUVmax, TBR, 18F-FDG distribution pattern, and VGS. Furthermore, to measure the ability of these parameters in predicting presence of AGI, a receiver operating characteristic curve (ROC) was plotted and area under the ROC curve (AUC) with 95% confidence interval (CI) was calculated. The diagnostic ability was classified by the AUC values as follows: 0.5 to 0.6 failed, 0.6 to 0.7 poor, 0.7 to 0.8 fair, and 0.8 to 1.0 good. Cutoff points with the highest sensitivity and specificity from the AUC curves were used to determine a threshold value for TBR and SUVmax. Next, as for the VGS, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

The diagnostic value of CTA for detecting AGI was assessed for the CTA characteristics of aortoenteric fistula, pseudoaneurysm, intergraft thrombus, hydronephrosis, perigraft fluid, perigraft air, perigraft soft tissue, focal bowel wall thickening and discontinuity of the aneurysmal wrap. For these CTA characteristics sensitivity, specificity, PPV, and NPV were calculated. Data were collected and processed using the IBM SPSS 20.0 software (IBM Corp, Armonk, NY).

**RESULTS**

**Patient selection.** We identified 37 patients who met the inclusion criteria. Specimens for microbiologic analysis were obtained in eight patients through percutaneous puncture and in 29 patients through surgery. Positive cultures were found in 21 patients during surgery (n = 15) or puncture (n = 6). The Fig shows the pathways for including patients with a suspected AGI.

**Baseline patient characteristics.** The 37 patients (73% male) were a mean age of 66 ± 8.0 years (range, 50-86 years) at the time the 18F-FDG PET examination took place. All implants were prosthetic grafts and implanted in the thoracoabdominal-iliac tract. Mean duration from graft implantation until 18F-FDG PET scanning was 5.3 ± 6.0 years (range, 0.05-18.31 years). Antibiotic treatment was initialized before surgical treatment in 89% of the patients. Of those patients with a positive culture, 20 (95%) received preoperative antibiotics compared with 13 of the patients (81%) with a negative culture result. Patient characteristics are described in Table I. The initial treatment in 23 patients (62%) was because of aneurysmal disease. Operative details are listed in Table II. An AGI was proven in 21 of 37 patients, yielding a prior probability for the presence of AGI of 57%.

<table>
<thead>
<tr>
<th>Table I. Baseline characteristics</th>
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<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
</tr>
<tr>
<td>Preoperative antibiotic use</td>
</tr>
<tr>
<td>Comorbidities&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetic</td>
</tr>
<tr>
<td>Current tobacco use</td>
</tr>
<tr>
<td>Hypertension, controlled by &gt;0 drugs</td>
</tr>
<tr>
<td>Cardiac disease (SVS class 1, 2 or 3)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Renal status (creatinine level &lt;2.4 mg/dL)</td>
</tr>
<tr>
<td>Pulmonary status (SVS class 1 or 2)</td>
</tr>
<tr>
<td><strong>SD,</strong> Standard deviation; <strong>SVS,</strong> Society for Vascular Surgery.</td>
</tr>
<tr>
<td><strong>a</strong>Defined according the Ad Hoc Committee on Reporting Standards.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table II. Graft location and material at the initial operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Underlying disease</td>
</tr>
<tr>
<td>Aneurysmatic</td>
</tr>
<tr>
<td>Occluding</td>
</tr>
<tr>
<td><strong>Graft location</strong></td>
</tr>
<tr>
<td>Aortoiliac</td>
</tr>
<tr>
<td>Axillofemoral</td>
</tr>
<tr>
<td><strong>Type of reconstruction</strong></td>
</tr>
<tr>
<td>Open</td>
</tr>
<tr>
<td>Endovascular</td>
</tr>
<tr>
<td><strong>Graft material</strong></td>
</tr>
<tr>
<td>Dacron&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Endurant&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>DuPont, Wilmington, Del.  
<sup>b</sup>Medtronic, Minneapolis, Minn.
Mean SUVmax for proven infections was 8.1 ± 3.7 (range, 3.6-18.5) compared with 5.0 ± 2.3 (range, 2.7-11.0) for the other group (Table III). The AUC of SUVmax was classified as fair, with a value of 0.78 (95% CI, 0.63-0.93). Sensitivity, specificity, PPV, and NPV, were calculated for SUVmax cutoff values of 4, 6, 8, and 10 (Table IV). When the cutoff point was set at a value $\geq$8 to indicate a positive test, the PPV was 80% and the NPV was 54%.

**TBR.** The mean TBR was 5.9 ± 2.7 (range, 1.7-13.0) for proven infections compared with 4.1 ± 2.1 (range, 1.7-8.5; Table III). The ability of TBR in predicting the presence of AGI was classified as fair, with an AUC of 0.70 (95% CI, 0.52-0.87). Sensitivity, specificity, PPV, and NPV, were calculated for TBR cutoff values of 2, 4, 6, and 8 (Table V). When we put the cut point at the value $\geq$6 to indicate a positive test, the PPV was 73% and the NPV was 52%.

**Visual 18F-FDG-PET interpretation.** The VGS showed suspicion for AGI high in 24 patients (65%). AGI was eventually proven in 18 of these 24 patients (75%), leading to a PPV of 73% and the NPV was 52%.

**DISCUSSION**

This study is among the first to report the use of (semi) quantitative (SUVmax and TBR) and qualitative (distribution patterns and VGS) parameters in the diagnostic workup of patients with suspected AGI. The ability of these four parameters to yield a definite proof of AGI is modest. The typical patient with AGI is fragile and with various comorbidities. A reliable imaging tool is essential for the diagnosis of AGI. A false-negative test result may refrain the patient from proper antibiotic or surgical treatment.

### Table III. (Semi-)quantitative 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) values

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total group (n = 37), mean ± SD (range)</th>
<th>Positive cultures (n = 21), mean ± SD (range)</th>
<th>Negative cultures (n = 16), mean ± SD (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUVmax</td>
<td>6.7 ± 3.5 (2.7-18.5)</td>
<td>8.1 ± 3.7 (3.6-18.5)</td>
<td>5.0 ± 2.3 (2.7-11.0)</td>
</tr>
<tr>
<td>TBR</td>
<td>5.1 ± 2.7 (1.7-13.0)</td>
<td>5.9 ± 3.0 (2.5-13.2)</td>
<td>4.1 ± 2.1 (1.7-8.5)</td>
</tr>
</tbody>
</table>

**Table IV. Cutoff for maximum standardized uptake value (SUVmax)**

<table>
<thead>
<tr>
<th>SUVmax value</th>
<th>Patients with positive test, No.</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>18</td>
<td>90 (77-100)</td>
<td>38 (14-61)</td>
<td>64 (7-82)</td>
<td>75 (45-100)</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>65 (44-85)</td>
<td>69 (46-92)</td>
<td>72 (52-93)</td>
<td>61 (39-84)</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>40 (19-62)</td>
<td>88 (71-100)</td>
<td>80 (55-100)</td>
<td>54 (34-73)</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>25 (6-44)</td>
<td>94 (82-100)</td>
<td>83 (54-100)</td>
<td>50 (32-68)</td>
</tr>
</tbody>
</table>

**Table V. Cutoff values for tissue-to-background ratio (TBR)**

<table>
<thead>
<tr>
<th>TBR value</th>
<th>Patients with positive test, No.</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>20</td>
<td>100 (100-100)</td>
<td>19 (1-38)</td>
<td>61 (44-77)</td>
<td>100 (100-100)</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>65 (44-86)</td>
<td>56 (32-81)</td>
<td>65 (44-86)</td>
<td>56 (32-81)</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>40 (19-62)</td>
<td>81 (62-100)</td>
<td>73 (46-99)</td>
<td>52 (32-72)</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>20 (3-38)</td>
<td>94 (82-100)</td>
<td>80 (45-100)</td>
<td>48 (31-66)</td>
</tr>
</tbody>
</table>

CI, Confidence interval; NPV, negative predictive value; PPV, positive predictive value.

**SUVmax value.** Mean SUVmax for proven infections was 8.1 ± 3.7 (range, 3.6-18.5) compared with 5.0 ± 2.3 (range, 2.7-11.0) for the other group (Table III). The AUC of SUVmax was classified as fair, with a value of 0.78 (95% CI, 0.63-0.93). Sensitivity, specificity, PPV, and NPV, were calculated for SUVmax cutoff values of 4, 6, 8, and 10 (Table IV). When the cutoff point was set at a value $\geq$8 to indicate a positive test, the PPV was 80% and the NPV was 54%.

**TBR.** The mean TBR was 5.9 ± 2.7 (range, 1.7-13.0) for proven infections compared with 4.1 ± 2.1 (range, 1.7-8.5; Table III). The ability of TBR in predicting the presence of AGI was classified as fair, with an AUC of 0.70 (95% CI, 0.52-0.87). Sensitivity, specificity, PPV, and NPV, were calculated for TBR cutoff values of 2, 4, 6, and 8 (Table V). When we put the cut point at the value $\geq$6 to indicate a positive test, the PPV was 73% and the NPV was 52%.

The interobserver agreements were calculated between the two nuclear medicine physicians and were excellent. The average ratings and standard deviations were quite equal, and the correlations among the ratings of SUVmax, TBR, and VGS were 0.89, 0.80, and 0.74, respectively. The interobserver agreement regarding the likelihood for AGI was 0.49 (fair).

**CTA characteristics.** On the basis of the CTA analysis, all of the 37 patients (100%) were judged positive for AGI. In 21 of these patients, AGI was eventually proven by positive cultures, yielding a PPV of 57%. The sensitivity, specificity, PPV, and NPV, of the various CT parameters are reported in Table VII.

**DISCUSSION**

This study is among the first to report the use of (semi) quantitative (SUVmax and TBR) and qualitative (distribution patterns and VGS) parameters in the diagnostic workup of patients with suspected AGI. The ability of these four parameters to yield a definite proof of AGI is modest.

The typical patient with AGI is fragile and with various comorbidities. A reliable imaging tool is essential for the diagnosis of AGI. A false-negative test result may refrain the patient from proper antibiotic or surgical treatment.
Table VI. Qualitative $^{18}$F-fluorodeoxyglucose positron emission tomography ($^{18}$F-FDG-PET) values

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal/diffuse</td>
<td>90 (78-100)</td>
<td>25 (4-46)</td>
<td>61 (44-78)</td>
<td>67 (29-100)</td>
</tr>
<tr>
<td>VGS$^a$</td>
<td>86 (71-100)</td>
<td>63 (39-86)</td>
<td>75 (58-92)</td>
<td>77 (54-100)</td>
</tr>
</tbody>
</table>

$^a$Grade 0, $^{18}$F-FDG uptake similar to that in the background; grade I, low FDG uptake, comparable with that by inactive muscles and fat; grade II, moderate FDG uptake, clearly visible and higher than the uptake by inactive muscles and fat; grade III, strong FDG uptake, but distinctly less than the physiologic urinary uptake by the bladder; grade IV, strong FDG uptake, comparable with the physiologic urinary uptake by the bladder. Grade 0, I, and II are considered low probability for AGI; grade III and IV are considered high probability for AGI.

Table VII. Diagnostic value of several computed tomography (CT) scan outcomes for detecting aorta graft infection (AGI)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortoenteric fistula</td>
<td>7</td>
<td>35 (14-56)</td>
<td>60 (35-85)</td>
<td>54 (27-81)</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
<td>4</td>
<td>21 (3-39)</td>
<td>64 (39-89)</td>
<td>44 (12-77)</td>
</tr>
<tr>
<td>Intergraft thrombus</td>
<td>9</td>
<td>45 (23-67)</td>
<td>53 (28-79)</td>
<td>56 (32-81)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>3</td>
<td>15 (0-31)</td>
<td>53 (28-79)</td>
<td>30 (32-81)</td>
</tr>
<tr>
<td>Perigraft fluid</td>
<td>7</td>
<td>35 (14-56)</td>
<td>73 (51-96)</td>
<td>64 (35-92)</td>
</tr>
<tr>
<td>Air</td>
<td>6</td>
<td>30 (10-50)</td>
<td>73 (51-96)</td>
<td>60 (30-90)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>20</td>
<td>100 (100-100)</td>
<td>7 (0-19)</td>
<td>59 (42-75)</td>
</tr>
<tr>
<td>Focal bowel wall thickening</td>
<td>4</td>
<td>20 (3-8)</td>
<td>67 (43-91)</td>
<td>44 (12-77)</td>
</tr>
<tr>
<td>Discontinuity of the aneurysmal wall</td>
<td>2</td>
<td>10 (0-23)</td>
<td>100 (100-100)</td>
<td>100 (100-100)</td>
</tr>
</tbody>
</table>

$^a$Confidence interval; NPV, negative predictive value; PPV, positive predictive value; VGS, visual grading scale.

and may negatively affect the prognosis. A false-positive test result may result in unneeded extensive surgical procedures.$^{16}$

Reports on the use of $^{18}$F-FDG PET in AGI are limited. These reports seem to indicate that $^{18}$F-FDG PET scanning has a better diagnostic accuracy than CTA for the detection of AGI and may very well prove to be the new gold standard for minimal invasive AGI diagnosis.$^6-10$ However, most evidence comes from case series rather than cohort studies. Focal uptake intensity compared with a diffuse or linear $^{18}$F-FDG distribution along the graft was studied earlier and was associated with a vascular graft infection with a PPV of 91% and a NPV of 95%. In this study, we could not confirm these high predictive values. The main difference between the studies is that we included only patients in whom AGI was proven through cultures, whereas Spacsek et al$^{10}$ also included clinically proven AGI, increasing the prevalence of AGI and with that potentially the PPV.

The intensity of $^{18}$F-FDG uptake is most commonly assessed using a grading scale of 1 to 5 points. This grading scale is analogous to the VGS of Deauville, originally developed for the interpretation of $^{18}$F-FDG PET scans made for lymphomas,$^{12}$ and to the scale of 0 to 4 points of Stumpe et al,$^{17}$ used for the detection of orthopedic infections. Because both scales only address the uptake intensity, they are unable to firmly differentiate between infection and inflammation. PPV and NPV of an $^{18}$F-FDG PET scan using only increased uptake as a marker for graft infection have been reported to be 56% and 93%, respectively.$^7$ In our study, the prior probability for the presence of AGI was 57%. Adding VGS information resulted in a PPV up to 75%. Therefore, the VGS may be of use in the assessment of presence of AGI in patients with suspected AGI. However, confirmation in larger studies is needed.

SUVmax measurements are known to be influenced by many different factors of a technical and biologic nature and are difficult to compare across hospitals.$^{18}$ Only one small case series (n = 8) reported the use of SUVmax in the diagnosis of AGI. A cutoff value of >8 showed a sensitivity of 100% and specificity of 80% whether or not an aortic graft was infected.$^{19}$ TBR seems to be more reproducible than the SUV.$^{18}$ We found TBR was fairly accurate in diagnosing AGI, with an AUC of 0.70; yet, a clinician uses cutoff values rather than AUC. The use of cutoff values, however, leads to a debate regarding overdiagnosis and underdiagnosis and its consequences. In AGI, we assume a high PPV is preferable to a NPV, therefore needing a relatively high value of SUVmax or TBR.

CTA is still considered the gold standard for diagnosing AGI.$^4,7,20$ The amount of false-negative CTA results, however, is considerably high, especially in the presence of low-grade infections. Overall specificity has been reported up to 100% and an overall sensitivity of 56%.$^{15}$ In our study, we were unable to confirm these results. The specificity of the various CT parameters ranged between 7% and 100%, the sensitivity ranged between
10% and 100%, PPV ranged between 30% and 100%, and NPV ranged between 32% and 100% (Table VII).

Some aspects of the study need to be addressed. Ideally in a diagnostic study, all patients are enrolled who are suspected to have the studied disease and undergo all of the diagnostic tests that are being investigated, together with a gold standard to assess the final diagnosis. Clearly, that is difficult in studies of AGI. Not all diagnostic tests are uniformly performed, and the gold standard cannot be obtained in all patients for several reasons. That diagnostic studies in AGI may yield biased results (underestimating or overestimating the accuracy) is therefore inevitable. The extent to which bias occurred in our study is difficult to estimate.

Furthermore, the difference in positive and negative cultures might be due to the use of antibiotic therapy in patients when AGI is suspected. Antibiotic therapy was started in 89% of the patients and might have yielded false-negative cultures. Routine microbiologic techniques started in 89% of the patients and might have yielded patients when AGI is suspected. Antibiotic therapy was expected to have the studied disease and undergo all of the diagnostic tests that are being investigated, together with a gold standard to assess the final diagnosis. Clearly, that is difficult in studies of AGI. Not all diagnostic tests are uniformly performed, and the gold standard cannot be obtained in all patients for several reasons. That diagnostic studies in AGI may yield biased results (underestimating or overestimating the accuracy) is therefore inevitable. The extent to which bias occurred in our study is difficult to estimate.

Furthermore, the difference in positive and negative cultures might be due to the use of antibiotic therapy in patients when AGI is suspected. Antibiotic therapy was started in 89% of the patients and might have yielded false-negative cultures. Routine microbiologic techniques can sometimes be insufficient in isolating the microorganism from perigraft material.\textsuperscript{21, 22} Use of sonication techniques have been described to identify indolent gram-positive microorganisms.\textsuperscript{21, 22} However, these sonication techniques were not applied in this retrospective study because they were not available in our hospital.

We restricted the present study to only those patients with all information available. However, this does not reflect current clinical practice because AGI may also be based on clinical symptoms and imaging only, irrespective of the culturing results. Therefore, our diagnostic test results may be an overestimation of what is found in real clinical life. Furthermore, this resulted in the loss of several patients during the process for which information was lacking. Whether this is selective loss (ie, different among those with and without AGI and different among those with and without clear imaging results) is unknown to us.

This study should also be conducted prospectively to prevent these kinds of limitations. Our study reflects the difficulties with performing diagnostic studies in patients with a rare but severe disease in whom the assessment of a diagnosis is difficult to establish. As such, we call for a well-developed protocol and (inter-) national collaboration to set up future diagnostic studies on AGI.

CONCLUSIONS

Our study, performed in a small sample of patients suspected of AGI, showed that the diagnostic ability of \textsuperscript{18}F-FDG parameters and VGS is modest.

We acknowledge Dr Andor W.J.M. Glaudemans, Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands, for technical evaluation of the \textsuperscript{18}F-FDG PET scans.

AUTHOR CONTRIBUTIONS

Conception and design: GB, CZ
Analysis and interpretation: IV, BK, EV, RS

Data collection: BS, PB
Writing the article: BS, PB
Critical revision of the article: BS, PB, IV, BK, EV, RS, GB, CZ

Final approval of the article: BS, PB, IV, BK, EV, RS, GB, CZ

Statistical analysis: IV

Obtained funding: Not applicable

Overall responsibility: CZ

B.S. and P.B. contributed equally and share first authorship.

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Submitted Sep 12, 2014; accepted Nov 9, 2014.

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