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Efficacy of 18F-fluorodeoxyglucose positron emission tomography/computed tomography in anticipating the progression of vascular graft and endograft infection: A retrospective multicenter study

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Abstract

Background

Vascular graft and endograft infection (VGEI) is a life-threatening complication. In this study, we evaluated the efficacy of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) in anticipating the clinical progression of VGEI in patients presenting with fever of unknown origin (FUO) after aortic surgery.

Methods

This retrospective multicenter study enrolled 29 patients with FUO after aortic surgery (2012–2020). Patients underwent FDG-PET/CT upon admission; the SUV_{max} at the site of the greatest pathological uptake surrounding the graft was measured. The primary endpoint was progression to "proven VGEI," defined by the Management of Aortic Graft Infection Collaboration criteria. Independent predictors of VGEI progression were identified using multivariable Cox regression.

Results

The median follow-up period was 771 [172–1418] days; the median interval from PET/CT to VGEI diagnosis was 19 [5–60] days. Progression to VGEI was observed in 13 patients (44.8%). Multivariable analysis identified SUV_{max} surrounding the graft as the sole independent predictor of VGEI progression (hazard ratio: 1.40; 95% confidence interval: 1.04–1.89). Receiver operating characteristic analysis revealed an optimal SUV_{max} cut-off of 6.675 (area under the curve = 0.937; sensitivity 100%, specificity 87.5%). In the High-SUV_{max} group ($\geqq$ 6.675, n = 15), 13 patients (86.7%) experienced VGEI progression, 10 underwent surgical intervention, and six died from VGEI-related causes. Conversely, no patients in the Low-SUV_{max} group (< 6.675) exhibited VGEI progression or VGEI-related death.

Conclusions

^{18}F-FDG-PET/CT is highly effective in predicting the clinical progression of VGEI. High FDG uptake strongly reveals a high risk of advancement, indicating that early surgical intervention should be considered to prevent catastrophic complications.

BACKGROUND

Vascular graft and endograft infection (VGEI) is a rare, but still catastrophic complication following aortic surgery, including both conventional graft replacement (GR) and endovascular repair, associated with high rates of mortality and morbidity. [1–5] Inflammation caused by VGEI can gradually spread to

adjacent organs, potentially leading to the formation of life-threatening fistulae between the aorta and neighboring structures. Such complications usually complicate radical surgical procedures as they necessitate additional resection of the perforated organs alongside complete removal of the prosthesis and subsequent aortic reconstruction. Consequently, these challenges often lead to a poor prognosis for those with VGEI. [1] Although early diagnosis and timely radical procedures are essential for the optimal management of VGEI, identifying VGEI in its initial stages remains clinically challenging as typical computed tomography (CT) findings are often absent during the early phase (Fig. 1). [1–2] The Management of Aortic Graft Infection Collaboration (MAGIC) criteria provide a robust framework for diagnosing established VGEI; however, the clinical imperative lies in the precise anticipation of disease progression before it reaches a catastrophic state, thereby facilitating earlier therapeutic decision-making. [6]

^{18}F-fluorodeoxyglucose positron emission tomography and CT (^{18}F-FDG-PET/CT) is a well-established modality widely used for clinical decision-making and staging in oncology. [7–8] Furthermore, it is highly effective at detecting metabolic activity in inflammatory cells during the acute phase of infection. [9–11] In cases of fever of unknown origin (FUO), FDG-PET/CT is reportedly superior to other scintigraphy techniques in localizing infectious foci. [10–11] Clinically, abnormal FDG uptakes surrounding native vessels or prostheses have been observed in those with various type of arteritis, [12–13] infected aneurysms, [13] and established VGEI. [14–18] However, the specific role of ^{18}F-FDG-PET/CT in anticipating the future clinical progression and severity of VGEI remains to be fully elucidated.

In this retrospective multicenter study, we aimed to assess the efficacy of ^{18}F-FDG-PET/CT in anticipating the progression of VGEI in patients presenting with FUO following aortic surgery.

METHODS

Patient recruitment

This retrospective multicenter study was approved by the Institutional Review Board (Ethics Committee) of our hospital. Informed consent was obtained from all patients through written and verbal forms.

Between May 2012 and September 2020, 34 patients with past aortic surgery were admitted with a high fever, and underwent FDG-PET/CT. To evaluate the efficacy of PET/CT in the undiagnosed phase, five patients were excluded based on the following criteria: two patients with suspected recurrence of VGEI after prior radical or palliative operations, two patients with ascending graft infection secondary to chronic osteomyelitis, and one patient with multiple cerebral abscess of known origin. Consequently, 29 FUO patients were enrolled in this study. The median age (interquartile range [IQR]) was 72.0 [63.0–78.0] years old, which included 25 men and 4 women. The details of the patient characteristicsand detailed history of previous aortic surgeries, including open GR, thoracic endovascular aortic repair (TEVAR), and endovascular aortic repair (EVAR), are summarized in Table 1 and 2. All clinical management and

imaging assessments were conducted by the OSCAR group, a specialized vascular surgery consortium, ensuring consistency in patient care and evaluation criteria across all participating centers.

Study protocol and clinical endpoint

Upon admission, all the patients underwent laboratory tests (including blood culture), contrast-enhanced CT, and ^{18}F-FDG-PET/CT. At that time, they could not be absolutely diagnosed with VGEI. All patients were initially treated with empirical antibiotic therapy.

The primary clinical endpoint was defined as the **progression of VGEI**, identified by the presence of at least one of the following criteria based on clinical and imaging findings:

1. Clinical progression: A further increase in inflammatory biomarkers such as C-reactive protein (CRP) level and white blood cell (WBC) count relative to baseline or the new onset of specific symptoms such as back, chest, or abdominal pain.

2. Imaging progression (CT findings): Based on previous literature, [1-2, 14-18] representative CT findings indicative of VGEI progression include the de novo appearance of aorto-pulmonary or aorto-enteric fistula, peri-graft air collection, anastomotic pseudo-aneurysm, intra-graft/stent-graft thrombus formation, new peri-graft fluid or soft-tissue attenuation, enlargement of aneurysmal sacs, or expansion of existing peri-graft fluid collections.

These findings were evaluated by an experienced radiologist blinded to the PET/CT results; the final clinical status was adjudicated by the OSCAR group via consensus, adhering strictly to the MAGIC criteria.[6] Accordingly, the 29 enrolled patients were categorized into the **Progression group** (n = 13) or **Non-progression group** (n = 16). Independent predictors of progression were identified using multivariable-adjusted Cox proportional hazards regression analysis.

Cut-off value of SUV_{max} concerning VGEI progression

To establish a clinically relevant threshold for risk stratification, the optimal cut-off value of SUV_{max} for predicting future VGEI progression was determined via receiver operating characteristic (ROC) curve analysis. On the basis of this value, the 29 patients were divided into High-SUV_{max} and Low-SUV_{max} groups. The prognostic impact of this stratification was then evaluated; overall survival and VGEI-related mortality were assessed using Kaplan–Meier survival curves, with differences between the High-SUV_{max} and Low-SUV_{max} groups compared using the log-rank test.

^{18}F-FDG-PET/CT protocol

All patients fasted for at least 6 hours before ^{18}F-FDG-PET/CT, and their blood glucose levels were within normal limits. PET/CT images were acquired 60 minutes after systemic administration of ^{18}F-FDG (185 MBq). PET and CT images were fused; radioactivity was reconstructed using Syngo.via (version VB60A;

Siemens Healthineers AG, Erlangen, Germany) at Osaka University and the VOX-BASE II system (J-MAC system, Japan) at Suita Tokushukai Hospital. The SUV_{max} in the area of the greatest pathological FDG uptake surrounding the prosthesis was measured. As SUV_{max} represents the single highest pixel intensity within the region of interest (ROI), this measurement is inherently robust against variations in ROI size, ensuring consistency in metabolic quantification across the study cohort. Measurements were reviewed by independent radiologists blinded to clinical outcomes.

Statistical analysis

Continuous variables are expressed as medians and IQRs, and categorical variables are presented as counts and proportions. The baseline characteristics of the Progression and Non-progression groups were compared using the Welch's *t*-test for continuous variables and Fisher's exact test for categorical variables. The association between potential parameters, including SUV_{max}, and the risk of VGEI progression was assessed using hazard ratios (HR) and 95% confidence intervals (CI) via Cox proportional hazards regression. Variables with $p < .10$ in the univariable analysis were included in the multivariable model to identify independent predictors. Statistical significance was set at $p < 0.05$. Subsequently, ROC curve analysis was performed to identify the optimal cut-off value of SUV_{max} for anticipating VGEI progression. All statistical analyses were performed using JMP Pro 19.0.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Clinical Outcomes and Progression of VGEI

Of the 29 patients, 13 were identified as having VGEI progression (Progression group), whereas 16 showed no evidence of progression (Non-progression group). In the Progression group, the median interval from PET/CT to the diagnosis of progression was 19.0 [8.5–57.5] days. Blood cultures were positive in 10 patients (76.9%). Regarding clinical management in the Progression group, ten patients underwent surgical intervention, six received radical procedures (complete resection of infected tissue with omental wrapping), three underwent palliative procedures (two abscess drainages and one bowel disconnection), and one underwent an emergent operation for rupture of anastomotic pseudoaneurysm. The remaining three patients received conservative antibiotic therapy alone owing to surgical contraindications. All three patients who received conservative treatment died of VGEI-related causes. Among the surgical cases, three deaths occurred: one following palliative therapy due to a subsequent aorto-duodenal fistula, one requiring an emergent operation for rupture of a pseudo-aneurysm leading to acute hemorrhagic shock, and another following radical procedure for sepsis. In contrast, all 16 patients in the Non-progression group were successfully discharged after receiving antibiotic therapy alone.

Optimal Predictors of VGEI Progression

Univariate and multivariate Cox proportional hazards regression analyses were performed to identify predictors of VGEI progression (Table 3). Univariable analysis identified five potential predictors: SUV_{max} around the graft (HR:1.19; 95% CI:1.05–1.34; p = 0.005), age (HR:0.939; 95% CI:0.894–0.985; p = 0.014), positive blood culture (HR:3.98; 95% CI:0.867–18.3; p = 0.043), platelet count (HR:0.952; 95% CI:0.890–1.00; p = 0.076), and left ventricular ejection fraction (HR:0.940; 95% CI:0.886–0.996; p = 0.037).

In the multivariable-adjusted model, SUV_{max} was identified as the sole independent predictor of VGEI progression (HR:1.40; 95% CI:1.04–1.89; p = 0.005) in the present study.

Prognostic Value of SUV_{max} and Kaplan–Meier Analysis

To measure the SUV_{max} cut-off value concerning VGEI progression, ROC curve analysis was conducted. ROC curve analysis yielded an optimal SUV_{max} cut-off value of **6.675** for anticipating VGEI progression (p < .0001), with an area under the curve (AUC) of 0.9369, a sensitivity of 100%, and a specificity of 87.5%, respectively.

Subsequently, the patients were categorized into the following two groups based on the cut-off value: Low-SUV_{max} group (< 6.675, n = 14) and High-SUV_{max} group (≧ 6.675, n = 15). In the Low-SUV_{max} group, no patients experienced VGEI progression or VGEI-related death. Although the all-cause mortality rate was 21.4% (n = 3) in this group, these deaths were entirely attributed to non-VGEI causes, including cancer (n = 2) and aspiration pneumonia (n = 1). In contrast, 13 of the 15 patients (86.7%) in the High-SUV_{max} group experienced VGEI progression. Kaplan–Meier analysis demonstrated a significantly higher rate of VGEI-related mortality in the High-SUV_{max} group compared with the Low-SUV_{max} group (log-rank test, p = 0.015; Figure 2). Overall survival rate was lower in the High-SUV_{max} groups than in the Low-SUV_{max} group; however, the difference was not significant (log-rank test, p = 0.153; Figure 2).

DISCUSSION

The present study demonstrates that the SUV_{max} around prosthetic grafts is a potent predictor of VGEI progression, providing a quantitative clinical signal that transcends systemic inflammatory biomarkers. In the human body, FDG, a glucose analog, is transported into cells by glucose transporters (GLUTs) via the same pathway as glucose. Although this mechanism is well-characterized particularly in malignant oncology, [7-8] GLUTs are also overexpressed in activated neutrophils, macrophages, and lymphocytes during the acute inflammatory phase.[9] Previous studies have already reported abnormal ^{18}F-FDG uptakes around the arterial walls in some types of arteritis, such as Takayasu arteritis. [12-13] Given these premises, we hypothesized that intense ^{18}F-FDG uptake around a prosthesis could reflect a significant local accumulation of active inflammatory cells, such as neutrophils and macrophages. Consequently, SUV_{max} could provide a more precise assessment of localized inflammation severity in VGEI than systemic inflammatory biomarkers such as WBC count or serum CRP levels. While the diagnostic utility of ^{18}F-FDG-PET/CT for VGEI has been previously reported, [13,17] to the best our

knowledge, the present study is the first to establish its efficacy as a prognostic tool for clinical progression instead of as a diagnostic tool in itself.

Despite recent advances in aortic surgery, VGEI remains a life-threatening complication with mortality rates ranging from 25% to 75%. [3-4] The primary clinical challenge lies in the difficulty of achieving an early and precise diagnosis. The MAGIC criteria have significantly improved diagnostic standards by integrating clinical, microbiological, and imaging evidence. [6] However, cases meeting the "proven" VGEI criteria, often characterized by definitive CT findings, frequently represent an advanced stage of the disease. By the time such structural findings are apparent, the infection may have already extended to neighboring tissues, inevitably increasing the complexity and risks of subsequent management. Therefore, analogous to the clinical paradigm in oncology where tumor marker thresholds provide critical indicators, early detection is essential to enable intervention at an optimal timing. Although the MAGIC criteria recognize FDG-PET/CT as a useful imaging modality, they are primarily positioned as a component of the diagnostic framework. [6] Previous studies have demonstrated that intense FDG uptake is often evident at a relatively early clinical phase, well before the appearance of specific CT findings (e.g., gas collection or fistula formation). [18-20] In our cohort, the median interval from PET/CT to VGEI diagnosis was 19 [IQR: 5–60] days, as highlighted in Figure 1. Thus, we propose that FDG-PET/CT should not be interpreted merely as a component for achieving a "proven" VGEI diagnosis according to the MAGIC criteria; instead, it functions as a potent predictive tool for identifying the progression toward "proven" VGEI at an early clinical phase, the critical window when empirical treatment is typically initiated. Notably, in most of the Progression group, the site of the maximal SUV_{max} on initial FDG-PET/CT spatially correlated with the anatomical site where subsequent structural complications, such as pseudoaneurysm or fistula formation, developed. This strong spatiotemporal correlation reinforces the utility of SUV_{max} as a reliable **“predictive alarm”** for localized graft infection.

Although FDG-PET/CT serves as a minor diagnostic criterion in the MAGIC framework, traditionally relying on subjective, qualitative descriptors such as “focal” uptake, our study shifts the paradigm toward objective quantitative analysis. [6,9-11] By identifying these high-risk patients earlier, clinicians can shift from a 'reactive' wait-and-see approach to a more 'proactive' surgical strategy, potentially preventing catastrophic complications. By establishing a validated SUV_{max} threshold, we introduce a proactive risk-stratification indicator conceptually distinct from the MAGIC diagnostic framework. Much like tumor markers in oncology, this quantitative cut-off acts as a "predictive alarm" for impending disease progression instead of defining the diagnosis itself. Although MAGIC remains the gold standard for diagnosing VGEI, our approach provides a complementary prognostic dimension. Identifying high-risk patients before the development of definitive "proven" VGEI, particularly those at risk of severe complications such as aorto-enteric fistula, facilitates earlier clinical vigilance and optimizes therapeutic timing. This strategy may mitigate the procedural complexity of late-stage interventions, ultimately leading to improved patient outcomes.

Limitations

The results of this study should be interpreted with caution because of certain limitations. First, the sample size was relatively small (n = 29), reflecting the rarity of VGEI. Although our SUV_{max} threshold demonstrates clinical potential, future large-scale, prospective multicenter studies are essential to validate its generalizability and establish a definitive optimal cut-off value. Second, the effects of pre-admission antibiotic therapy should be considered. Most patients were referred to our center after receiving empiric antibiotics for FUO, which may have attenuated ^{18}F-FDG uptake and potentially led to an underestimation of the SUV_{max}.

Finally, although our findings support earlier therapeutic intervention, VGEI outcomes are multifactorial, being influenced by bacterial virulence (e.g., MRSA), host immune status, and frailty. [1, 21] The European Society for Vascular Surgery (ESVS) guidelines currently categorize partial excision as Class IIb and Level C. [2] Therefore, extended follow-up is essential to precisely determine the long-term durability and safety of surgical strategies tailored through quantitative PET assessment.

CONCLUSION

In conclusion, this study identifies SUV_{max} as a potent, objective prognostic indicator for VGEI progression. By shifting from subjective visual interpretation to quantitative risk stratification, ^{18}F-FDG-PET/CT serves as a critical "predictive alarm" that allows for the identification of high-risk patients before the development of definitive "proven" VGEI. Although the MAGIC criteria remain the gold standard for clinical diagnosis, our findings suggest that integrating SUV_{max}-based prognostic assessment into clinical pathways facilitates earlier surgical vigilance and optimizes therapeutic timing. This quantitative approach may mitigate the procedural complexity associated with late-stage radical interventions and potentially improve long-term outcomes for patients with VGEI.

Abbreviations

AUC: Area under the curve; CI: Confidence interval; CRP: C-reactive protein; CT: Computed tomography; EVAR: Endovascular aortic repair; FDG: Fluorodeoxyglucose; FUO: Fever of unknown origin; GLUTs: Glucose transporters; GR: Graft replacement; HR: Hazard ratio; IQR: Interquartile range; MAGIC: Management of Aortic Graft Infection Collaboration; MRSA: Methicillin-resistant Staphylococcus aureus; PET: Positron emission tomography; ROC: Receiver operating characteristic; ROI: Region of interest; SUV_{max}: Maximal standardized uptake value; TEVAR: Thoracic endovascular aortic repair; VGEI: Vascular graft and endograft infection; WBC: White blood cell;

Declarations

Ethics Approval and Consent to Participate: This study was approved by the ethics committee of our hospital (IRB approval Number in Osaka university Graduate School of Medicine, and Osaka General Medical Center: 16105-5, and 26-2001, respectively). Written and verbal informed consent was obtained from all enrolled patients.

Consent for Publication: Not applicable.

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Author Contributions:

Conceptualisation: TG, KS, TS

Data collection: TG, TS, YW

Analysis: TG, RS

Methodology: TG, KS, TS

Supervision: KS, RS, SM

Writing – original draft: TG

Writing – review and editing: KS, RS, SM

Critical review and revision: all authors

Final approval of the article: all authors

Accountability for all aspects of the work: all authors

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Tables

Tables 1 to 3 are available in the supplementary files section.

Figures

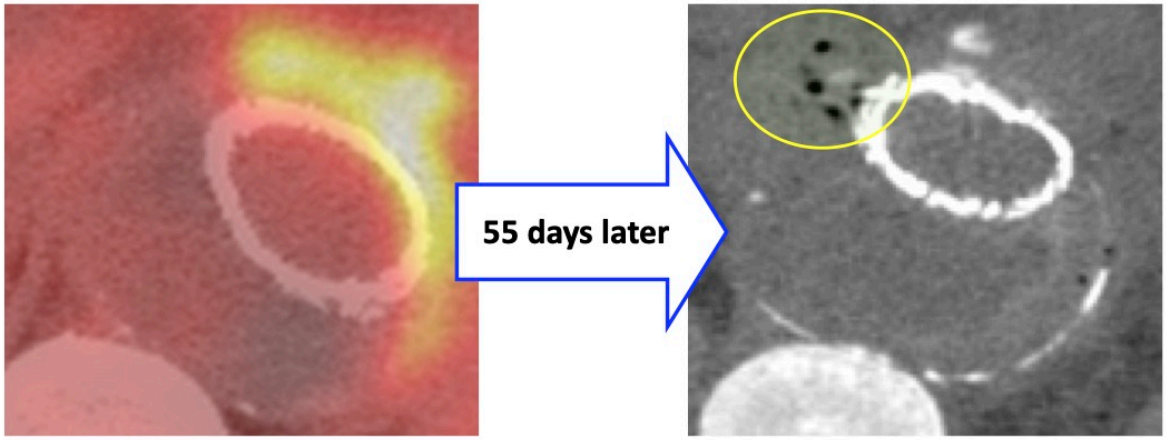


Figure 1

Representative Case illustrating the prognostic value of ^{18}F-FDG-PET/CT.

Initial ^{18}F-FDG-PET/CT demonstrates intense FDG uptake around the endograft, whereas concurrent conventional CT shows no structural findings suggestive of VGEI. Follow-up CT performed 55 days later reveals definitive VGEI progression, including air collection around the graft. This case highlights how high FDG uptake serves as a predictive marker that identifies high-risk patients well before the emergence of structural changes on conventional imaging, thereby facilitating earlier clinical vigilance.

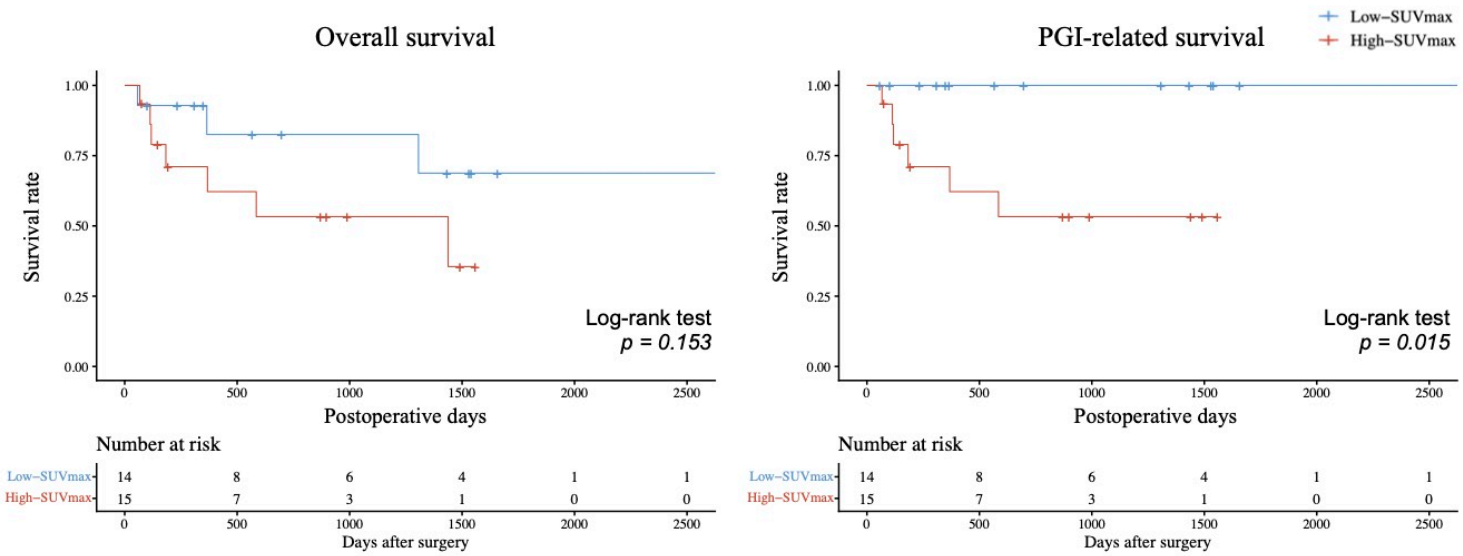


Figure 2

Kaplan-Meier curve between High- and Low-SUV_{max} group.

Overall survival was higher than in Low-SUV_{max} group than in High-SUV_{max} group, but not significantly (log-rank test; p = 0.153). VGEI-related mortality was significantly lower in Low-SUV_{max} group than in High-SUV_{max} group (log-rank test; p = 0.015).

VGEI: vascular graft and endograft infection; SUV_{max}: maximal standardized uptake value.

Supplementary Files

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