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Positron Emission Tomography (PET) Evaluation of Abdominal Aortic Aneurysm (AAA)

N. Sakalihasan[1], H. Van Damme[1], P. Gomez[4], P. Rigo[2], C. M. Lapiere[3], B. Nusgens[3] and R. Limet[1]

Departments of [1]Cardiovascular Surgery, [2]Nuclear Medicine and [3]Laboratory of Connective Tissues Biology, University Hospital of Liège, CHU Sart-Tilman, 4000 Liege, [4]Department of Nuclear Medicine, St-Joseph Hospital, Rue de Hesbaye, 75, 4000 Liege, Belgium

Abstract

Background: aneurysmal disease is associated with an inflammatory cell infiltrate and enzymatic degradation of the vessel wall.

Aim of the study: to detect increased metabolic activity in abdominal aortic aneurysms (AAA) by means of positron emission tomography (PET-imaging).

Study design: twenty-six patients with AAA underwent PET-imaging

Results: in ten patients, PET-imaging revealed increased fluoro-deoxy-glucose (18-FDG) uptake at the level of the aneurysm. Patients with positive PET-imaging had one or more of the following elements in their clinical history: history of recent non-aortic surgery (n = 4), a painful inflammatory aortic aneurysm (n = 2), moderate low back pain (n = 2), rapid (>5 mm in 6 months) expansion (n = 4), discovery by PET-scan of a previously undiagnosed lung cancer (n = 3) or parotid tumour (n = 1). Five patients with a positive PET scan required urgent surgery within two to 30 days. Among the 16 patients with negative PET-imaging of their aneurysm, only one had recent non-aortic surgery, none of them required urgent surgery, only two had a rapidly expanding AAA, and in only one patient, PET-imaging revealed an unknown lung cancer.

Conclusion: these data suggest a possible association between increased 18-FDG uptake and AAA expansion and rupture.

Key Words: Tomography, emission-computed; Aortic aneurysm, abdominal; Metalloendopeptidases.

INTRODUCTION

The risk of rupture increases with the diameter of AAA,[1] however, rupture also occurs in small AAA; it would therefore be useful to define criteria of accelerated growth and impending rupture in smaller AAA. An increased number of inflammatory cells and elevated levels of cytokines within the aneurysm wall have been observed.[2] Cytokines may trigger an increased production of matrix metalloproteinases (MMP) by macrophages and smooth muscle cells. We observed a relationship between the level of inflammatory infiltrate and activation of MMP_2.[3] The risk of rupture can be correlated with the level of biologic markers (matrix metalloproteinases (MMP-2 and -9) and their tissue inhibitors (TIMP 1 and 2)).

We investigated the potential of whole-body positron emission tomography (PET) to detect increased metabolic activity of the aneurysm wall. Such hypermetabolism could possibly reflect changes in the aneurysm wall portending rupture.

Positron emission tomography (PET) is a diagnostic method that creates high resolution, three-dimensional tomographic images of the distribution of positron emitting radionuclides in the human body. The radiolabelled compounds used include substrates, ligands, drugs, antibodies, neurotransmitters and other biomolecules that are tracers for specific biological processes. The resulting PET images can be considered as "functional images" of these biochemical or physiological processes. Biochemical processes are altered in most diseases, and these alterations usually precede gross anatomical changes.

Historically, the initial PET studies focused on cerebral and myocardial metabolism. Now, PET is often used for oncological investigation. The most widely applied substrate is fluorodeoxyglucose, (18-FDG) a marker of glycolysis. 18-FDG uptake into malignant cells is enhanced by an increased expression of glucose transport molecules on the tumour cell surface. However, FDG uptake is not specific for tumors. FDG-PET scan can also be positive in inflammatory disease.[5] Within tumours, as well as in inflammatory lesions, part of FDG is taken up by macrophages and other blood cells, and up to 25% of the signal reaching the scanner could be due to glycolysis from macrophages within the tumour.[6] FDG uptake in atherosclerotic lesions has been described primarily in spumous cells of the atherosclerotic plaque.[7]

In this study, we analysed PET images in 26 patients with a documented AAA in order to correlate the clinical course of the AAA with the rate of 18-FDG uptake.

MATERIAL AND METHODS

Patients

The study population consisted of a non-consecutive series of 26 patients with AAA (23 males and 3 females) documented by CT-Scan, for whom a complementary investigation by PET imaging was performed between March 1999 and August 2001. The patients presented an AAA with one or more of the following characteristics: large size (70 mm or more) (n = 11), painful AAA (n = 11), familial history of AAA (n = 1), inflammatory AAA (n = 4), rapid expansion (n = 6). PET-imaging was performed depending on the availability of the PET imaging system of the hospital.

Mean age was 72 (range 56-85) years. The mean diameter of AAA was 63 mm (range 45-78 mm).

Methods

Radiopharmaceutical

After a minimum 6 h fasting, 3.7mBq F-18-FDG per kilogram body weight was injected into a peripheral vein.

PET protocol

Static whole-body PET was performed with either an ADAC E-PET or a GE Advance tomograph. Beginning 60 min after tracer injection, emission and transmission images were recorded at each couch position (5-8) for 4-5 and 2-3 minutes, respectively. Coronal, sagittal and transaxial images were based on the use of an ordered subset expectation maximization iterative reconstruction algorithm (OSEM) including post-injection segmented attenuation correction.

Image interpretation

Two experienced investigators interpreted the PET images. The images were reviewed on hard copy and on a computer workstation (SUNSparc, SUN Microsystem, Palo Alto, CA, U.S.A.).

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Table 1. *Patient characteristics with positive FDG uptake.*

Patients			Diameter of AAA		Delay between diagnosis and	Remarks	
No.	Sex	Age	Initial	Last	surgery		
1	F	64	_	71	<l month	Low back pain	
2	M	60	-	76	< 2 months	Painful inflammatory AAA	
3	M	70	42	51	36 months	Painful inflammatory AAA, rapidly expanding	
4	M*	79	32	70	96 months	Rapidly expanding AAAy prostatectomy	Parotid tumour†
5	M*	73	60	64	6 months	Recent nephrectomy for hypernephroma, leaking AAA	
6	M*	77	35	70	24 months	Recent bilateral carotid TEA, rapidly expanding AAA	Pulmonary CAf
7	M*	82	54	60	6 months	Recent sigmoidectomy, rapidly expanding AAA	
8	M	74	-	70	<l month	Low back pain	
9	M	69	-	70	2 days	Thoracic aneurysm, painful AAA	Pulmonary CAf
10	M	84	-	50	unoperated	Asymptomatic	Pulmonary CAf

* Patients who had emergency surgery. † Lesions revealed by PET scan.

RESULTS

Among the 26 patients, PET scan revealed visible 18-FDG uptake over the infrarenal aorta in ten. The details are shown in Table 1.

Four of these patients (cases 4, 5, 6, 7) had a past history of a recent (within 6 months) operation excluding aortic surgery (carotid endarterectomy, nephrectomy, prostatectomy, sigmoidectomy). Each of these four patients with positive PET imaging and a positive history of recent operation required urgent aneurysmectomy for rupture (case 6), leaking (case 5), severe back pain and rapid growth (cases 4 and 7). One of these four AAA patients (case 6), with a history of three previous vascular interventions, ruptured his aneurysm eight days after the PET and had emergent surgery (Fig. 1). Another patient (case 5), who underwent nephrectomy six months prior to PET imaging, had emergency surgery for leaking AAA 20 days after the examination. Another patient (case 4) with recent resection for prostatic carcinoma had a known AAA. He did not have elective surgery because of pulmonary disease, and had to be operated on one month later for back pain and an increase in size of the aneurysm of 12 mm (Fig. 2).

A positive PET image was also observed in two of the four inflammatory aortic aneurysms (IAAA) diagnosed on CT scan. Both IAAA were painful (cases 2 and 3).

In three other patients (cases 6, 9, 10) with positive 18-FDG uptake of their AAA, PET imaging also revealed a previously undiagnosed lung cancer. One of them (case 10) benefited from pulmonary lobectomy and will be followed further for his AAA. Another patient (case 9) underwent urgent AAA resection two days after PET imaging, because of severe back pain related to his 70 mm AAA. His lung cancer is treated by chemotherapy. In this patient, 18-FDG uptake was also observed at the level of an aneurysmal thoracic aorta (45 mm in diameter). In the third patient (case 6), the lung cancer showed rapid evolution after AAA resection and was managed by palliation. He died 4 months later.

The remaining two patients (cases 1 and 8) with positive PET imaging of the aneurysm had moderate low back pain preoperatively (Fig. 3). Their past history was unremarkable.

The data concerning the 16 patients with negative PET imaging are summarized in Table 2 (cases 11 to 26). Only one of these patients had recent (within 6 months) surgery (coronary artery bypass grafting three months prior). Two of the four inflammatory AAA revealed by CT scan showed no 18-FDG uptake (cases 16 and 22). These IAAA were asymptomatic. One of them presented with silent ureterohydrone-phrosis. In one patient (case

25), PET imaging was negative at the level of the aortic aneurysm, but revealed a stage IV lung cancer. He did not have surgery for the AAA.

Fig. 1. *This partially ruptured AAA is characterised by increased metabolic activity of the aneurysmal wall as evidenced by positive PET imaging. On the right side, the upper image corresponds to the emission image, the second one is a transmission image area; and the third one is a fusion of the two previous images.*

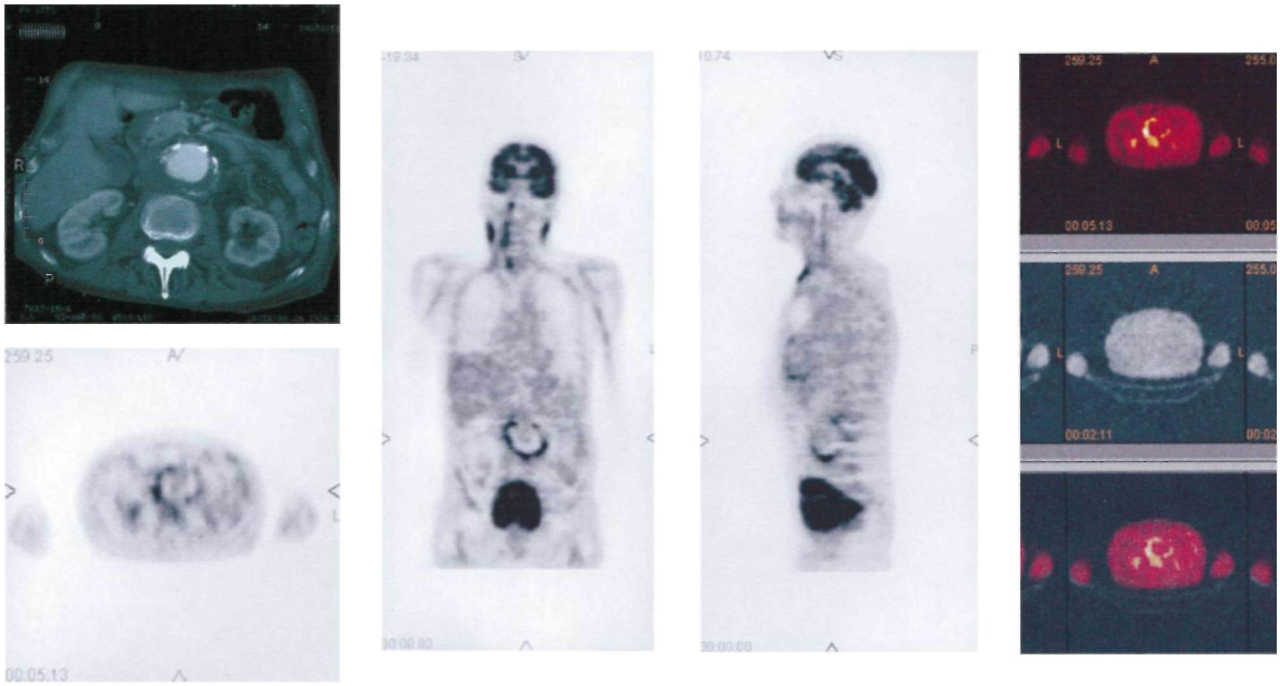

Fig. 2. *This painful rapidly expanding aneurysm of 70 mm displays 18-FDG uptake at the level of the aneurysmal wall.*

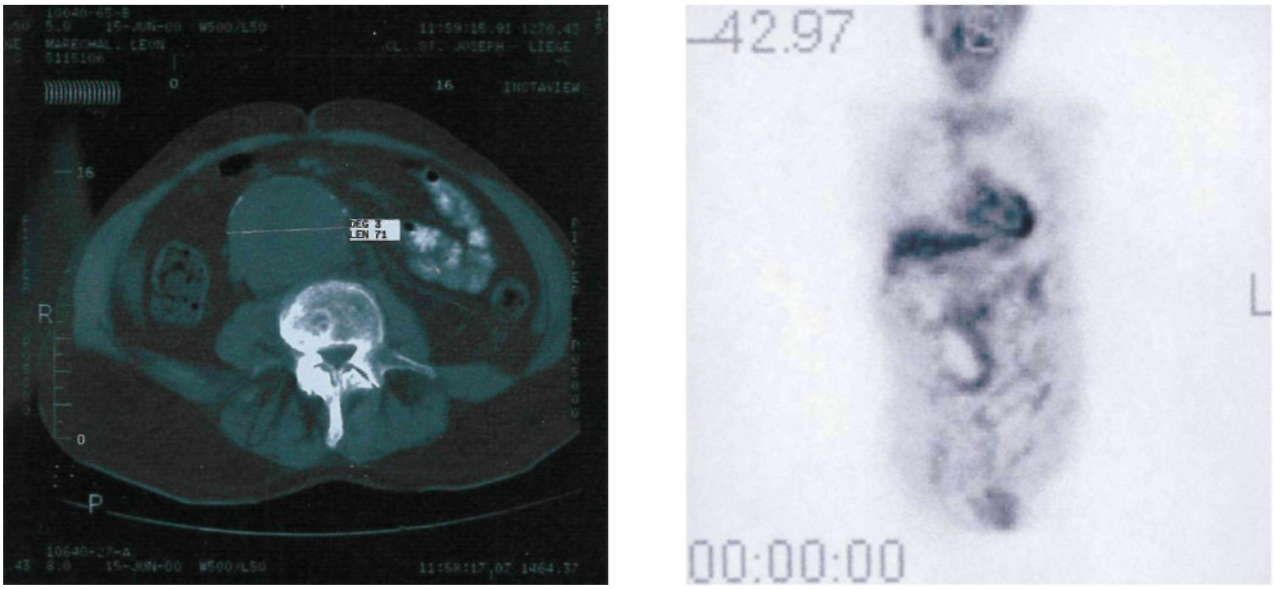

Fig. 3. *This aneurysm is mainly filled with a parietal thrombus. The thrombus does not manifest FDG uptake, in contrast to the aneurysm wall where we observe moderate uptake of FDG.*

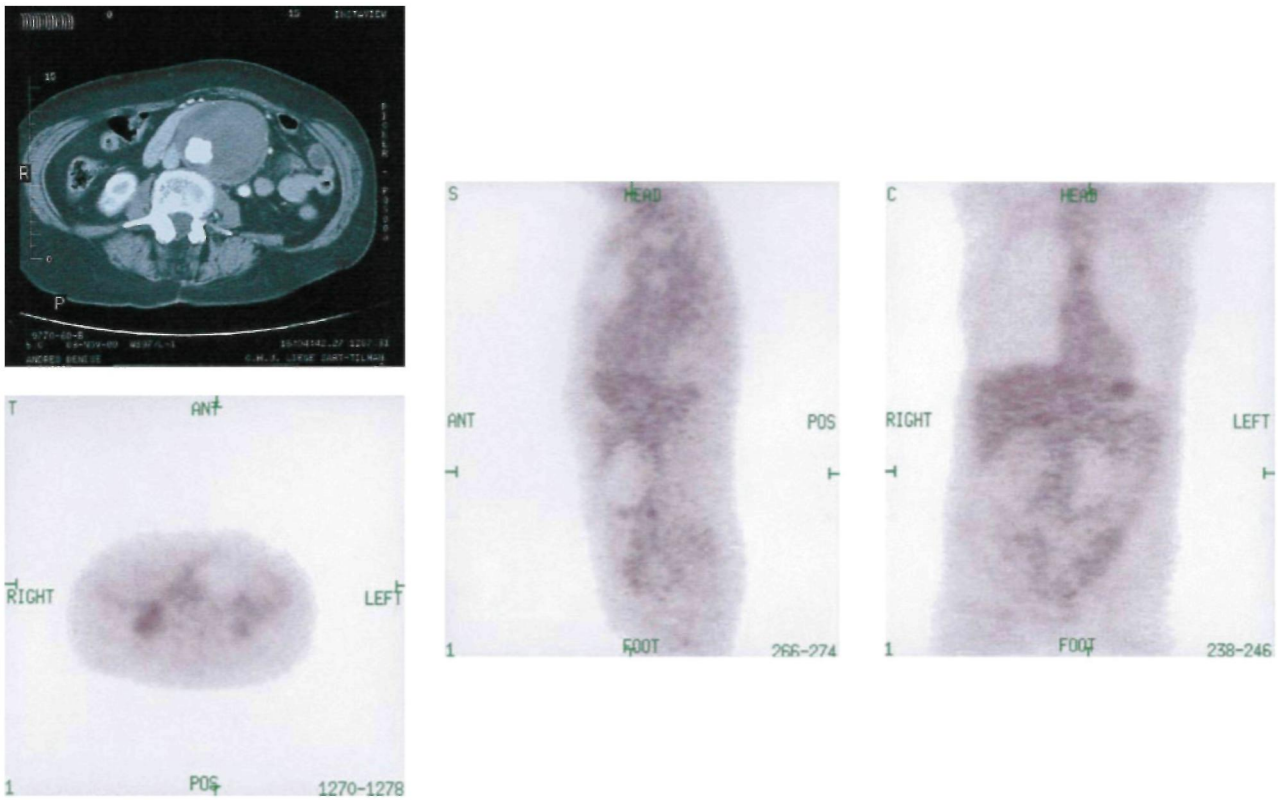

Table 2*. Patient characteristics without positive FDG uptake.*

Patients			Diameter of AAA		Delay between diagnosis and surgery	Remarks
No.	Sex	Age	Initial	Last		
11	M	56	66	70	20 month	Asymptomatic
12	M	69	-	60	<l month	Moderate back pain
13	M	78	56	60	7 months	Moderate back pain
14	F	73	-	45	<l month	AAA with associated aortoiliac artery disease
15	M	68	50	70	17 months	Rapidly expanding AAA
16	M	60	50	50†	7 months	IAAA (asymptomatic)
17	M	70	40	52	36 months	Rapidly expanding AAA
18	F	77	-	65	<l months	Moderate back pain
19	M*	66	30	47	60 months	Positive familial history for AAA
20	M	85	34	66	30 months	Moderate back pain
21	M	78	-	60	< 2 months	Asymptomatic
22	M	77	-	51†	< 2 months	IAAA (asymptomatic) with hydronephrosis
23	M	75	-	78	<l months	Moderate back pain
24	M	64	-	60	<3 months	Asymptomatic, CABG 3 months before
25	M	74	-	70	unoperated	Pulmonary CA with metastasis
26	M	63	-	70	<l month	Moderate back pain

* Familial AAA.
† Inflammatory AAA.

DISCUSSION

This preliminary study of PET imaging of AAA suggests an association between 18-FDG uptake by the aneurysm wall, rapid expansion of the aneurysm, recent (within 6 months) surgery, and malignancy. Indeed, five of the nine operations among patients with positive PET imaging were done on an urgent or emergent basis. No urgent surgery was required among the 15 operated patients with negative PET imaging. In this series, malignancy was also more common among patients with positive PET-imaging of the AAA.

A surgical intervention may activate inflammatory cells, producing collagenase and elastase activity within the aortic wall. Swanson[8] was the first to report an increased growth of AAA as well as an increased tendency to rupture in the postoperative period of an unrelated operation. This interrelationship between AAA rupture and any operation has been well documented in other observational studies.[9]

Aneurysmal degeneration of the aortic wall and malignancy could have a common underlying histo-pathological process. An altered turnover of connective tissue proteins has been documented in AAA as well as in malignant tumors. Bernstein correlated tumor growth to degradation of the interstitial matrix.[10] Our group (and others) reported increased metalloproteinase (MMP) activity within the aneurysm wall.[3] Immunohistological analysis showed that these MMP are produced by inflammatory cells infiltrating the aortic wall.[11,12] The MMP positive cells however represent a subset of only 10-20% of the inflammatory cells within the aneurysm wall.[11] It is possible that this proportion increases in case of unstable aneurysms, prone to rupture (rapid growth and activation of inflammatory processes under certain circumstances). The triggering mechanism of this increased activity however remains unclear.

In inflammatory aortic aneurysms (IAAA), a lymphocytic infiltrate is present in the periadventitial tissue. These lymphocytes produce cytokines, known to regulate MMP expression by macrophages.[12-14] Some IAAA contain a dense macrophage infiltrate associated with the predominant lymphocyte infiltrate. In these cases, the regulation of MMP is altered and protein catabolism is initiated.[12-14] IAAAs with macrophage infiltrate are to be considered as unstable. Activated macrophages can be detected by PET imaging. In one recent report, PET imaging revealed 18-FDG uptake in unstable carotid atherosclerotic plaques. The authors compared the histology of the endarterectomised plaque with the PET imaging. Intraplaque haemorrhage correlated with 18-FDG uptake, indicating a focally increased metabolic activity.[15]

This report is preliminary and will be completed by investigations of the metabolic activity of the aneurysm wall. A comparison of PET imaging with morphological and biochemical analyses of specimens of excised aneurysm wall should provide more insight in the pathogenesis of aneurysmal disease. Positron emission tomography could also help the clinician to proceed to operation electively However, this specialised investigational procedure is not routinely available, and has not yet acquired a definitive place in the diagnosis or treatment of aortic aneurysms.

CONCLUSION

Our preliminary report shows the capacity of PET imaging to assess increased metabolic activity within the aneurysm wall. A subset of aneurysms shows an increased 18-FDG uptake, suggestive of a focally accelerated metabolism. This could predispose to rapid growth and/or imminent rupture.

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