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Emerging Evidence

Value of CT and ^{18}F-FDG PET/CT Imaging for Preoperative Screening in Advanced Heart Failure Therapy Candidates

Xavier Rabbath,[a] Matthieu Pelletier-Galarneau, MD. MSc,[a] Maxime Tremblay-Gravel, MD,[b] Pierre-Emmanuel Noly, MD, PhD,[c] Normand Racine, MD,[b] and Stephanie Tan, MD[a]

[a] *Department of Medical Imaging, Montreal Heart Institute, Montréal, Quebec, Canada*

[b] *Department of Medicine, Montreal Heart Institute, Montréal, Quebec, Canada*

[c] *Department of Surgery, Montreal Heart Institute, Montréal, Quebec, Canada*

ABSTRACT

This study assesses the impact of contrast-enhanced chest and abdominal computed tomography (CT) and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET)/CT in preoperative screening of heart transplantation or ventricular assist device candidates. Patients who underwent both studies within a 6-month interval at our institution between 2014 and 2021 were reviewed for significant findings, defined as possible contraindications or actionable findings. Among the 79 included patients, significant findings were found in 38 (48.1%) with CT and in 18 (22.8%) with FDG-PET/CT ($P = 0.0015$). FDG-PET/CT identified 10 additional significant findings, but none of these precluded patient listing for heart transplantation. Use of FDG-PET/CT may lead to unnecessary investigations when performed indiscriminately in all patients.

RÉSUMÉ

La présente étude se penche sur l'incidence du recours à une tomodensitométrie (TDM) thoracique et abdominale avec produit de contraste et à une tomographie par émission de positrons au fluorodésoxyglucose marqué au fluor 18 (TEP-^{18}FDG) lors d'évaluation préopératoire de candidats à une transplantation cardiaque ou à l'implantation d'un dispositif d'assistance ventriculaire. Les résultats obtenus de 79 patients qui ont subi ces deux examens dans un intervalle maximal de six mois à notre établissement entre 2014 et 2021 ont été analysés à la recherche de conclusions pertinentes, définies comme des contre-indications possibles à l'intervention ou des résultats ayant un impact direct sur la prise en charge du patient. De telles conclusions ont été constatées chez 38 participants (48,1 %) suite à une TDM et 18 participants (22,8 %) suite à une TEP-^{18}FDG ($p = 0,0015$). La TEP-^{18}FDG a permis de relever 10 résultats d'importance supplémentaires, mais aucun d'entre eux n'aurait entraîné l'inadmissibilité du patient à une transplantation cardiaque. L'utilisation de la TEP-^{18}FDG pourrait donner lieu à des examens non nécessaires lorsqu'elle est réalisée sans distinction chez tous les patients.

Advanced heart failure carries a poor prognosis, with a 5-year survival rate of only 20%,[1] with current therapeutic options limited to heart transplant (HTx) or ventricular assist devices (VADs).[2] Given that fewer than 6000 donor hearts are available worldwide annually and that VADs are a costly life-saving therapy,[3,4] patient selection is crucial for appropriate resource allocation. Patient selection and surgical planning are also key to improving outcomes.[2] Active malignancy, with some exceptions, requiring oncological opinion, represents a contraindication to HTx.[5] Evaluation for malignancies is also recommended (class I) in VAD candidates.[6] However, with no specific guidelines and a lack of conclusive evidence on how to exclude malignancy, screening strategies prior to transplant listing vary from institution to institution.[7] Certain centres such as ours at the Montreal Heart Institute perform chest radiograph, computed tomography (CT), Doppler, and ^{18}F-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) for potential candidates. Other centres require only chest radiographs or chest and/or abdominal CT with or without contrast, and some opt for abdominal ultrasound.[8-16] Advanced imaging tests, such as contrast-enhanced chest and abdominal CT and FDG-PET/CT have already proven useful in cancer screening in asymptomatic individuals.[17-19] In HTx/VAD candidates, CT and FDG-PET/CT also can document vascular anatomy, which is of importance in surgical planning.[5] However, systematic use of

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Ethics Statement: This study was approved by our institutional research ethics board (#ICM2023-2999), and the requirement to obtain informed consent was waived, given the retrospective nature of the study.

Corresponding author: Dr Stephanie Tan, Department of Medical Imaging, Montreal Heart Institute, 5000 Rue Bélanger, Montréal, Quebec H1T 1C8, Canada. Tel.: 1-514-376-3330 x4400; fax: +1-514-593-2592.

E-mail: stephanie.tan@icm-mhi.org

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contrast-enhanced CT and FDG-PET/CT for screening of potential HTx recipients has not been studied. The purpose of this study is to assess their value in this setting.

Methods

Study population

This study is a retrospective single-centre medical records review of potential HTx and VAD candidates evaluated at the Montreal Heart Institute between January 2014 and July 2021. Patients who underwent both contrast-enhanced chest-abdomen-pelvis CT and FDG-PET/CT within a 6-month interval for pretransplantation or VAD evaluation were included. Patients were identified by cross-matching the list of patients who underwent a pretransplant workup and the hospital radiologic database. Those with noncontrast or incomplete chest-abdomen-pelvis CT, including absence of a portal phase acquisition for the abdomen and pelvis, were excluded. Whole-body FDG-PET/CT imaging was performed following a fasting period of $\geq$ 6 hours, from the base of the skull to the mid thighs, roughly 60 minutes after intravenous injection of 370 MBq (10 mCi) of FDG.

Data collection

The following data were retrieved from medical records: patient demographic information (sex, date of birth, weight, height); risk factors for cancer (smoking status, alcohol consumption, use of recreational drugs, history of cancer including radiation therapy, previous solid organ transplant, family history); risk factors for cardiovascular disease (diabetes, hypertension, dyslipidemia, renal disease); type of complex congenital heart disease if any; and indication for transplant or a VAD.

All CT and FDG-PET/CT reports were reviewed. Significant findings were defined as any of the following: possible contraindications for transplant/VAD (eg, cancer, large or complicated infection, etc.)[5]; findings having an impact on their medical or surgical management (eg, venous thrombosis, vessels immediately retrosternal in patients with previous sternotomy, etc.); or actionable findings (eg, ventricular thrombus, pulmonary embolism, etc.). The absence on the second test (CT or FDG-PET/CT) of a finding suspected on the first test (FDG-PET/CT or CT, respectively) was not counted as a significant finding, because some patients underwent FDG-PET/CT first, whereas others underwent CT first.

Subsequent confirmatory imaging, biopsies, and diagnostic interventions for findings described on CT and FDG-PET/CT were retrieved from the medical records. The decision and timing of whether or not to list patients on the transplant list or to proceed to a VAD implantation were recorded.

This study was approved by our institutional research ethics board (#ICM2023-2999), and the requirement to obtain informed consent was waived, given the retrospective nature of the study.

Statistical analysis

The primary objective of this study is to compare the proportions of tests with significant findings on CT vs FDG-PET/CT. The secondary objective is to assess the added value of FDG-PET/CT when used in addition to CT, by reporting the number of common significant findings seen on both CT and FDG-PET/CT, and the number of additional findings found on FDG-PET/CT. Continuous variables are expressed as median and interquartile range (IQR), and categorical variables are expressed as frequencies and percentages. Proportions were compared using Fisher's exact test, using a significance level of 0.05.

Results

Study population

A total of 316 patients underwent pretransplant/VAD workup during the study period (Fig. 1). Of these, 107 (34%) did not undergo FDG-PET/CT; 19 (6%) did not undergo CT; and 64 (20%) did not undergo either FDG-PET/CT or CT, leaving 78 patients (25%) who met the inclusion criteria. Of the 78 eligible patients, one patient underwent 2 separate pretransplant/VAD workups 21 months apart. Indications for performing FDG-PET/CT and/or CT were based entirely on clinician judgement. Study sample characteristics are presented in Table 1. The median time interval between CT and FDG-PET/CT was 4 days (interquartile range [IQR] = 1-13.5; range: 0-80 days). In 22 patients, FDG-PET/CT was performed before CT (median interval: 6.5 days [IQR: 3-14.8]; range: 1-80 days).

Significant imaging findings

The proportion of imaging studies with significant findings was greater with CT than with FDG-PET/CT (48.1% vs 22.8%, $P = 0.0015$). Contrast-enhanced CT identified more vascular findings than FDG-PET/CT (39% vs 6%; $P = 0.011$; eg, thrombosis, pulmonary embolism). No statistically significant difference was present between CT and FDG-PET/CT for lesions suspicious for cancer (42% vs 61%; $P = 0.254$), infection (11% vs 28%; $P = 0.129$), or other diseases (8% vs 17%; $P = 0.374$; e.g., interstitial lung disease, severe emphysema).

Of the 18 significant findings identified on FDG-PET/CT, 8 (44%) were common findings seen on both CT and FDG-PET/CT. Therefore, 10 significant findings (56%) were found only on FDG-PET/CT (Supplemental Table S1). These 10 patients underwent further investigation consisting of breast ultrasound, mammogram, prostate biopsy, rhinopharyngolaryngoscopy, bronchoscopy, repeat PET imaging, additional CT imaging, echocardiography, thyroid ultrasound, and thyroid nodule biopsy. Of those, 7 had lesions suspicious for cancer; upon further investigation, 6 were found to be false positives, and 1 had a final diagnosis still pending; this finding is related to a focal hypermetabolic area in the prostate in a patient with prior surgical history for benign prostatic hyperplasia, and the patient was deemed a noncandidate to HTx before a final diagnosis was available. Four patients had additional FDG-PET/CT findings suggestive of infection (pulmonary parenchyma [n = 2], mitral ring, and oropharynx and paratracheal lymph nodes uptake). Findings exclusive to FDG-PET/CT allowed diagnoses of pneumonia treated with antibiotics, pneumonia of viral

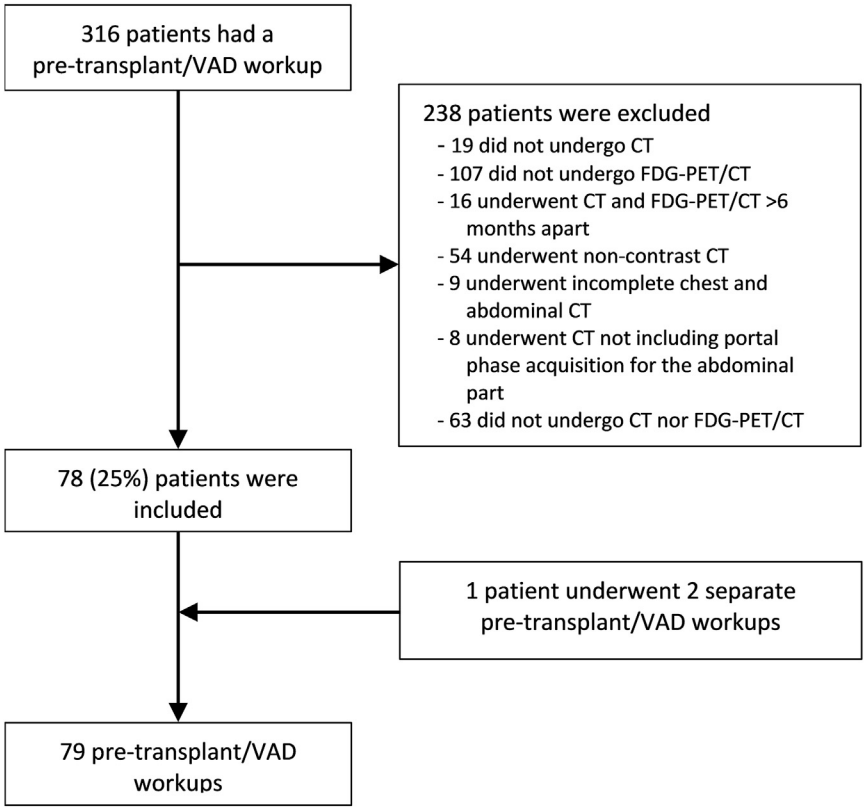

Figure 1. Selection of pretransplant/ventricular assist device (VAD) workups. CT, computed tomography; FDG-PET, ^{18}F-fluorodeoxyglucose positron emission tomography.

origin, and mitral ring thrombus without infectious endocarditis. For patients who had significant findings found only on FDG-PET/CT, the median interval between the 2 imaging studies was 2 days (IQR = 0-7) and ranged from 0 to 48 days (pneumonia treated by antibiotics: FDG-PET/CT 2 days after CT; pneumonia of probable viral origin: FDG-PET/CT 1 day after CT; and mitral ring thrombus: FDG-PET/CT 48 days before CT).

Transplant-listing decision outcome of candidates

Figure 2 presents listing outcomes for the 46 patients with significant findings on CT and/or FDG-PET/CT. Four of them (9%) were not listed, because of contraindication found on CT and/or FDG-PET/CT. Of these 4 critical findings, 2 were suspected on both CT and FDG-PET/CT (interstitial lung disease and high suspicion for lymphoma), and 2 were seen only on CT (severe peripheral arterial disease).

Discussion

This study is the first to our knowledge to compare the value of contrast-enhanced CT and FDG-PET/CT in the workup of pretransplant/VAD patients. Our data indicate that performing systematic contrast-enhanced chest-abdomen-pelvis CT allows identification of HTx/VAD contraindications in a significant proportion of patients. Contraindications to advanced therapy found on FDG-PET/CT were also identified on CT. Additionally, routine FDG-PET/CT would lead to several false-positive studies and additional investigations that could result in therapy delays.

In HTx/VAD candidates whose preassessment workup included both CT and FDG-PET/CT, the proportion of studies with significant findings was statistically greater with CT, compared to that with FDG-PET/CT, due mainly to vascular findings, such as stenosis, variants, and precarious location, such as vessels immediately retrosternal, best assessed on CT. In our study, diseases diagnosed from findings that were observed only on FDG-PET/CT (pneumonia and mitral ring thrombus) could easily be diagnosed on CT. The fact that these acute events were observed only on FDG-PET/CT is likely related to the timing of the imaging. Important to note is that, despite being characterized as significant, these findings do not represent absolute contraindications to HTx/VAD. Seven patients with findings exclusive to FDG-PET/CT underwent further investigation for cancer suspicion. Although 1 had final diagnosis still pending, 6 were false positives. This finding is not surprising, as FDG-PET/CT is not specific for malignancies and can be abnormal in a broad range of benign conditions. Thus, screening FDG-PET/CT performed in low-risk populations is associated with a high rate of false-positive studies. The results of this study therefore do not support the routine use of PET as a first-line screening tool for contraindications to HTx or VAD in all patients.

For patients with a contraindication to iodinated-contrast, such as severe allergy, FDG-PET/CT could potentially

Table 1. Selected demographic and clinical characteristics of sample patients

Characteristic	Study patients (N = 79)
Age, y	52 (43−60)
Sex	
Female	20 (25)
Male	59 (75)
BMI	27.1 (23.8−29.9)
History of smoking	48 (61)
History of alcohol consumption	
None	42 (53)
Occasional (≤ 10/wk [F] or ≤ 15/wk [M])	36 (46)
Frequent (> 10/wk [F] or > 15/wk [M])	1 (1)
Use of recreational drugs	
None	59 (75)
Active	6 (8)
Past	14 (18)
History of cancer	9 (11)
History of radiation therapy to the chest	3 (4)
Previous solid organ transplant	6 (8)
Family history of cancer	
Yes	14 (18)
No	18 (23)
Unknown	47 (59)
Diabetes	20 (25)
Hypertension	39 (49)
Dyslipidemia	42 (53)
CKD	21 (27)
Congenital cardiopathy	9 (11)
Indication for transplant / primary diagnosis	
Dilated CM	28 (35)
Ischemic CM	24 (30)
Hypertrophic CM	6 (8)
Refractory or recurrent arrhythmia	13 (16)
Toxic CM	9 (11)
Infiltrative CM	4 (5)
Congenital malformation	3 (4)
Other	17 (22)

Values are n (%), or median (interquartile range).

BMI, body mass index; CKD, chronic kidney disease; CM, cardiomyopathy; F, female; M, male.

represent an alternative in intermediate- to high-risk patients. In patients without contraindications to iodinated-contrast, FDG-PET/CT should probably be used as a second-line test for those with abnormalities on CT that need further characterization, or it could be targeted to candidates with a high pretest risk of cancer (eg, smokers, patients with familial history, etc.).

Selected use of FDG-PET/CT may also represent a more cost-effective strategy, as FDG-PET/CT imaging costs are significantly higher than those of enhanced CT alone (approximately twice as much at our institution).

Limitations

Our study has limitations that must be acknowledged. First, this a single-centre retrospective study from an institution with a low to moderate volume of HTx patients (15 to 20 annually). The study population was, however, representative of adult HTx recipients, as reported in the International Society for Heart & Lung Transplantation Registry data.[20] Second, this analysis was based on significant findings identified by the report of each modality, but it did not account fully for the proportion of these significant findings that turned out to be true. Third, the images were not reviewed, and our analysis relied on the official report. Considering that reader expertise affects the value of imaging tests, an important point to note is that all studies were performed in a specialized centre with a limited number of expert readers (4 radiologists and 3 nuclear medicine physicians, all fellowship-trained) and are representative of real-life interpretation.

Fourth, some patients underwent FDG-PET/CT before CT, and in exams performed on different dates, cases in which the second study refutes a condition suspected on the first study are not reported as significant. This approach is used to better reflect the individual value of each modality. Finally, a high proportion of patients were excluded. Indications for performing FDG-PET/CT and/or CT were based on clinician judgement and personal routine workup. Consequently, a potential test-referral bias was present, and this may lead to an overestimation of the proportion of patients in whom routine CT and/or FDG-PET/CT would provide incremental useful information. However, this bias stems from the lack of clear guidelines in patient workup for pre-VAD and pre-HTx patients, causing heterogeneity in clinician practices. In our cohort, we observe that the impression of the clinician alone is probably not sufficient to justify use of the 2 modalities.

Conclusion

Our study suggests that use of imaging has a value in preassessment for patients awaiting cardiac transplant or VAD, as planning and management were impacted for over half of assessed candidates. Contrast-enhanced thorax-abdomen-pelvis CT identified more significant findings, compared to FDG-PET/CT. Furthermore, FDG-PET/CT was associated with nonspecific findings leading to additional investigation. A progressive approach, consisting of CT followed by FDG-PET/CT as needed for very specific cases, may be a more effective strategy. Further prospective studies with a larger sample size are required to determine the optimal strategy for the evaluation of pre-HTx/VAD patients.

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Disclosures

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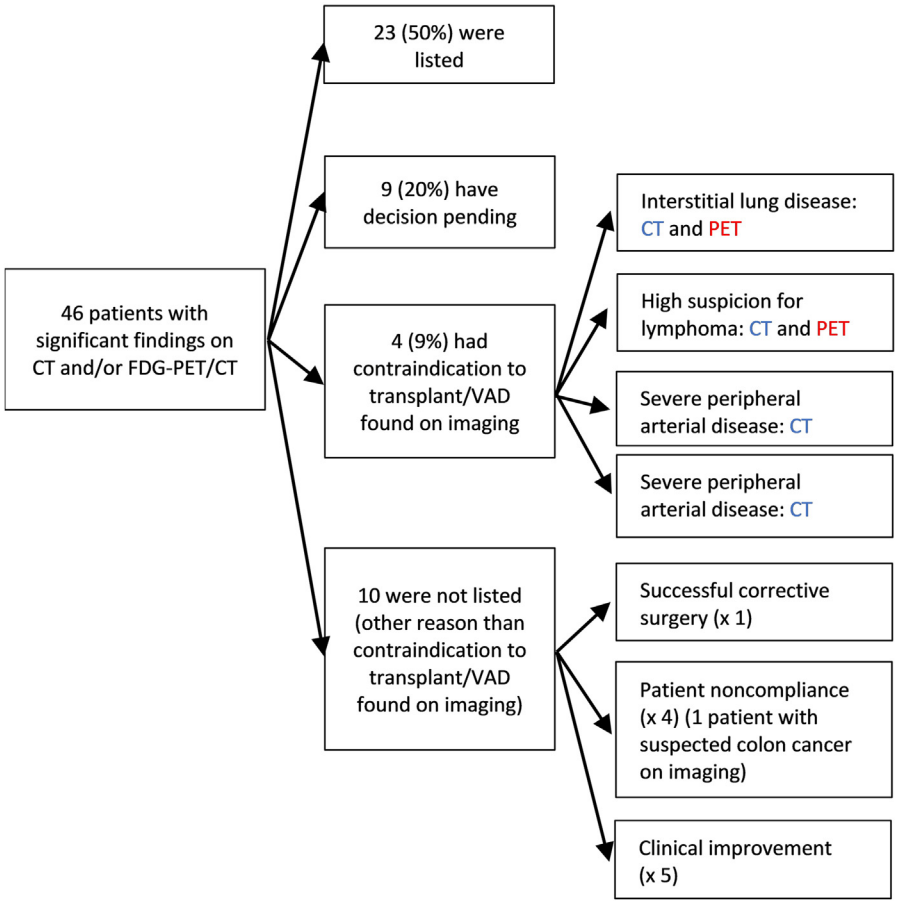

Figure 2. Transplant-listing outcomes of patients with significant findings on computed tomography (CT) and/or ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET/CT). VAD, ventricular assist device.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.03.012.