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ORIGINAL ARTICLE

FDG atrial uptake is associated with an increased prevalence of stroke in patients with atrial fibrillation

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Abstract

Purpose Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with an increased risk of stroke. Indeed, silent AF is frequently identified in unexplained ischemic stroke. ^{18}F-FDG-PET/CT is a powerful tool for assessing myocardial metabolic shift and inflammation, both potentially at stake in AF. This case–control study investigated whether AF could promote FDG uptake in atria after physiological myocardial glucose uptake suppression, and the potential relationship between FDG atrial uptake and prevalence of stroke.

Methods We retrospectively enrolled 128 patients (64 consecutive patients with AF and 64 without AF as the control group, matched for age and sex) who underwent ^{18}F-FDG-PET/CT after a high-fat low-carbohydrate diet. We analyzed visual and quantitative FDG uptake parameters of the right and left atria (RA/LA) and the right and left appendages (RAA/LAA), and selected clinical features including history of stroke.

Results Diffuse right atrial uptake was present in a third of patients with AF and only two patients in the control group. FDG uptake intensity of both atria was significantly associated with the underlying heart rhythm. The occurrence of stroke was strongly associated with detectable atrial uptake in multivariate analysis, with an odds ratio superior to that of other known risk factors.

Conclusions This study shows a significant correlation between FDG atrial uptake and AF. While inconsistent, this pattern seems to be associated with an increased prevalence of cardioembolic stroke.

Keywords Atrial fibrillation · Stroke · Positron emission tomography (PET) · FDG · Inflammation

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, responsible for approximately one-third of hospitalizations for heart rhythm disturbances [1]. The estimated prevalence is approximately 1.5–2% in the general population in industrialized countries, higher in men and increasing with age [2, 3]. AF without antithrombotic therapy remains associated with ischemic strokes and peripheral thromboembolic events [4, 5]. More than 33 million people live with AF [1], but the diagnosis is still a challenge, with almost 40% of silent AF [6] and AF identified in 25% of patients with an unexplained ischemic stroke [7]. Diagnosing AF before the occurrence of a first complication is a recognized priority in the prevention of stroke [4].

AF provokes a structural remodeling involving both atrial cardiomyocytes and microenvironment changes [8, 9]. Histological examinations have shown metabolic changes with a switch in cardiomyocyte metabolism [10], also referred to as cardiomyocyte dedifferentiation [8]. Recent genetic data support this "atrial-to-ventricular switch" with up-regulation of ventricular genes and downregulation of atrial genes in atrial walls [8]. Subsequently, atrial patchy fibrosis [11] appears progressively in the right atrium and right appendage, associated with lymphomononuclear [12] and epicardial

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adipose tissue inflammation (EAT) [13, 14]. Of note, several studies have suggested a link between inflammation and thromboembolic events [15].

Quantification of inflammatory activity in atrial walls remains a challenge. Molecular imaging could provide crucial information, especially [^{18}F]fluorodeoxyglucose-positron emission tomography combined with computed tomography (^{18}F-FDG-PET/CT). This technique has proven its ability to identify, with high sensitivity, myocardial inflammatory involvement in cardiac sarcoidosis and is now part of the diagnostic workup [16]. While atrial walls are usually devoid of FDG uptake [16], a few studies have reported the presence of atrial FDG signal in patients with AF [17, 18]. The recent study by Lange et al. [19] did not show significantly greater FDG uptake in atrial walls in patients with AF, but showed a strong association between atrial and left ventricular myocardial signal, supporting the hypothesis of a common metabolic shift from free fatty acids to glucose as the main substrate. In addition, patients enrolled in previous studies did not undergo a high-fat low-carbohydrate (HFLC) diet designed to suppress nonspecific myocardial FDG uptake, so there may have been multiple etiologies of atrial uptake [19, 20].

We hypothesized that AF could promote FDG uptake in atria, independently of nonspecific myocardial uptake, and we sought to identify a potential relationship between FDG atrial uptake and the occurrence of embolic events in patients with AF. Hence, we performed a case–control study that enrolled 64 patients with and 64 without a history of AF (matched for sex and age), who underwent [^{18}F]FDG-PET/CT after HFLC diet and fasting to achieve a myocardial glucose physiological uptake suppression. We characterized the FDG atrial uptake pattern in both groups and assessed the relationship with cardioembolic events.

Material and methods

Study population

This single center study retrospectively enrolled adult patients referred to our Department between April 2011 and October 2017 for the assessment of cardiac inflammation or infection (suspected cardiac sarcoidosis or infective endocarditis or infection of a cardiac implantable electronic device), that required the suppression of physiological FDG myocardial uptake by an HFLC diet and > 12-h fasting as previously reported [21]. Group 1 consisted of consecutive patients with AF history. For every included patient in group 1, one control patient was matched for sex and age. Patients were included if they met the following criteria: age ≥ 18 years, HFLC diet followed by > 12-h fasting, follow-up ≥1 year. CHA_2DS_2-VASc risk factors of stroke and a history of proven stroke (symptomatic embolic event confirmed on resonance magnetic imaging) were systematically noted [4]. Left atrial dilation was defined by an area > 20 cm^2 [22] on echocardiogram. In addition, potential confounders such as atrial thrombus in the appendages were excluded. We used the last ECG (n = 50) or Holter ECG monitoring (n = 14) to characterize the arrhythmia. Most of the patients had permanent AF (n = 48) and a few patients had paroxysmal AF (n = 16). The average duration of the arrhythmia was 6.8 ±2.6 years, and 79% of the patients in the group with AF were treated with anticoagulants.

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

Acquisitions were performed on a PET/CT hybrid system (Discovery 690; General Electric Medical Systems, Buc, France), 60 min after ^{18}F-FDG injection at a dose of 4 MBq/kg. Imaging started with non-enhanced, low-dose CT (120 kV, 80 mA) for attenuation correction in all patients and was followed by whole-body PET acquisition in three-dimensional time-of-flight mode, with an acquisition time of 3 min per bed position. PET images were reconstructed with an ordered-subset expectation–maximization 3D iterative algorithm, using two iterations and 24 subsets, a 256 × 256 matrix size and a post-reconstruction Gaussian filtering with 6.4 mm full width at half maximum.

Image analysis

Image analysis was performed using Advantage Workstation software (GE Healthcare) by a nuclear medicine physician blinded to patients' medical records. The efficiency of the HFLC diet was visually graded as previously described [21]: 0 = absence of uptake or FDG uptake on cardiac walls was lower than that of blood pool; 1 = faint or heterogeneous when uptake was the same level as the mediastinum or greater, but with areas with no uptake; and 2 = intense when left ventricular uptake was intense and homogeneous. The assessment of FDG uptake on atrial walls was performed on horizontal long axis slices after oblique reorientation, comparing FDG uptake of atrial walls and blood pool (0 = no uptake, 1 = uptake superior to mediastinum). A quantitative analysis was then performed using a 20 mm^3 volume of interest (VOI) to measure the maximum standardized uptake value (SUV_{max}) on right atrium (RA), left atrium (LA), right appendage (RAA) and left appendage (LAA) walls. FDG uptake has been specifically assessed in atrial appendages, since they are areas of low blood flow, particularly in the case of AF, which promotes thrombus formation. Also, LAA is the most frequent location of thrombus in the setting of cardioembolic stroke. Mean blood pool SUV was measured within the right ventricle distant from any wall uptake, and the atrial wall-to-background ratio (TBR) was calculated by dividing atrial SUV_{max} by blood pool SUV_{mean}. The left ventricle FDG uptake [19] and

the SUV_{mean} in the spleen [22] were also assessed, as previously reported.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and compared using of Student's *t* test. Categorical variables are presented as percentages and compared using Fisher's exact test. Pearson's correlation coefficients were calculated to assess the association between two continuous variables. Predictors of stroke were determined using logistic regression analysis. Given the close correlation of parameters assessing the intensity of FDG atrial uptake (presence of atrial uptake, atrial SUV_{max} and appendage SUV_{max}), only the presence of atrial uptake was retained for multivariate analysis. Otherwise, variables with a p value ≤0.1 on univariate analysis were retained for multivariate analysis that used a backward stepwise selection of variables. Statistical analysis was performed using MedCalc Statistical Software version 17.2 (MedCalc Software, Ostend, Belgium). A p value ≤0.05 was considered statistically significant.

Results

Study population

Group 1 consisted of 64 consecutive patients with a history of AF (56% male, 70 ± 14 years, 75% with chronic AF, 25% with paroxysmal form). Group 2 consisted of 64 patients without AF matched for age and sex (53% male, 69 ± 14 years). A substantial proportion of patients presented with valvular heart disease (37% in group 1 and 28% in group 2; $p = 0.42$) or a history of coronary artery disease (22% in group 1 and 11% in group 2; $p = 0.15$). In both groups, a small proportion of patients had a final diagnosis of definite endocarditis (20% in group 1 and 9% in group 2, $p = 0.14$) or cardiac sarcoidosis (2% in group 1 and 5% in group 2, $p = 0.62$). Other baseline characteristics are presented Table 1. As expected, most patients in group 1 were under treatment with anticoagulants, in contrast to group 2. The quality of physiological glucose uptake suppression was good in both groups, with 50 (78%) and 44 (69%) patients, respectively, with complete myocardial suppression, 4 and 10 with low uptake (grade 1), and 10 and 10 with grade 2 uptake. As expected, significant dilation of left and right atria was present in the group with AF (Table 1).

FDG uptake pattern

One-third (24/64) of patients with AF presented diffuse atrial FDG uptake, involving at least the right atrial wall ($n = 24/24$), while left atrial uptake was significant in nine patients (14%, $p = 0.01$ compared with RA uptake). Only two patients in the group without known AF exhibited detectable right atrial uptake ($p < 0.0001$) (Fig. 1). In this group with AF, four patients with atrial positive uptake presented proven CIED infection. No association was found between infectious status and the atrial uptake pattern ($p = 0.52$), and none of the five patients diagnosed with cardiac sarcoidosis had positive atrial uptake.

In agreement with the visual analysis, RA, LA, RAA and LAA FDG uptake intensity was significantly associated with the underlying heart rhythm. The normalized values RA TBR and LA TBR were also significantly greater in group 1 than in group 2. All results are presented in Table 2.

There were more patients with atrial dilation in group 1 (62 vs. 22%, $p < 0.01$), but atrial uptake was not correlated with atrial area, for example, between LA area and visual LA uptake ($p = 0.84$) or LA SUV_{max} ($r = -0.26$; $p = 0.11$). Neither age, gender, presence of CIED, cardiovascular risk factors, nor blood markers of inflammation were significantly associated with RA uptake.

In the whole population, a significant but modest correlation was found between left ventricular uptake and RA uptake ($r = 0.25$; $p = 0.005$), suggesting a small impact of physiological glucose utilization in atrial uptake. Indeed, the ventricular uptake was higher in group 1 than in group 2, with SUV_{max} of 4.56 ± 3.47 and 3.79 ± 2.65, respectively ($p = 0.16$), with no correlation between ventricular uptake and heart rate ($r = 0.12$; $p = 0.88$) (Table 2). The mean heart rate during acquisition was 83 beats per minute (bpm) in group 1 and was not correlated with atrial uptake parameters ($r = 0$; $p = 0.95$).

Atrial uptake and stroke

As expected, a history of stroke of cardioembolic origin was more frequent in the group with AF than in the group without AF (17 patients vs. 2 patients respectively; $p < 0.0001$). Interestingly, the occurrence of stroke was frequently associated with detectable atrial uptake (Table 3). A similar pattern was present in the group of patients with AF (LA uptake present in 35 vs. 6% of patients with/without stroke, respectively ($p = 0.02$); RA uptake present in 65 vs. 28% of patients with/without stroke, respectively ($p = 0.08$). One patient of group 2, without documented AF, presented both a history of stroke and right atrial uptake. In the study population, RA SUV_{max} was higher in the case of history of stroke as well as LA SUV_{max} (Table 3). Conversely, there was no association between history of stroke and CHA_2DS_2-VASc risk factors (Table 3). In the multivariate analysis, RA uptake and active smoking were the only independent variables associated with the occurrence of stroke, including when history of AF was retained in the model (Table 4).

Table 1 Baseline characteristics of the 128 patients enrolled

Characteristics	Total population ($N = 128$)	Group 1 ($N = 64$)	Group 2 ($N = 64$)	p value
Age [years, mean (SD)]	70.1 (14)	70.2 (14)	69.9 (14.57)	0.91
Male [*n* (%)]	70/128 (55)	36/64 (56)	34/64 (53)	0.85
History of CAD [*n* (%)]	21/128 (16)	14/64 (22)	7/64 (11)	0.15
Valvular heart disease [*n* (%)]	42/128 (33)	24/64 (37)	18/64 (28)	0.42
Atrial dilation	54/128 (42)	40/64 (62)	14/64 (22)	<0.01
Hypertension [*n* (%)]	64/128 (50)	38/64 (59)	26/64 (41)	0.22
Diabetes [*n* (%)]	42/128 (33)	24/64 (37)	18/64 (28)	0.42
Dyslipidemia [*n* (%)]	35/128 (27)	17/64 (27)	18/64 (28)	0.88
Current smoker [*n* (%)]	13/128 (10)	9/64 (14)	4/64 (06)	0.18
Obesity [*n* (%)]	16/128 (12)	7/64 (11)	9/64 (14)	0.64
Referral indication				
- Endocarditis [*n* (%)]	110/128 (86)	55/64 (86)	55/64 (86)	1
- Sarcoidosis [*n* (%)]	8/128 (6)	1/64 (1)	7/64 (11)	0.04
Final diagnosis				
- Endocarditis [*n* (%)]	19/128 (15)	13/64 (20)	6/64 (9)	0.14
- Sarcoidosis [*n* (%)]	4/128 (3)	1/64 (2)	3/64 (5)	0.62
CIED [*n* (%)]	35/128 (27)	22/64 (34)	13/64 (20)	0.18
Steroid anti-inflammatory treatment [*n* (%)]	18/128 (14)	10/64 (15)	8/64 (12)	0.66
Anticoagulant treatment [*n* (%)]	56/128 (44)	51/64 (79)	5/64 (8)	<0.0001
Biological inflammatory syndrome				
- Leukocyte count [$\times 10^9$.L(SD)]	8.89 (9.83)	7.49 (4.45)	11.23 (13.27)	0.11
- C-reactive protein [mean, (SD)]	45.58 (48.98)	37.69 (45.49)	58.08 (52.59)	0.15
Atrial flutter [*n* (%)]	2/128 (2)	2/64 (3)	0/64 (0)	0.16
Permanent AF	48/128 (37.5)	48/64 (75)	–	
Paroxysmal AF	16/128 (12.5)	16/64 (25)	–	
History of stroke	19/128 (15)	17/64 (26)	2/64 (3)	<0.001
Left atrial area [cm2, (SD)]	24.7 (10.8)	30.5 (11.6)	19 (4.5)	<0.001
Blood glucose [mmol/L (SD)]	6 (1.5)	6 (1.4)	5.9 (1.6)	0.79

SD standard deviation; *CAD* coronary artery disease; *CIED* cardiovascular implantable electronic device (pacemaker/implantable cardiac monitor)

Discussion

This case–control study performed in patients who underwent HFLC diet and prolonged fasting substantiates the relationship between history of AF and FDG uptake in the atrial walls. Atrial uptake pattern is highly suggestive of AF, present in one-third of patients with AF and in only two patients of the control group. The uptake intensity was greater in the right atrium than in the left, as described in previous retrospective studies that did not include a specific diet to suppress myocardial uptake [23]. In addition, increased atrial FDG uptake was associated with increased prevalence of stroke in the overall population, suggesting that this pattern may be regarded as a risk marker of stroke.

Myocardial FDG uptake varies considerably between patients or even according to fasting duration due to its reliance on metabolic conditions. The results of the present study corroborate previous reports, which described a trend toward increased atrial uptake in patients with AF [17, 20], but in addition, all patients in the present study underwent the HFLC diet followed by a fasting period. Myocardial glucose uptake suppression is now widely used for cardiac FDG PET studies, since it increases the diagnostic accuracy in infective or inflammatory processes [21]. However, FDG uptake in the ventricular walls may persist, as glucose can still account for 30–40% of the energy derived from oxidation [24]. Conversely, there is no uptake in normal atria, because metabolism derived from carbohydrates is markedly lower than in ventricles [25].

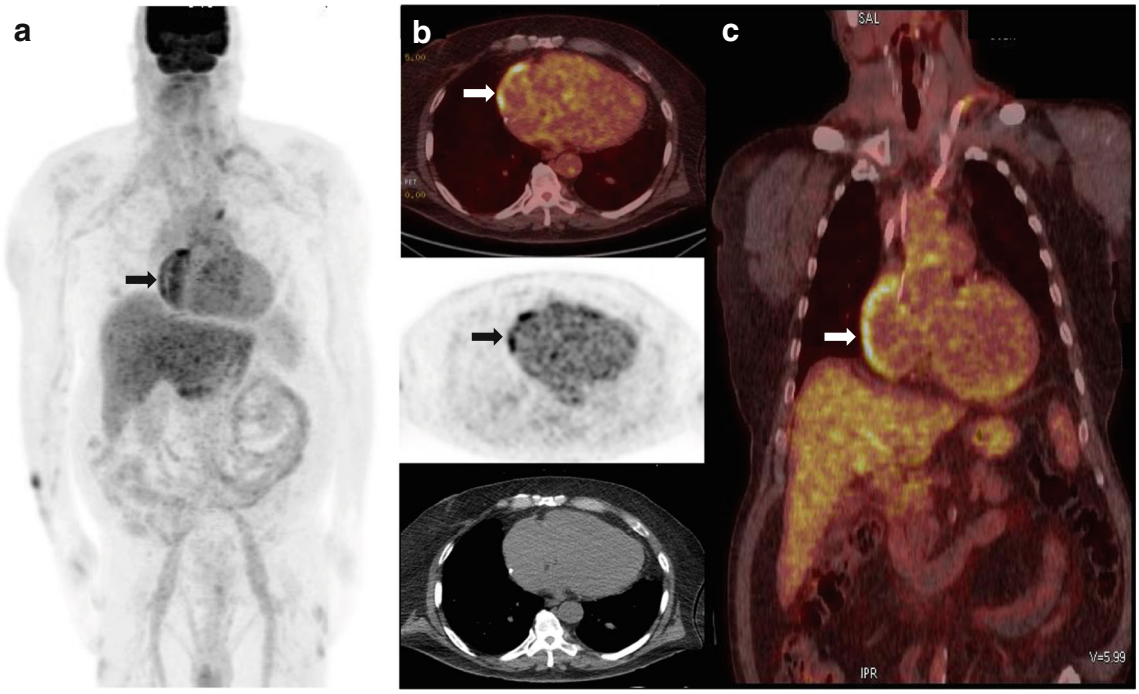

Fig. 1 A 60-year-old patient with diffuse right atrial FDG uptake, representative of an atrial fibrillation metabolic pattern. Interestingly in this patient, atrial fibrillation has been detected during the diagnostic workup of ischemic stroke. A: Maximum intensity projection of ^{18}F-FDG-PET/CT, B: axial views, C: coronal view

The pathophysiology of increased glucose utilization by atria during AF that may involve different levels of transient metabolic shift, chronic metabolic remodeling and inflammation, as well as its predominance in the RA, is not precisely elucidated. Indeed, transcriptomic studies have demonstrated high expression of ventricular genes in the atrial cells of patients with chronic AF [8]. This novel approach suggests that the cellular dedifferentiation toward a fetal-like phenotype is a protection mechanism developed by myocytes. Various reasons for this switch have been proposed, including local ischemia, calcium homeostasis breakdown and passive stretch [26, 27]. Xie et al. [28] found that persistent AF was an independent factor predicting increased activity of the atrium. We did not find such an association, although the small number of patients with

Table 2 FDG-uptake values and corresponding TBR values in AF or without AF

	Total population (N = 128)	Atrial fibrillation (N = 64)	No atrial fibrillation (N = 64)	*p* value
Right visual uptake	26 (0.20)	24 (0.38)	2 (0.03)	<0.001
Left visual uptake	9 (0.07)	9 (0.14)	0 (0.00)	0.004
RA SUV_{max}	2.98 (0.97)	3,35 (1.16)	2.62 (0.55)	<0.001
RAA SUV_{max}	3.08 (1.19)	3.51 (1.46)	2.65 (0.46)	<0.001
LA SUV_{max}	2.84 (0.68)	3.07 (0.72)	2.61 (0.55)	<0.001
LAA SUV_{max}	2.75 (0.69)	3.03 (0.76)	2.47 (0.53)	<0.001
Left ventricle FDG uptake	4.17 (3.1)	4.56 (3.47)	3.79 (2.65)	0.16
Blood pool in the right ventricle	1.89 (0.46)	1.97 (0.51)	1.81 (0.39)	0.46
Mean splenic SUV_{max}	2.24 (0.51)	2.22 (0.51)	2.26 (0.52)	0.67
TBR right atrial	1.59 (0.39)	1.73 (0.45)	1.49 (0.26)	<0.001
TBR right appendage	1.58 (0.52)	1.80 (0.63)	1.39 (0.19)	<0.001
TBR left atrial	1.52 (0.32)	1.61 (0.36)	1.46 (0.19)	<0.01
TBR left atrial appendage	1.51 (0.29)	1.57 (0.30)	1.46 (0.22)	0.02

Data are presented as mean (SD)

TBR target-to-background ratio, *AF* atrial fibrillation, *RA* right atrial FDG-uptake, *RAA* right atrial appendage

Table 3 Relationship between FDG uptake and risk factors of stroke

		Stroke ($N = 19$)	No stroke ($N = 109$)	p value
Heart rhythm status	Atrial fibrillation	17 (0.89)	47 (0.43)	<0.0003
FDG uptake	Left uptake, *n* (%)	6 (0.32)	3 (0.03)	0.001
	Right uptake, *n* (%)	12 (0.63)	14 (0.13)	<0.001
	RA SUV_{max} (SD)	3.91 (1.55)	2.84 (0.73)	<0.01
	LA SUV_{max} (SD)	3.21 (0.80)	2.78 (0.64)	0.01
	RAA SUV_{max} (SD)	3.97 (1.84)	2.82 (0.96)	<0.01
	LAA SUV_{max} (SD)	3.03 (0.77)	2.78 (0.67)	0.16
Stroke risk factors	Hypertension, *n* (%)	10 (0.53)	59 (0.54)	0.95
	Age ≥ 75 years, *n* (%)	10 (0.53)	49 (0.45)	0.71
	Diabetes, *n* (%)	6 (0.32)	36 (0.33)	0.93
	Vascular disease, *n* (%)	4 (0.21)	17 (0.16)	0.74
	Sex (female) *n* (%)	8 (0.42)	50 (0.46)	0.85
	Left atrial dilation, *n* (%)	3 (0.16)	24 (0.22)	0.49
Other CV risk factors	Dyslipidemia, *n* (%)	5 (0.26)	30 (0.27)	0.93
	Current smoker, *n* (%)	4 (0.21)	9 (0.08)	0.23
	Obesity, *n* (%)	1 (0.05)	15 (0.14)	0.69

SD standard deviation,*AF* atrial fibrillation, *RA* right atrial FDG-uptake, *RAA* right atrial appendage FDG-uptake, *LA* left atrial FDG-uptake, *LAA* left atrial appendage FDG-uptake, *CV* cardiovascular

paroxysmal AF might represent a limitation to this finding. An animal model of persistent AF showed that the first molecular change appeared 2 weeks after onset of the arrhythmia, while structural remodeling appeared progressively with gradual re-expression of alpha-smooth muscle actin [29].

Table 4 Univariate and multivariate analysis of risk factors of stroke

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Heart rhythm status				
Atrial fibrillation	11.21 (2.47–51.02)	0.0017		
FDG uptake				
Right atrial uptake	11.63 (3.92–34.53)	<0.0001	14.36 (4.43–46.51)	<0.0001
Left atrial uptake	16.30 (3.64–73.15)	0.0003		
RA SUV_{max}	2.52 (1.50–4.23)	0.0001		
LA SUV_{max}	2.33 (1.173–4.62)	0.015		
RAA SUV_{max}	1.84 (1.24–2.74)	0.0007		
LAA SUV_{max}	1.61 (0.82–3.15)	0.17		
Stroke risk factors				
Hypertension	1.06 (0.40–2.82)	0.90		
Age ≥ 75 years	1.36 (0.51–3.61)	0.54		
Diabetes	0.94 (0.33–2.67)	0.90		
Vascular disease	1.44 (0.43–4.88)	0.56		
Sex (female)	0.86 (0.32–2.30)	0.76		
Left atrial dilation	0.50 (0.12–2.04)	0.33		
Other CV risk factors				
Dyslipidemia	0.94 (0.31–2.84)	0.91		
Current smoker	2.96 (0.81–10.84)	0.10	5.24 (1.12 to 24.49)	0.035
Obesity	0.35 (0.04–2.80)	0.32		

AF atrial fibrillation, *RA* right atrial FDG-uptake, *RAA* right atrial appendage FDG-uptake, *LA* left atrial FDG-uptake, *LAA* left atrial appendage FDG-uptake, *CV* cardiovascular

The present study suggests a relationship between the presence and intensity of FDG atrial uptake and the occurrence of cardioembolic stroke. On multivariate analysis, RA uptake was associated with the highest odds ratio. Conversely, there was no correlation between left atrial dilation, hypertension, diabetes or dyslipidemia and stroke occurrence. One hypothesis is that increased atrial FDG uptake detected by PET may be a marker of local inflammation in addition to metabolic shift, and as such may constitute a pro-thrombotic factor. Several studies have shown a link between thrombogenesis and inflammation [15]. Supporting this assumption, systemic biomarkers such as interleukin-6 (IL-6) and C-reactive protein (CRP) have already shown an association with the occurrence of vascular events in the case of AF [30, 31]. In our study, active smoking (but not CRP) was also an independent predictor of stroke. All these findings seem to support the hypothesis of inflammation in the atrial wall microenvironment mediated by local factors (fibrosis, inflammation and cardiomyocyte degeneration) [32], possibly maintained by systemic inflammation [31]. The design of the study and the relatively short duration of follow-up are limiting factors, but the results suggest that increased atrial FDG uptake may be an independent risk marker of thromboembolic events. In the future, a prospective study must be carried out to assess this hypothesis.

Limitations of the study

In order to avoid nonspecific FDG myocardial uptake, we selected patients who underwent the specific no-carbohydrate diet in the setting of routine care, i.e., in patients with suspected cardiac sarcoidosis or infective endocarditis or infection of a cardiac implantable electronic device. Those diseases and the associated confounders may have influenced atrial uptake, although the diagnosis was rejected in most patients, and positive atrial uptake was not associated with any of the suspected diseases.

Due to the inclusion of patients with atrial arrhythmia, 42% of the study population had atrial dilation. Atrial uptake was inversely correlated with atrial area, possibly due in part to a partial volume effect [33–35]. However, this bias should have led to an underestimation of the true FDG atrial uptake in patients with AF, and therefore the differences between the two groups should have been greater than those reported.

Similarly, the prevalence of patients implanted with a cardiac device was relatively high in the group with AF (although not significantly different between groups). Most of those patients had sinus node dysfunction, which is often associated with atrial fibrillation. Atrial pacing is inhibited during AF episodes, but it could be relevant to consider the impact of atrial electro-stimulation in patients with sick sinus syndrome.

Another limitation of the study is the absence of ECG recording at the time of FDG administration, which explains that paroxysmal atrial arrhythmia could have been missed in the two patients in the control group who presented an atrial FDG uptake.

Conclusion

This case–control study shows a significant association between FDG atrial uptake and atrial fibrillation. While inconsistent in patients with AF, this pattern seems to be associated with increased prevalence of cardioembolic stroke. Future studies should seek to evaluate prospectively whether FDG atrial uptake is a marker of increased risk of stroke in patients with known or silent AF.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval and consent The institutional review board of Bichat Hospital approved this study, and all subjects gave informed consent for review of their records.

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