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Evaluation of 18-FDG PET diagnostic capabilities for cancer screening in heart transplant patients, a retrospective study

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Abstract

Evaluate 18-FDG positron emission tomography (PET) diagnostic capabilities for cancer screening in heart transplant patients. We conducted an anonymized retrospective observational study of heart transplant patients followed in the University Hospital of Montpellier, France. We analyzed 303 18-FDG PET from 158 patients. We compared demographic and clinical characteristics through uni- and multivariate analysis: in the cancer-free group, comparisons were made between the PET false positive (FP) group versus true negative (TN), and in the cancer group, comparisons were made between the PET false negative (FN) group versus true positive (TP). Out of the 303 exams, we found 245 TN, 26 TP, 26 FP and 6 FN. The sensitivity rate was calculated at 81%, the specificity rate at 90%, the positive predictive value at 50%, and the negative predictive value at 97%. The multivariate analysis showed an association between FP diagnosis and graft-PET delay (*P* value = .046, OR = 5.14, 95% CI [1.18–32.4]) and creatine reactive protein (CRP) ≥ 10 mg/L (*P* value = .042, OR = 4.21, 95% CI [1.02–17.2]). The estimated probability of FP by logit regression was 0.48 with 95% CI [0.21–0.77] when graft-PET delay ≥ 6 years and CRP ≥ 10 mg/L. No significative statistical link was found for the demographic or clinical characteristics in the FN group of patients with cancer, except for sex (all FN were men). 18-FDG PET performed very well in the follow-up of heart transplant patients for neoplasia screening, with better specificity than sensitivity. However, the study showed that almost 50% of FP can be predicted by considering only the graft-PET delay and CRP.

Abbreviations: CRP = creatine reactive protein, EBV = Epstein-Barr virus, FN = false negative, FP = false positive, PET = positron emission tomography, PPV = positive predictive value, PTLD = posttransplant lymphoproliferative disease, TN = true negative, TP = true positive.

Keywords: 18-FDG PET, heart transplant patients, neoplasia screening

1. Introduction

Heart transplant patients are treated for life with immunosuppressant drugs to prevent graft rejection. It has been well documented that these treatments increase the risk of cancer.[1–3] According to several studies, transplant patients, including heart transplant patients, have 2 to 4 times more risk of developing cancers than the general population.[4–9] Consequently, mortality due to cancer is also increased compared to the general population. Indeed some have estimated that cancer mortality will become the leading cause of death among transplant recipients ahead of cardiovascular mortality.[1,10–14] The most frequent neoplasia in transplant patients in descending order of frequency is as follows: skin cancer, post-transplant hemopathy, and lung, liver and kidney neoplasia. Other localizations are also more frequent than in the general population such as otorhinopharyngeal sphere, stomach and colon. In view of this high risk of neoplastic events, cancer screening in this population seems important. The guidelines adapted for transplant recipients are mainly available for kidney transplant patients and are based on the current guidelines for the general population.[15–20] In a review concerning cancer screening in renal transplant patients, Wong et al[21] concluded that the recommendations should quantify the benefits and risks (mortality benefits, harm, screening test accuracy, and cost-effectiveness) to decide the best screening strategy. Regarding heart transplant patients, the International Society for Heart and Lung Transplantation Guidelines for the Care of Heart Transplant Recipients were published in 2010[22]: they suggest that the general population recommendations for screening for colon, breast and prostate cancers should be

There are no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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followed. They also recommend regular dermatological and hematological follow-up by physicians specialized in posttransplant cancers. These recommendations remain insufficiently specific.

In view of the lack of dedicated guidelines, the cardiology and nuclear medicine departments of the University Hospital of Montpellier, France, decided to screen consenting heart transplant patients followed for neoplasia, based on annual 18-FDG positron emission tomography (PET).

The benefits of 18-FDG PET are well known in oncology, particularly for the initial assessment and follow-up of hematological, colon or lung cancers, for example. However, it is not systematically used to screen neoplasia. We were interested in its contribution in this screening context, which has not yet been studied, particularly in transplant patient. This study is the first of its kind for heart transplant patients.

We thus evaluated the 18-FDG PET diagnostic capabilities in the context of cancer screening in order to determine whether this type of examination has its place in the management of these patients.

2. Materials and method

2.1. Study details and characteristics of interest

We conducted a monocentric anonymized retrospective cohort study and retrieved data on sex, age, weight, height, transplant date, PET date, cardiopathy etiology, tobacco consumption, and the creatine reactive protein (CRP) value at the screening. We stipulated that the first (i) 18-FDG PET had to have been done after at least 1 year of immunosuppressive therapy, a time after which the risk of neoplasia is significantly increased[2–4] and (ii) patients had to have been followed for at least 1 year after the 18-FDG PET.

2.2. 18-FDG PET acquisition settings

The acquisitions were performed on a Siemens Healthineers Biograph mCT 20Flow (Knoxville, USA) PET/CT scanner in the Nuclear Medicine Department of the University Hospital Center of Montpellier, France. PET acquisition included brain, cervical-thoracic and abdominal-pelvic regions. Tomographic reconstructions were performed with 3D TOF OSEM using 2 iterations, 21 subsets including point spread function correction, and Gaussian post-filtering with a full width -at -half maximum of 3 mm. The images were sampled on a 400 × 400 matrix with a voxel size of 2-2-2 mm3. The PET attenuation correction was based on the CT -generated μmaps.

2.3. Population study

Our cohort comprised 210 heart transplant patients monitored at one of the University Hospitals of Montpellier, France. We retrieved all PET scans from cardiac transplant patients between October 2012 and February 2022. The initial prescription for PET monitoring for the detection of neoplasia following post-cardiac transplant immunotherapy was broad, with no clinical exclusion criteria. For our study, the 3 primary inclusion criteria were: an interval of more than 1 year between the PET scan and the initiation of immunotherapy, the PET scan must have been performed at our center, the clinical follow-up of at least 1-year post-PET scan to monitor for the occurrence of cancer. Examinations that did not meet these inclusion criteria were excluded.

From these criterions, 28 patients were excluded because they had not had an 18-FDG PET, 15 patients were excluded because they had not had 1 year of clinical follow-up post 18-FDG PET, 1 patient had an uninterpretable 18-FDG PET because of hyperinsulinism, and 1 patient refused a biopsy to confirm the cancer. For the 165 remaining patients, 416 18-FDG PET were performed. Among these examinations, 88 PET were excluded because of the lack of the 1 year follow-up, 8 PET were excluded because the diagnostic confirmation was still underway or because we did not find the result in our database, 4 PET were excluded because it was performed as part of a cancer follow-up and not as screening, and 13 PET were excluded because they had been performed before 1 year of immunosuppressive treatment. In total, we analyzed 303 18-FDG PET. Because some patients had only one 18-FDG PET scan, the exclusion of some of these scans excluded some patients. Therefore, we had a total of 158 patients. A flowchart is presented in Table 1.

No patient refused to participate in this study. Approval of the nuclear medicine research ethics committee was obtained and our confirmation of anonymized was declared to the "*Commission Nationale de l'Informatique et des Libertés*" according to the regulations in force.

2.4. Analyzed groups and variable dichotomization

Except for body mass index, continuous variables were dichotomized. We chose 65 years as the age cut-off as this threshold is often used in questions related to aging. Regarding the graft-PET delay, we chose the median of the sample as the cut-off. We did the same to classify cigarette smoking. We distinguished inflammation rates according to-: (i) no or minor inflammation when CRP < 10 mg/L, and (ii) significant inflammation when CRP ≥ 10 mg/L.[23]

The comparisons were performed on 2 distinct groups: patients with cancer and those without it. In each of these groups, we were interested in the diagnostic performance of PET. In the cancer-free group, the features of interest were compared according to the PET diagnostic status: false positive (FP) versus true negative (TN). Similarly, in the cancer group, comparisons were made between the PET false negative (FN) group versus true positive (TP). The distributions of the characteristics of interest in the groups are described in Table 2 for both the 303 PET exams and the cancer group. Our cohort had a majority of men (76%) but the distribution of sex in the cancer group was not significantly different. The cohort also had a majority of active or former smokers (55%) (distributed statistically differently in the cancer group) and the initial cardiopathy was mostly ischemic or dilated, which are 2 of the most frequent cardiopathies in the general population. Other etiologies of cardiopathy were grouped into an "other" group. Note also that the age at-graft was statistically different between patients with and without cancer. Other characteristics were statistically balanced between the cancer groups.

Distribution of the characteristics of interest as a function of PET diagnostic results in our cohort are presented in Table 3.

2.5. Statistical analysis

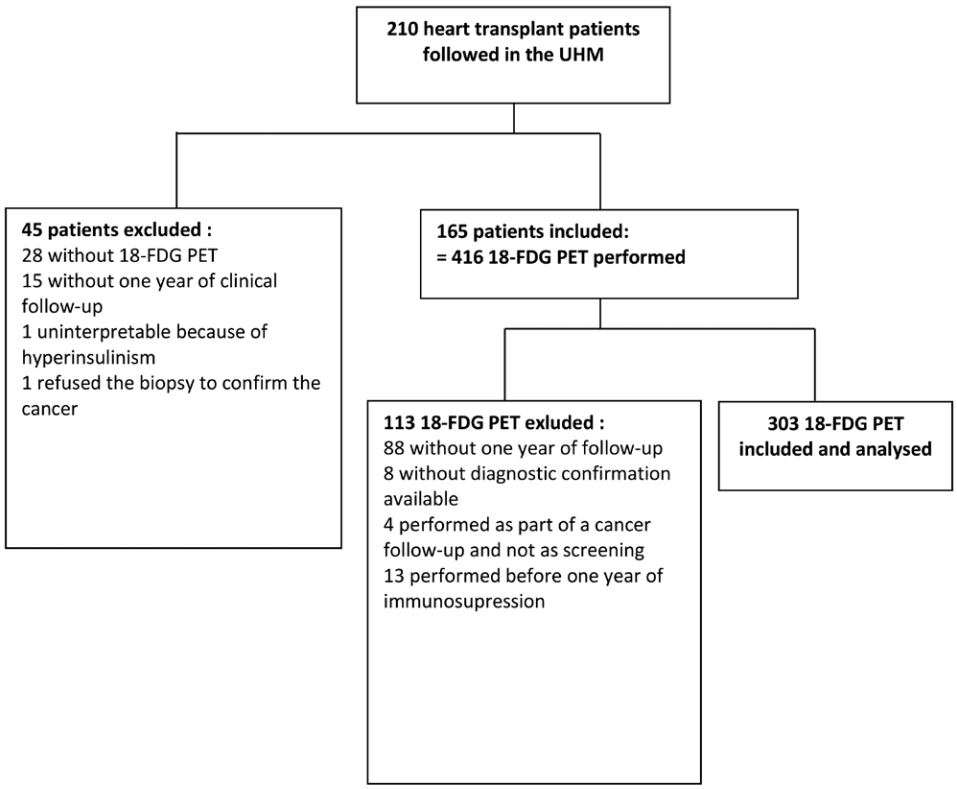
The Pearson's Chi-squared test (if N < 5) and the Fisher exact test (if N ≥ 5) were used to evaluate the association between the presence or absence of cancer with the characteristics of interest that were categorical variables. The Wilcoxon rank sum test was used to evaluate the quantitative distribution of cancer in our database across the demographic and clinical characteristics.

In the cancer group (comparing FN and TP groups), univariate logistic regression was carried out on the characteristics of interest. The variables were not dichotomized for this study because of the small population size of these groups.

In the group without cancer (comparing FP and TN groups), an analysis using a univariate logistic regression model was conducted to determine the independent variables associated with FP diagnoses. We included all independent variables ($P < .2$) associated with FP diagnosis in the multivariate analysis. A forward procedure was used to obtain the final multivariate model

Table 1

Flow chart.



UHM = University Hospital of Montpellier.

selecting only the variables significantly associated with FP. To account for the observation that more than 1 PET scan could be associated with 1 patient, a multivariate generalized linear mixed model with random intercepts over patient identification was run.

A logistic regression prediction model enabled us to compute the probability of FP among the patients without cancer taking into account the selected significant variables, this was extracted and described.

Statistical tests were performed using R (version 4.2, R Foundation for Statistical Computing, Vienna, Austria). The significance was considered reached when $P \leq .05$.

3. Results

The diagnostic properties of 18-FDG PET in our dataset are presented in Table 4. Among the 303 exams, we found 245 TN, 26 TP, 26 FP, and 6 FN. The sensitivity rate was 81%, with a specificity rate of 90%, a positive predictive value (PPV) of 50%, and a negative predictive value of 97%. The patients were 8 times more likely to have a positive 18-FDG PET if they had a cancer than if they did not. Also, they were almost 21 times more likely to have a cancer if the 18-FDG PET was positive than if it was not. Almost 90% of the 18-FDG PET gave the right diagnosis with a detection rate of 17% in our cohort.

Although the diagnostic capabilities of PET were good for detecting post-heart transplant cancers, there were nevertheless some cases that were misdiagnosed. These were the cases that particularly interested us in this study. We assumed that the causes of misinterpretation were not the same for FP and FN of PET diagnosis. Thus, we conducted 2 further analyses: one for FP in patients who did not develop cancer and one for FN in patients who did.

3.1. FP in patients without cancer

In order to extract the demographic and clinical parameters having a statistically significant link with the occurrence of an erroneous diagnosis of the FP type, we used a logistic regression model to compare these characteristics between the FP and TN groups. The characteristics and their distribution across the categorical variables of interest can be found in Table 3.

In Table 5, the univariate analysis showed that 3 main characteristics were positively and significantly associated with the diagnosis of cancer in an unaffected patient: age over 65 years at the time of the transplant, being a smoker over 30 pack-years and CRP ≥ 10 mg/L at the time of the PET scan. All the 95% confidence intervals of the odd ratios of these characteristics exclude 1.

In addition to these characteristics, the graft-PET delay was added to the multivariate analysis.

The multivariate analysis showed an association between FP diagnosis and graft-PET delay ($P = .046$, OR = 5.14 with 95% CI of [1.18–32.4]) and CRP ≥ 10 mg/L ($P = .042$, OR = 4.21 with 95% CI of [1.02–17.2], Table 4). The conditions for application and validity of this analysis were verified. Also, the multivariate generalized linear mixed model with random intercepts over patient identification gave ORs and P values similar to the regular multivariate logistic regression. Only the confidence intervals were slightly but not significantly different.

Table 2

Population characteristics.

Characteristics	Overall population N = 303*	Populatio`n in function of cancer status		
		Cancer, N = 32*	No cancer, N = 271*	*P* value
Sex				.3†
Female	72 (24%)	5 (16%)	67 (25%)	
Male	231 (76%)	27 (84%)	204 (75%)	
Age at graft				<.001†
< 65 yr	186 (61%)	10 (31%)	176 (65%)	
> 65 yr	117 (39%)	22 (69%)	95 (35%)	
Graft-PET delay				.056†
< 6 yr	143 (47%)	10 (31%)	133 (49%)	
> 6 yr	160 (53%)	22 (69%)	138 (51%)	
Cardiopathy				.072†
Others	48 (16%)	3 (9.4%)	45 (17%)	
CMD	123 (41%)	9 (28%)	114 (42%)	
CMI	132 (44%)	20 (62%)	112 (41%)	
BMI	24.82 (4.27)	25.66 (4.06)	24.72 (4.29)	.3‡
(Missing)	29	2	27	
Cigarette smoking (PY‖)				<.001§
Non smoker	111 (45%)	3 (12%)	108 (49%)	
[0;30]	98 (40%)	14 (58%)	84 (38%)	
>30	36 (15%)	7 (29%)	29 (13%)	
(Missing)	58	8	50	
Inflammation level (CRP¶)				>.9§
No or minor inflammation	144 (84%)	20 (87%)	124 (83%)	
Inflammation	28 (16%)	3 (13%)	25 (17%)	
(Missing)	131	9	122	
Cancer				
Cancer	32 (11%)			
No cancer	271 (89%)			

BMI = body mass index, PY = pack-year.

* n (%); Mean (SD).

† Pearson Chi-squared test.

‡ Wilcoxon rank sum test.

§ Fisher exact test.

‖ Pack-year.

¶ C-reactive protein.

Table 3

TEP diagnostic properties in function of population characteristics.

Characteristics	Population without cancer		Population with cancer	
	FP, N = 26	TN, N = 245	FN, N = 6	TP, N = 26
Sex				
Female	4 (15%)	63 (26%)	0 (0%)	5 (19%)
Male	22 (85%)	182 (74%)	6 (100%)	21 (81%)
Age at graft				
< 65 yr	12 (46%)	164 (67%)	2 (33%)	8 (31%)
> 65 yr	14 (54%)	81 (33%)	4 (67%)	18 (69%)
Graft-PET delay				
< 6 yr	9 (35%)	124 (51%)	0 (0%)	10 (38%)
> 6 yr	17 (65%)	121 (49%)	6 (100%)	16 (62%)
Cardiopathy				
Others	3 (12%)	42 (17%)	2 (33%)	1 (3.8%)
CMD	10 (38%)	104 (42%)	1 (17%)	8 (31%)
CMI	13 (50%)	99 (40%)	3 (50%)	17 (65%)
BMI	24.80 (3.46)	24.71 (4.37)	25.26 (4.03)	25.76 (4.14)
(Missing)	5	22	0	2
Cigarette smoking (PY)				
Non smoker	9 (43%)	99 (50%)	3 (75%)	0 (0%)
[0;30]	5 (24%)	79 (40%)	1 (25%)	13 (65%)
>30	7 (33%)	22 (11%)	0 (0%)	7 (35%)
(Missing)	5	45	2	6
Inflammation level (CRP)				
No or minor inflammation	9 (56%)	115 (86%)	4 (80%)	16 (89%)
Inflammation	7 (44%)	18 (14%)	1 (20%)	2 (11%)
(Missing)	10	112	1	8

BMI = body mass index, CRP = C-reactive protein, FP = false positive, FN = false negative, PY = pack-year, PET = positron emission tomography, PY = pack-year, TN = true negative, TP = true positive.

The logit model was also used to conduct a predictive analysis and thus estimate the probability of positively misdiagnosing a patient without cancer; it is denoted *P* (PET positive/no cancer). Considering the 2 statistically associated variables highlighted in the multivariate analysis, this probability was computed with the following equation:

$$p\,(PET\ positive|no\ cancer) = \frac{\mathrm{A}}{1 + A}_{(1)}$$

with:

•$A = e^{(-a+b.\omega_1+c.\omega_2)}$
•a = 2,1551
•b = 1,553
•c = 1,170
•ω_1 = 1 if graft-PET delay ≥ 6 years, 0 otherwise.
•ω_2 = 1 if CRP ≥ 10mg/L, 0 otherwise.

Table 6, shows the probabilities of diagnosing a FP with the combinations of graft-PET delays and CRP values (< or ≥ to 10 mg/L) with 95% confidence intervals. The predictions were validated by k-fold cross-validation.

An overview of the detailed pathologies misdiagnosed as cancers is proposed here: we found 3 suspicions of lymphoma invalidated by echography or biopsy, 2 suspicion of gastritis, one of esophageal tumor invalidated by endoscopy, 8 pulmonary infections without germ identification, 1 bartonellosis, 1 suspicion of lingual tumor that turns out to be a canker sore, 1 parotid tumor suspicion found to be an intraparotid inflammatory node, 1 bone tumor suspicion found to be a fibrous dysplasia, and suspicions of 1 thyroid tumor (Fig. 1), 1 tonsillar tumor, 1 ovarian tumor, 1 renal tumor, 1 breast tumor, 1 spleen tumor, 1 gallbladder tumor, 1 liver tumor, all of which were refuted by other imaging.

3.2. Analysis of patients with cancer

In the group of patients who developed cancer, a small number (N = 6) were misdiagnosed on PET. The small number of these patients was insufficient to justify using the same categories as for the analysis of the patient group without cancer. The univariate analysis was therefore conducted on the continuous variables and is presented in Table 7. The "sex" variable was not included because the 6 FN patients were all men. In this analysis, only masculine sex can therefore be considered as significantly associated, as all other estimated OR CIs include 1.

The 6 patients whose cancer was not initially detected by 18-FDG PET had the following cancers: 1 mucinous pulmonary adenocarcinoma (Fig. 2) (known to be associated with a low uptake on 18-FDG PET), 1 colonic adenoma with low grade dysplasia, 1 scalp squamous cell carcinoma, 2 cheek squamous cell carcinomas and 1 squamous cell carcinoma of the ear. Two of the squamous cell carcinomas (1 on the cheek and one of the scalp) were visible on the 18-FDG PET after review but not interpreted at first reading.

Among the TP PET, we found 1 non-Epstein-Barr virus (EBV) induced diffuse large cell B lymphoma, 3 pulmonary adenocarcinomas (1 acinar, 1 papillary, one without histological precision found), 4 pulmonary squamous cell carcinomas, 1 non-small cell lung carcinoma, 1 pleural desmoid tumor, 8 digestive

Table 4

18-FDG PET diagnosis properties in cancer screening.

	Positive 18-FDG PET	Negative 18-FDG PET	Total
Cancer	26	6	32
No cancer	26	245	271
Total	52	251	303
Se (%)	81,25		
Sp (%)	90,41		
PPV (%)	50		
NPV (%)	97,6		
Odds for positive PET	8,47		
Odd for cancer	20,92		
Accuracy (%)	89,44		
Detection rate (%)	17,16		

NPV = negative predictive value, PET = positron emission tomography, PPV = positive predictive value, Se = sensitivity, Sp = specificity.

Table 5

Uni- and multivariate analysis comparing characteristics among patients without cancer (false positive vs true negative).

		Univariate			Multivariable		
Characteristics	**N**	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Sex	271						
Female		-	-				
Male		1.90	0.70, 6.70	.3			
Age at graft	271						
< 65 yr		-	-		-	-	
> 65 yr		2.36	1.04, 5.42	.039	1.33	0.37, 4.72	.7
Graft-PET delay	271						
< 6 yr		-	-		-	-	
> 6 yr		1.94	0.85, 4.70	.13	5.14	1.18, 32.4	.046
Cardiopathy	271						
Others		-	-				
CMD		1.35	0.39, 6.22	.7			
CMI		1.84	0.56, 8.32	.4			
BMI	244	1.00	0.90, 1.11	>.9			
Cigarette smoking (PY)	221						
Non smoker		-	-		-	-	
[0;30]		0.70	0.21, 2.10	.5	0.77	0.17, 2.99	.7
>30		3.50	1.14, 10.4	.024	1.71	0.18, 11.9	.6
Inflammation level (CRP)	149						
No or minor inflammation		-	-		-	-	
Inflammation		4.97	1.60, 15.1	.004	4.21	1.02, 17.2	.042

BMI = body mass index, CI = confidence interval, CMD = cardiomyopathy dilated, CMI = cardiomyopathy ischemic, CRP = C-reactive protein, OR = odds ratio, PET = positron emission tomography, PY = pack-year.

adenocarcinomas (2 colonic lieberkuhnian adenocarcinomas, 2 tubolo-villous adenomas with low grade dysplasia, 3 tubular adenomas with low grade dysplasia, one without histological precision found), 1 non-dysplastic colonic polyp (considered a true positive because of the risk of long-term degeneration), 1 squamous cell carcinoma of the vocal cord, 3 cutaneous squamous cell carcinomas, 1 endometrioid carcinoma, 1 peritoneal carcinosis of unknown origin at diagnosis, and 1 Wharthin parotid tumor.

4. Discussion

Our study shows that 18-FDG PET has good diagnostic capabilities in the detection of neoplasia in heart transplant patients such as good specificity, sensitivity and negative predictive value but low (50%) PPV. The 2 most frequently detected cancers in our study were gastrointestinal and pulmonary neoplasia, which are among the most common cancers in the general population. We found only 1 lymphoma, in our cohort, although, it is one of the most frequent cancers described after solid organ transplantation. This difference in prevalence could be explained by the small size of our cohort.

The low PPV of 18-FDG PET in our cohort was investigated through multivariate analysis. We found an association between the FP diagnoses and a graft-PET delay ≥ 6 years and with a CRP ≥ 10 mg/L. Moreover, even though the confidence intervals of the FP predictor were quite wide, we also found the PPV could be reduced by considering only these 2 easy to access parameters: a graft-PET delay ≥ 6 years and CRP ≥ 10 mg/L had a 48% [21%, 77%] chance of being FP as opposed to a 3% [0.8%, 11%] if the graft-PET delay was < 6 years CRP was < 10 mg/L. This encourages us to recommend close follow-up with 18-FDG PET in the first years after heart transplant and careful interpretation of the exams of patients with inflammation and a long graft-PET delay.

One limitation of our study was the monocentric anonymized retrospective observational design. It would be interesting to enrich our database with more 18-FDG PET to reduce the size of the confidence intervals. Other studies have been performed in heart transplant patients in the evaluation of posttransplant lymphoproliferative disease (PTLD), not in a screening context but in cases of clinical suspicion of progressive disease. Sica et al[24] evaluated the clinical use of 18-FDG PET in the detection of PTLD and other neoplasms when they showed a clinical or laboratory suspicion of malignancy, and they reported that 18-FDG PET was of great interest for the early identification of malignancy. Many of their patients had greater susceptibility to EBV, human papillomavirus and human immunodeficiency virus, which are infectious agents known to promote the onset of malignancy. Yoon Gy et al[25] retrospectively evaluated 12 transplanted patients (one with a heart transplant) suffering with PTLD and found that most of their patients EBV encoded ribonucleic acid in the pathological specimen. We did not explore this link because of the lack of this type of accessible data in our cohort but it would be interesting to evaluate whether the virological status influences 18-FDG PET capabilities. Vali R et al[26] used 18-FDG PET at the PTLD diagnosis in order to guide the biopsy. Graute V et al[27] evaluated the capability of 18-FDG PET to determine the etiology of nonspecific symptoms (such as adenopathies, fever, weight loss or abdominal pain) in 17 patients: an etiology was found in half the patients (7 malignancies and 2 infections). Their sensitivity, specificity, positive predictive value and negative predictive value were, respectively, 0.9, 0.4, 0.69, and 0.75. These results cannot be directly compared with ours because their study was not focused on screening asymptomatic patients, but they do show that a positive 18-FDG PET should be explored.

The number of FN PET images indicated that we could reliably conduct association tests. This proportion was thankfully

Table 6

Predictions of the logistic regression estimated in probability of false positive in percent with its 95% confidence interval.

	Graft-PET delay < 6 yr	Graft-PET delay > 6 yr
No or minor inflammation	0.031 [0.008, 0.11]	0.11 [0.05, 0.24]
Inflammation	0.19 [0.07, 0.43]	0.48 [0.21, 0.77]

PET = positron emission tomography.

Table 7

Univariate analysis comparing characteristics among patients with cancer (false negative vs true positive).

Characteristics	N	OR	95% CI[1]	*P* value
Age at graft	32	0.99	0.86, 1.15	>.9
Graft-PET delay	32	1.01	1.00, 1.03	.043
Cardiopathy	32			
Others		-	-	
CMD		0.06	0.00, 1.19	.087
CMI		0.09	0.00, 1.19	.078
BMI	30	0.97	0.74, 1.21	.8
Cigarette smoking	24	0.85	0.70, 0.95	.024
CRP	23	1.01	1.00, 1.08	.3

BMI = body mass index, CI = confidence interval, CMD = cardiomyopathy dilated, CMI = cardiomyopathy ischemic, CRP = C-reactive protein, N = number of 18-FDG PET, OR = odds ratio, PET = positron emission tomography.

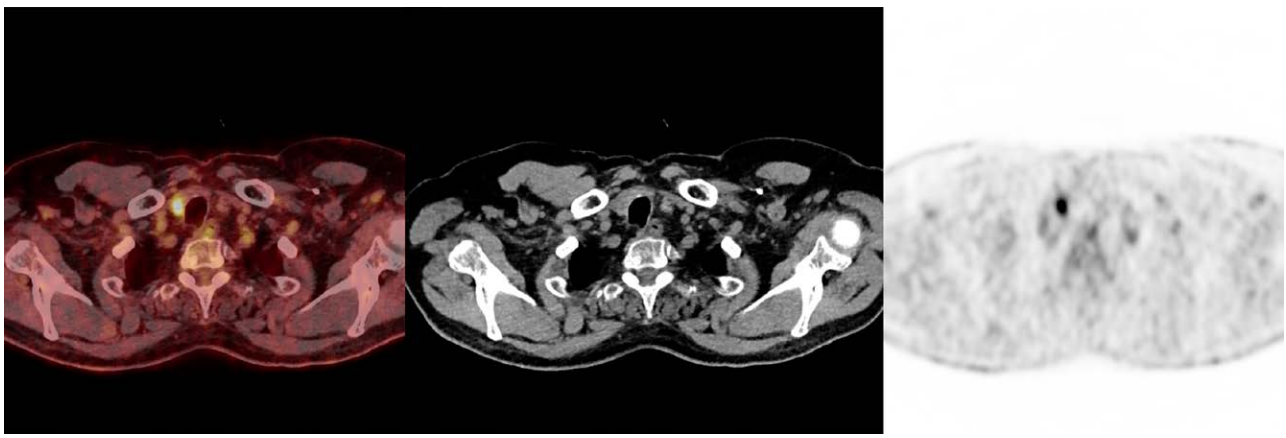


Figure 1. False positive 18-FDG PET: suspicion of thyroid neoplasm. PET = positron emission tomography.

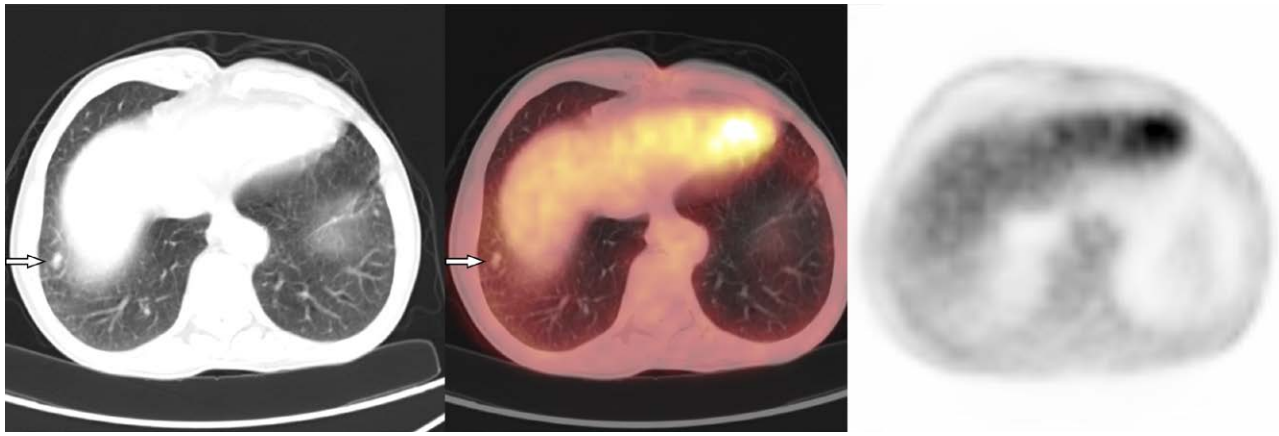


Figure 2. False negative 18-FDG PET: a mucinous pulmonary adenocarcinoma. PET = positron emission tomography.

low in our study and concerned only tumors known to be associated with low 18-FDG uptake and cutaneous neoplasia. This means that systematic dermatological examination is probably necessary in addition to 18-FDG PET (we found 3 cutaneous squamous cell carcinomas). Most of the FP tests were corrected by clinical examination, other imaging modalities, or on subsequent imaging examination, which was minimally invasive for the patient and low risk. However, some patients required lymph node biopsies (on suspected lymphoma) or endoscopy (on the suspected esophageal tumor). These techniques remain invasive and potentially lead to complications. This should be considered as part of the benefit-risk balance of screening.

5. Conclusion

We demonstrate that an 18-FDG PET might be interesting for neoplasia screening in the follow-up of heart transplant patients, as it showed high specificity, high negative predictive value and good sensitivity. We propose that a focus on a short graft-PET delay and elevated CRP would significantly enhance the positive predictive value of 18-FDG PET for cancer detection in heart transplanted patients. Other studies are needed to support our results and evaluate the clinical benefits, such as the impact on life expectancy, the risks of harm, and the cost-effectiveness of this type of screening.

Author contributions

Conceptualization: Julie Sagnes, Tom Paunet, Pascal Battistella, Denis Mariano Goulart, Florentin Kucharczak.
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