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Longitudinal Assessment of Inflammatory Activity in Acute Type B Aortic Dissection with Integrated Fluorodeoxyglucose Positron Emission Tomography/Magnetic Resonance Imaging

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WHAT THIS PAPER ADDS

The aim of this study was to characterise the inflammatory response in the aortic wall over time in acute type B aortic dissection by means of fluorodeoxyglucose (FDG) positron emission tomography/magnetic resonance imaging (MRI). The highest FDG uptake was found in the acute phase (less than two weeks after onset) in the descending aorta, but also involving the aortic arch and ascending aorta, indicating a hyperinflammatory state in the whole thoracic aorta. This inflammation subsided early in the ascending aorta and the arch (three to four months), while it is stabilised later in the descending aorta (nine to 12 months). MRI inflammatory changes were more frequent in patients who required surgical intervention and merit further investigation as possible biomarkers for disease progression.

Objective: The significance of the inflammatory response in the natural course of acute type B aortic dissection (ATBAD) is unknown. The aim was to characterise inflammation and its transformation over time in ATBAD using ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) with contrast enhanced magnetic resonance imaging (MRI).

Methods: Ten patients underwent FDG-PET/MRI within two weeks of ATBAD (acute phase), three to four months (subacute phase), nine to 12 months (early chronic phase), and 21 to 24 months (late chronic phase) after ATBAD. Target background ratios (TBRs) were measured in the ascending aorta, aortic arch, and descending aorta. MRI inflammatory markers were assessed in the descending aorta.

Results: Ten patients were included: median age 69 years, median clinical follow up 32 months. In the acute phase there was increased FDG uptake in the descending aorta (maximum TBR 5.8, SD [standard deviation] 1.3) compared with the ascending aorta (TBR 3.3, SD 0.8, $p < .010$) and arch (TBR 4.2, SD 0.6, $p = .010$). The maximum TBR of the descending aorta decreased from the acute to subacute phase (TBR 3.5, SD 0.6, $p = .010$) and further to the early chronic phase (TBR 2.9, SD 0.4, $p = .030$) but was stable thereafter. The acute phase maximum TBR in the ascending aorta (TBR 3.3) and arch (TBR 4.2) decreased to the subacute phase (ascending: TBR 2.8, SD 0.6, $p = .020$; arch: TBR 2.7, SD 0.4, $p = .010$) and was stable thereafter. Four patients underwent surgical aortic repair (three for aortic dilatation at one, five, and 28 months and one for visceral ischaemia at three weeks). MRI signs of inflammation were present in all surgically treated patients *vs.* two of six of medically treated patients ($p = .048$).

Conclusion: ATBAD is associated with increased FDG uptake in the acute phase primarily in the descending aorta, but also involving the aortic arch and ascending aorta, indicating an inflammatory response in the whole aorta. Inflammation subsides early in the ascending aorta and arch (three months), whereas it stabilised later in the descending aorta (nine to 12 months). MRI signs of inflammation were more frequent in patients who later needed surgical treatment and merit further investigation.

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INTRODUCTION

Aortic dissection is a relatively common life threatening aortic event, with an incidence of 3.5 — 12 cases per 100 000 inhabitants per year.[1] Uncomplicated type B dissections are often primarily treated by best medical treatment.[2] However, randomised trials suggest that early thoracic endovascular aortic repair (TEVAR) of uncomplicated type B dissection may result in a benefit in terms of improved aortic remodelling and survival over time.[3,4] Thus, pre-emptive TEVAR may prevent aortic related deaths and disease progression in the long term in some patients, but is also associated with early per-operative hazards, and it is unclear which patients will benefit from early intervention. Early detectable prognostic factors for disease progression would help with individual stratification of patients for either meticulous follow up or TEVAR. Timing for early TEVAR treatment of uncomplicated type B aortic dissection is another issue, as the intervention should be performed early to allow for better remodelling, while the risks with TEVAR may be increased in the acute setting with a fragile aortic wall and hyperinflammatory activity in the dissection area.

Inflammation plays an important role in medial wall degeneration in aortic dissection disease, which has been shown on surgical specimens with extensive inflammatory cell infiltrates.[5,6] Increased ^{18}F-fluorodeoxyglucose (FDG) uptake in the aortic wall of patients with acute type B aortic dissection (ATBAD) has been observed in previous positron emission tomography (PET) computed tomography (CT) studies, but reports are scarce.[7,8] Furthermore, the longitudinal transformation of inflammation in the natural course of aortic dissection disease is unknown. Magnetic resonance imaging (MRI) specific signs of aortic wall inflammation (such as gadolinium enhancement [GE]) are recognised features in other vascular inflammation pathologies,[9—11] and have recently been studied by this group on abdominal aortic aneurysms,[12] but have not been thoroughly investigated in the setting of aortic dissection. Combination of both PET and MRI, integrated PET/MRI, enables the use of multiple imaging techniques to study different aspects of the inflammatory process as GE is a marker for angiogenesis and FDG is a marker for increased metabolic activity, mostly seen in inflammatory cells. Such imaging markers may help better understand the pathophysiology of aortic dissection disease and monitor its evolution from acute to chronic phase. In addition, temporal changes in patterns of FDG uptake in ATBAD are important to consider when performing FDG imaging studies aiming to evaluate potential pharmacological interventions[13] or predict high risk patients who may benefit from early surgical intervention.[14] They may also have implications with regards to timing for intervention in type B aortic dissection.

The aim of this study was to characterise inflammation and its transformation over time in the aortic wall of patients with ATBAD by means of integrated ^{18}FDG-PET/MRI.

MATERIALS AND METHODS

Patients

Ten patients with uncomplicated ATBAD, referred to Uppsala University Hospital, were consecutively included in the study between January 2017 and January 2021. Patients were repeatedly examined with FDG-PET/MRI: (1) within two weeks of index event (acute phase), (2) after three to four months (subacute phase), (3) after nine to 12 months (early chronic phase), and (4) after 21 — 24 months (late chronic phase). No patients who entered the study and underwent their PET/MRI examinations were excluded.

ATBAD was primarily diagnosed by means of contrast enhanced CT performed within 24 hours from the onset of symptoms. ATBAD was defined according to the recently published European Society for Vascular Surgery guidelines.[2] All patients received medical treatment with antihypertensive agents and pain management according to current clinical guidelines.[2]

In addition, CT angiography surveillance was performed according to the routine protocol: at 72 hours, one week, and one month, and after discharge at six months, one year, and then yearly thereafter or more frequently, depending on patient clinical status and imaging results. This CT surveillance was also maintained for patients included in the study and performed regardless of the PET/MRI examination results.

Positron emission tomography/magnetic resonance imaging protocol

Examinations were performed using a Signa PET MR unit with digital PET detectors (GE Healthcare, Waukeesha, WI). FDG was used as the PET tracer, 6 MBq/kg body weight, administered intravenously three hours before PET acquisition of a single bed position with a transaxial field of view (FOV) of 60 cm during 25 minutes. Patients fasted overnight and blood tests showed a normal glucose level. PET data were reconstructed with VUE Point FX-S using 28 subsets, four iterations, 192 × 192 pixel matrix, and a 3 mm sharpness filter. Attenuation correction was done with the vendor two point Dixon approach.

MRI sequences were acquired as follows: transversal T2 weighted (w) fatsat (FS) propeller with respiratory triggering (slice thickness 6 mm, FOV 38 cm); transversal diffusion weighted images with b value 0, 50, 200, 500, and 800; transversal LAVA-Flex breath hold with in and out phase, water and fat reconstructions (scan duration 18 seconds, matrix 224 × 200, FOV 40 cm); angio sequences consisted of axial LAVA FS pre-contrast. A dynamic sequence 3D TRICKS yielded nine datasets in 32 seconds. Axial LAVA FS at three minutes post-contrast followed by a coronal and sagittal and an axial LAVA FS at six minutes (LAVA FS scan duration 18 seconds, matrix 256 × 180, FOV 40 cm, slice thickness4 mm. 3D TRICKS 30 sagittal slices, slice thickness 3 mm and 1.5 mm gap, matrix 384 × 192, FOV 40 cm, TR 3.9 ms, TE 1.3 ms, 30 degrees flip angle). Gadolinium contrast agent Dotarem (Guerbet, Roissy, France) was given at a dose of 0.2 mL/kg and a flow rate of 3 mL/s.

Visual analyses of positron emission tomography/magnetic resonance imaging data and ^{18}F-fluorodeoxyglucose uptake

The images were analysed with Carestream software version 12.1.5.7014 (Carestream Healthcare, Rochester, NY).

On visual evaluation, FDG activity was considered elevated when the FDG signal in the aortic wall was higher than the FDG signal in the surrounding tissue. MRI scans were assessed visually for the presence of markers of mural inflammation in the wall of the dissected descending aorta: GE on the six minute post-contrast T1 weighted images, and increased signal on T2 weighted images (*vs.* back muscle). The status of the false lumen was assessed on the contrast enhanced MRI and categorised into patent, partially thrombosed (even if marginal thrombus/contrast was present), or completely thrombosed.

Quantitative analyses of ^{18}F-fluorodeoxyglucose uptake at three levels of the aorta

The aorta was divided into three segments: ascending aorta, aortic arch, and descending aorta. A region of interest was drawn to include only the aortic wall on volume matched PET and MR T2 weighted images on every transaxial slice along the entire length of each aortic segment. The maximum and mean standard uptake values (SUVs) were annotated for each axial slice and the SUVs were then added and divided by the total number of axial images to provide an average maximum and mean SUV for the entire ascending aorta, aortic arch, and descending aorta. Because the SUVs in the aortic wall can be influenced by the remaining FDG in the blood, the target to background ratio (TBR) was also calculated by dividing the averaged aortic SUVmax and SUVmean by blood pool SUV. This methodology is recommended by Rudd *et al.* as it has been proven to be highly reproducible.[15]

Follow up with PET/MRI was discontinued whenever patients underwent open surgical repair during the study period. However, patients treated with TEVAR underwent a single follow up examination with FDG-PET/CT, 12 — 14 months after the TEVAR procedure. PET/CT was used as the TEVAR grafts were deemed to cause too much image distortion on MRI making the attenuation correction difficult. However, the protocol for PET data collection was identical and hence the PET data were comparable for both modalities.

Statistical analyses

All analyses were performed using SPSS Statistics software version 27 (IBM, Armonk, NY). Normality was assessed with a histogram. Values of continuous variables were expressed as median and range. The Fisher exact test was used for proportions. The Mann—Whitney U test was used for comparison of the mean and maximum TBR for each aortic segment at each time point, and the Wilcoxon signed rank test for comparison between time points. A p value $< .050$ was considered significant.

Ethics

The study was performed with the approval of the Regional Ethics Committee of Uppsala (Dnr 2016/201) and the regional radiation committee. All patients gave written consent prior to study participation.

Table 1. Baseline characteristics of the 10 study patients

Characteristics	Patients (n = 10)
Median age — y	69 (55—82)
Body mass index	24 (20—33)
Male	8 (80)
DeBakey classification	
IIIA	4 (40)
IIIB	6 (60)
Status false lumen	
Patent	3 (30)
Partially thrombosed	6 (60)
Completely thrombosed	1 (10)
Largest aortic diameter	43 (31—47)
Diabetes	0 (0)
Coronary heart disease	3 (30)
Hypertension	7 (70)
Chronic obstructive pulmonary disease	2 (20)
Prior cerebral event	1 (10)
Smoking	
Current	1 (10)
Prior	5 (50)
Never	4 (40)
Connective tissue disease	0 (0)
Previous aortic surgery	0 (0)

Data are presented as median (range) or n (%).

RESULTS

Baseline characteristics and clinical outcome

Ten patients (median age 69, range 55 — 82, eight men) with ATBAD were included. The median time from onset of symptoms related to the acute dissection and first PET/MR investigation was a median 13 days (range 4 — 21; only one patient was examined after 14 days). Clinical follow up was a median 32 months (13 — 44). No patients had connective tissue disease. Baseline characteristics are presented in Table 1. During the study inclusion period (January 2017 to January 2021), 27 patients were treated with TEVAR for complications following ATBAD (n = 11 for visceral or extremity ischaemia and n = 16 for aortic dilatation). These patients were all operated on within 12 months of the index event.

Four patients suffered complications during follow up resulting in surgical repair: the first patient with a large proximal entry tear experienced rapid aortic dilatation (> 10 mm) and was treated with TEVAR five months after the index event; the second patient was re-admitted with renewed chest pain and CT showed progressive aortic dilatation which led to a left carotid to left subclavian artery bypass followed by TEVAR one month after the index event; the third patient with a bovine brachiocephalic trunk had a compressed true lumen at the visceral level and clinical suspicion of dynamic visceral ischaemia. This patient had no suitable proximal landing zone for a standard TEVAR and was therefore treated with a frozen elephant trunk, with a good result; the fourth patient suffered progressive aortic dilatation and was treated with staged TEVAR and branched EVAR 28 months after the index event. See Table 2 for

Table 2. Aortic dissection characteristics and outcome for the 10 study patients

Case no.	Sex/Age	DeBakey	False lumen morphology	Outcome
1	M/69	IIIB	Patent	Endpoint reached*, no events
2	F/69	IIIA	Partial thrombosis	Endpoint reached, aortic dilatation, BEVAR 28 mo
3	M/75	IIIA	Patent	Endpoint reached, no events
4	M/65	IIIB	Partial thrombosis	Endpoint reached, no events
5	M/82	IIIB	Partial thrombosis	Aortic dilatation, TEVAR 6 mo
6	F/64	IIIA	Complete thrombosis	Endpoint reached, no events
7	M/63	IIIA	Partial thrombosis	Aortic dilatation, TEVAR 1 mo
8	M/55	IIIB	Partial thrombosis	Visceral ischaemia, open repair elephant trunk 3 wk
9	M/75	IIIB	Partial thrombosis	Endpoint reached, no events
10	M/71	IIIB	Patent	Endpoint reached, no events

TEVAR = thoracic endovascular aortic repair; BEVAR = branched endovascular aortic repair; PET = positron emission tomography; MRI = magnetic resonance imaging.
* Endpoint reached refers to the completion of all four PET/MRI examinations within the intended two year imaging follow up period

aortic dissection characteristics, imaging, and clinical outcome.

Visual analyses of ^{18}F-fluorodeoxyglucose uptake and magnetic resonance imaging markers of inflammation

On visual assessment, increased FDG uptake was observed in the dissected descending aorta on the initial PET/MR scan in all patients in the acute phase. In eight patients (80%) this FDG activity was evenly dispersed throughout the entire length and circumference of the dissected descending aorta, whereas in two patients (20%) it was localised to the aortic wall adjacent to the suspected primary entry tear. Decline in visible FDG activity in the dissected descending aorta was observed in all patients over time (see Fig. 1). Interestingly, also the non-dissected ascending aorta and or the arch had visually increased FDG activity in six patients (60%) in the acute phase.

GE and increased T2 signal in the aortic wall of the dissected descending aorta was detected in six of 10 patients (60%) in the acute phase. The GE was not focal but rather global, with a uniform and circumferential or semilunar pattern involving the false lumen wall of the dissected descending aorta. When present, GE area and thickness did not seem to change over time, except in one patient who had a complete resolution of GE. See Table 3 for PET/MRI characteristics of descending aorta.

Quantitative analyses of ^{18}F-fluorodeoxyglucose uptake

Comparison of ^{18}F-fluorodeoxyglucose activity between different aortic segments at each time point. In the acute phase, the maximum TBR of the descending aorta was significantly increased (TBR 5.8, SD 1.3) compared with the ascending aorta (TBR 3.3, SD 0.8, $p < .010$) and the aortic arch (TBR 4.2, SD 0.6, $p = .010$). The maximum TBR of the arch was also significantly increased (TBR 4.2, SD 0.6) compared with the ascending aorta (TBR 3.3, SD 0.8, $p = .020$). In the subacute phase, the maximum TBR of the descending aorta remained higher (TBR 3.5, SD 0.6) compared with the arch (TBR 2.7, SD 0.4, $p < .010$) and ascending aorta (TBR 2.8, SD 0.6, $p = .010$). There was no significant difference between the aortic segment maximum TBRs in the early chronic phase (descending: TBR 2.9, SD 0.4; arch: TBR 2.5, SD 0.2; ascending: TBR 2.8, SD 0.3) and late chronic phase (descending: TBR 3.0, SD 0.3; arch: TBR 2.5, SD 0.3; ascending: TBR 2.8, SD 0.4).

The maximum TBR in the dissected descending aorta in the acute phase was 6.2 (SD 0.9) in patients who had their first examination 10 days or earlier compared with 3.9 (SD 1.8) in patients who had their first examination after 10 days ($p = .20$).

Longitudinal development of ^{18}F-fluorodeoxyglucose activity for each aortic segment. The maximum TBR of descending aorta decreased significantly from the acute phase (TBR 5.8, SD 1.3) to the subacute phase (TBR 3.5, SD 0.6, $p = .010$) and further to the early chronic phase (TBR 2.9, SD 0.4, $p = .030$), but was thereafter stable until the late chronic phase (TBR 3.1, SD 0.4, $p = .30$). The maximum TBR of the arch decreased significantly from the acute (TBR 4.2, SD 0.6) to the subacute phase (TBR 2.7, SD 0.4, $p = .010$) to then be stable. Similarly, the maximum TBR of ascending aorta decreased significantly from the acute (TBR 3.3, SD 0.8) to the subacute phase (TBR 2.8, SD 0.6, $p = .020$) and was thereafter unchanged.

The mean and maximum TBR values for each aortic territory and their longitudinal development are displayed in Figure 2A,B. A separate TBR analyses was performed for patients who were not operated on within the imaging follow up period of two years (Supplementary Figure S1).

Correlation between clinical outcome, lumen morphology, and ^{18}F-fluorodeoxyglucose positron emission tomography magnetic resonance imaging inflammatory changes in dissected descending aorta. MRI specific inflammatory changes where present in all four patients (100%) who experienced complications requiring surgical repair compared with two of six (33%) patients who remained on medical treatment ($p = .048$). MRI inflammatory changes were more frequent in patients with partial false lumen thromboses than in those with patent false lumen (83% *vs.* 0%, $p = .048$). The proportion of patients with MRI inflammatory changes in the acute phase was the same for

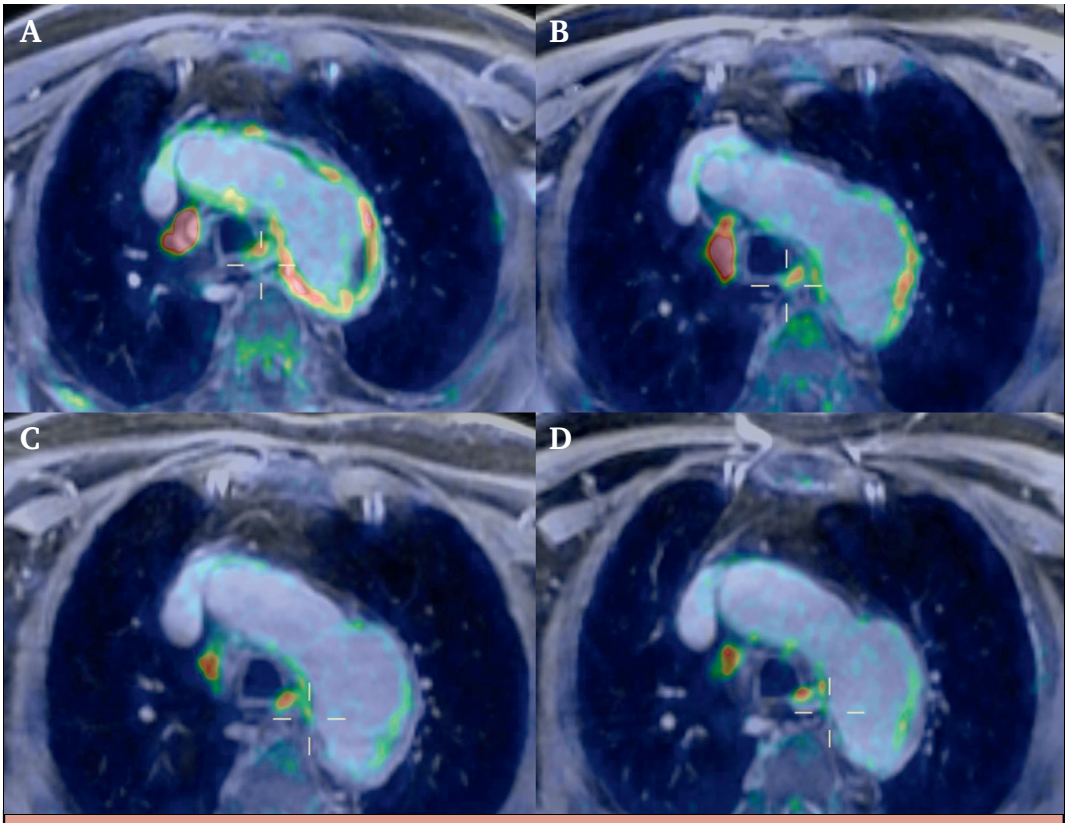

Figure 1. Positron emission tomography magnetic resonance imaging with fluorodeoxyglucose characteristics of a patient with acute type B dissection in different phases of dissection (A) within two weeks of the index event (acute phase), (B) three months (subacute phase), (C) 12 months (early chronic phase), and (D) 24 months (late chronic phase)

DeBakey type IIIA and IIIB dissections (75% *vs.* 50%, $p = .60$) (see Fig. 3).

Complications occurred in four of six patients with partial false lumen thromboses (67%) whereas none of the three patients with patent false lumen (0%) had complications ($p = .11$). Only one patient demonstrated complete false lumen thrombosis and remained without complications. There was no difference in FDG activity between patients with partial false lumen thromboses *vs.* patent false lumen in the acute phase ($p = .38$). There was no difference in maximum FDG activity between patients with type IIIA *vs.* IIIB dissections in the acute phase (5.8 *vs.* 5.9, $p = .83$). The

Table 3. Positron emission tomography magnetic resonance imaging longitudinal characteristics of descending aorta for the 10 study patients

Case no.	Maximum TBR for each time point				MRI inflammatory markers for each time point			
	<2 wk TBR	3–4 mo TBR	9–12 mo TBR	21–24 mo TBR	<2 wk GE/T2	3–4 mo GE/T2	9–12 mo GE/T2	21–24 mo GE/T2
1	3.9	3.3	2.8	3.1	Neg/Neg	Neg/Neg	Neg/Neg	Neg/Neg
2	3.9	2.0	2.9	3.3	Pos/Pos	Pos/Pos	Pos/Pos	Pos/Pos
3	5.3	3.6	3.1	3.1	Neg/Neg	Neg/Neg	Neg/Neg	Neg/Neg
4	6.3	4.2	3.8	3.2	Pos/Pos	Pos/Pos	*/Pos	*/Pos
5	6.3	4.2	TEVAR	TEVAR	Pos/Pos	Pos/Pos	TEVAR	(EVAR
6	6.2	4.1	2.8	2.6	Pos/Pos	Neg/Neg	Neg/Neg	Neg/Neg
7	7.2	TEVAR	TEVAR	TEVAR	Pos/Pos	TEVAR	TEVAR	TEVAR
8	7.2	OR	OR	OR	Pos/Pos	OR	OR	OR
9	4.0	3.2	2.9	2.9	Neg/Neg	Neg/Neg	Neg/Neg	Neg/Neg
10	5.4	3.1	2.7	2.7	Neg/Neg	Neg/Neg	Neg/Neg	Neg/Neg

TBR = target to background ratio; OR = open repair; TEVAR = thoracic endovascular aortic repair; GE = gadolinium enhancement; T2 = hyperintensity on T2 weighted images; MRI = magnetic resonance imaging.
* Gadolinium could not be administered due to increased creatinine levels on follow up.

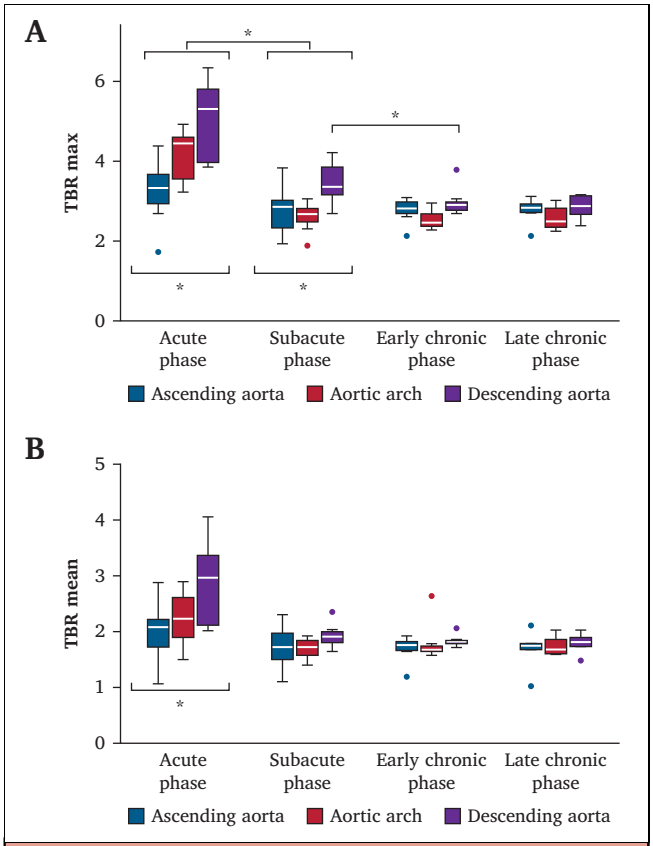

Figure 2. (A) Maximum tissue to background ratio (TBR) for each aortic segment and phase of the aortic dissection. Lower brackets represent significance of difference in TBR between aortic segments at each phase of the dissection and upper brackets represent significance of longitudinal change in TBR. In the acute phase, there was a significant difference in TBR between the three aortic segments. TBR in all three aortic segments decreased significantly from acute to subacute phase, but the descending aorta remained increased compared with the ascending aorta and the aortic arch. Although the TBR of the descending aorta continued to decrease significantly from the subacute to early chronic phase, the TBR of the ascending aorta and the aortic arch was stable. (B) Mean TBR for each aortic segment and phase of the dissection. In the acute phase, the maximum TBR of the descending aorta was significantly higher than the ascending aorta and the aortic arch. *$p<$ .050.

maximum TBR in the dissected descending aorta in the acute phase was 6.8 (SD 1.6) in patients who later had surgical repair compared with 5.4 (SD 1.0) in patients who remained on medical treatment alone ($p = .33$). See Table 3 for FDG-PET/MRI characteristics and clinical outcome for the entire cohort.

DISCUSSION

The current study depicts the inflammatory response in the aortic wall over time after an ATBAD, using functional imaging with integrated FDG-PET and MRI. Although all patients had a strong uptake of FDG in the dissected aorta in the acute phase, it rapidly diminished in the subacute phase and continued to decrease into the early chronic phase, whereupon it stabilised. Interestingly, the inflammatory activity visualised with FDG uptake was also increased in the adjacent aortic arch in the acute setting of the dissection, already stabilising in the subacute phase.

TBAD is most commonly defined as acute $<$ 14 days from index event, and chronic thereafter.[2] Recent studies however indicate that many dissection related complications occur beyond 14 days,[16] suggesting that there is an unstable or dynamic subacute phase 15 — 90 days after onset. The present findings of increased inflammatory activity during this subacute phase support the hypothesis that the descending aorta remains fragile and unstable during this time period. In addition, even the non-dissected ascending aorta and aortic arch showed quantitatively increased FDG uptake in the acute phase, with visually increased FDG activity in six of 10 patients (60%). This increased activity at 14 days significantly declined and stabilised within three to four months after onset. Whether this increased inflammation in the ascending aorta and arch early on in the dissection increases the risk of proximal progression of the dissection and or retrograde type A dissection in the case of acute endografting in this subgroup of patients remains unknown.

Globally increased inflammatory activity in the aortic wall within 90 days after onset of ATBAD raises the question of optimal timing for pre-emptive TEVAR to prevent late false lumen expansion. Performing TEVAR early, within one month after onset, in an unstable dissection, is related to increased mortality and complication rates.[17] It is possible that the dissected aorta, with increased inflammatory activity during this early time period, might be more fragile and thus susceptible to mechanical damage induced by the endograft. Gorla *et al.* showed that enhanced FDG uptake in the acute phase was associated with an increased mortality rate, disease progression, and re-intervention following TEVAR.[18] A recent large study on 805 patients undergoing TEVAR for acute TBAD showed that a high degree of systemic inflammation predicted major adverse events in hospital and during follow up. On the other hand, waiting too long with treatment might reduce the potential for aortic remodelling after TEVAR. Hejman *et al.* showed that endograft induced aortic remodelling was the same between one and three months,[19] and there are suggestions that the aorta can remodel also in the chronic phase.[20] The exact time point when the aorta loses its plasticity is unknown. Over time, however, fibrosis in the aortic wall progresses, with increased presence of less metabolically active cells (fibroblasts), leading to flap stiffness and decreased potential to remodulate after TEVAR.[21] In this perspective, it seems plausible that as the FDG uptake in the dissected aorta decreases so does the plasticity and thus the capacity of the aorta to remodel. This possibility, together with the inflammatory patterns in this series, showing the greatest magnitude of the FDG decrease within three to four months, could indicate that performing TEVAR beyond this time point might be safer; however, waiting beyond the early chronic phase (nine to 12 months) might decrease the aorta's ability to remodel.

Although some investigators suggest a possible link between increased TBR in dissected aortic wall in the acute

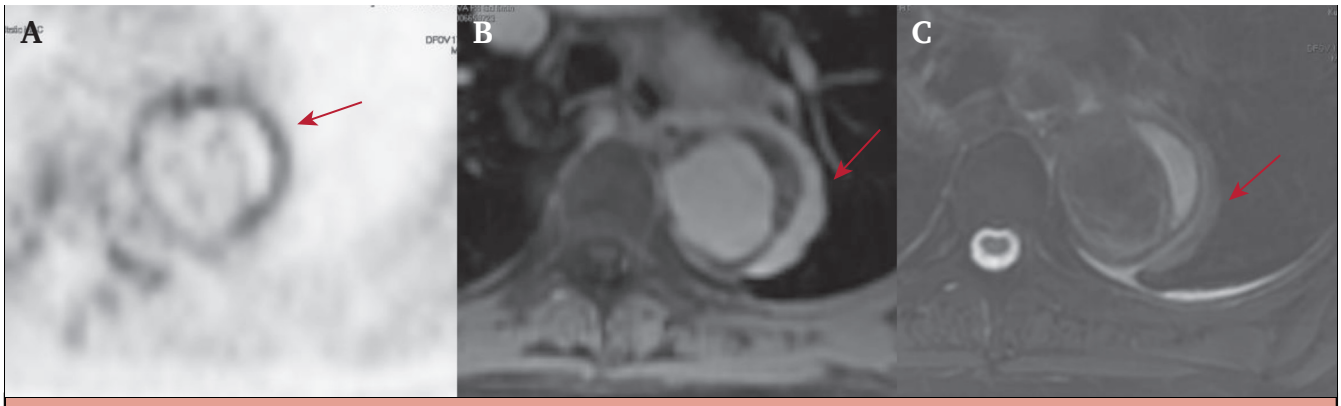

Figure 3. Positron emission tomography (PET) magnetic resonance imaging (MRI) characteristics in the acute phase of a patient with DeBakey type IIIA aortic dissection who suffered aortic dilatation and was operated on with a branched endograft 28 months after the index event. (A) PET inverted grey scale reveals increased fluorodeoxyglucose uptake in the aortic wall (arrow). (B) T1 weighted MRI showing wall thickening and gadolinium enhancement six minutes after injection. (C) T2 weighted MRI showing increased signal indicative of oedema.

phase and increased risk of disease progression, this cannot be corroborated by the present study.[8,18,22–24]

In current histopathological understanding of acute aortic dissections, the intimal injury triggers an inflammatory response with influx of inflammatory cells,[25] inducing proteolytic and apoptotic activity, which may lead to pathological remodelling, with medial degeneration and replacement fibrosis.[21] Neo-angiogenesis, shown to promote inflammation,[5] is also a common histological feature in TBAD disease.[6] GE is used for detecting fibrosis in ischaemic cardiomyopathy,[26] but also serves in the assessment of vascular inflammation,[9] and is associated with neo-angiogenesis and high inflammatory cell content on histology.[11] Thus, it is possible that the presence of GE in the dissected aortic wall could partly serve as a marker of angiogenetic inflammation and or indication of increased medial scaring related to acute injury and the following repair process. In this study, GE was detected in the dissected aortic wall in six of 10 patients (60%) in the acute phase, suggesting increased inflammatory activity in these patients. In addition, GE was significantly more frequent in patients requiring surgical intervention than in patients who remained stable on medical therapy. Patients who did not have GE or T2 hyperintensity in the acute phase did well on medical therapy only; however, if there was GE or hyperintensity, four of six patients needed surgical repair ($p = .048$). This finding indicates that the presence of MRI inflammatory signs in the dissected aortic wall could potentially be a marker of more active pathological remodelling with increased risk of disease progression. Furthermore, it emphasises the feasibility and possible future role of MRI in the assessment of aortic mural inflammation in TBAD, as a complementary addition to metabolic assessment with FDG-PET, in identifying higher risk patients.

While FDG uptake declined in all patients, MRI inflammatory signs did not seem to resolve over time, except in one patient. Interestingly, this patient had complete thrombosis of the false lumen with morphological resolution of the dissection on follow up. This apparent discordance between GE and FDG in aortic aneurysms has previously been addressed by other authors,[27] and as discussed in a recent published paper by this group,[12] is probably explained by the different aspects of the inflammatory process studied by the two different modalities. FDG is an established marker of increased glucose metabolism, predominantly based on uptake in macrophages, whereas GE is a marker of vascular leakage, and is not only associated with inflammation but also linked to angiogenesis and fibrosis. Investigators have reported that collagen deposits (fibrosis) in the adventitia increase with the chronicity of the dissection, which may in part account for the continued enhancement of scar tissue on MRI.[21]

A partially thrombosed false lumen has been associated with a poor clinical outcome in patients with type B dissections.[28] An increased FDG signal in the dissected aortic wall and biomarkers of thrombus formation and degradation are both associated with disease progression, suggesting an interaction between inflammatory activity and thrombus biological turnover.[23] In the present study MRI inflammatory changes were more frequent in patients with a partially thrombosed false lumen, which supports the hypothesis that thrombus may in part drive inflammatory activity in type B dissections.

The limitations of the current study include the sample size, which albeit being similar to other studies in this field, is still small, resulting in difficulties to assess the long term correlation between imaging findings and clinical outcome. The possibility for functional imaging findings in predicting aortic outcome over time would require larger cohorts of patients. Furthermore, as PET/MRI examinations are a large undertaking for severely ill patients and or patients who are unstable due to a long acquisition time (2 — 3 hours), such patients had to be excluded from this study, potentially leading to pre-selection bias. In addition, the cost (1500 euro) of PET/MRI and its lack of availability limits the employment of PET/MRI as a routine examination in clinical practice. The clinical course of patients who underwent surgery is variable, and hence despite efforts to select a

homogeneous cohort of uncomplicated aortic dissections in this study, there are patient variations that may affect the findings. However, this is the clinical reality of ATBAD, and some patients deemed to have uncomplicated dissection at the time of inclusion may later require surgery. The patients who were treated surgically were excluded from further imaging follow up and do not, from the point of exclusion, contribute further to the longitudinal data on inflammation development. Setting TBR thresholds is challenging as there is no appropriate standard cut off value for arterial inflammation; however, earlier observations indicate that averaged maximum TBR values could be somewhere between 1.7 and 3.1 in seemingly healthy aorta.[12,29] Lastly, the potential link between peripheral plasma biomarkers for inflammation and PET/MRI needs to be assessed in future studies.

Conclusions

The degree of inflammation in the aortic wall after type B dissections can be visualised with integrated PET/MRI. The inflammatory activity in the aortic wall quantified as FDG uptake is highest in the descending aorta in the acute phase, decreasing radically in the subacute phase (three to four months) but not stabilising until early chronic phase (nine to 12 months). Additionally, ascending aorta and the aortic arch showed increased inflammatory activity in the acute phase that stabilised at three to four months indicating a dynamic hyperinflammatory state in the whole thoracic aorta. MRI signs of inflammation in the acute phase were highly prevalent in patients who later needed surgical intervention and may be of interest as a biomarker in future studies.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2023.05.039

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COUP D'OEIL

Don't Stop Pulling the Leg (of the Graft)!

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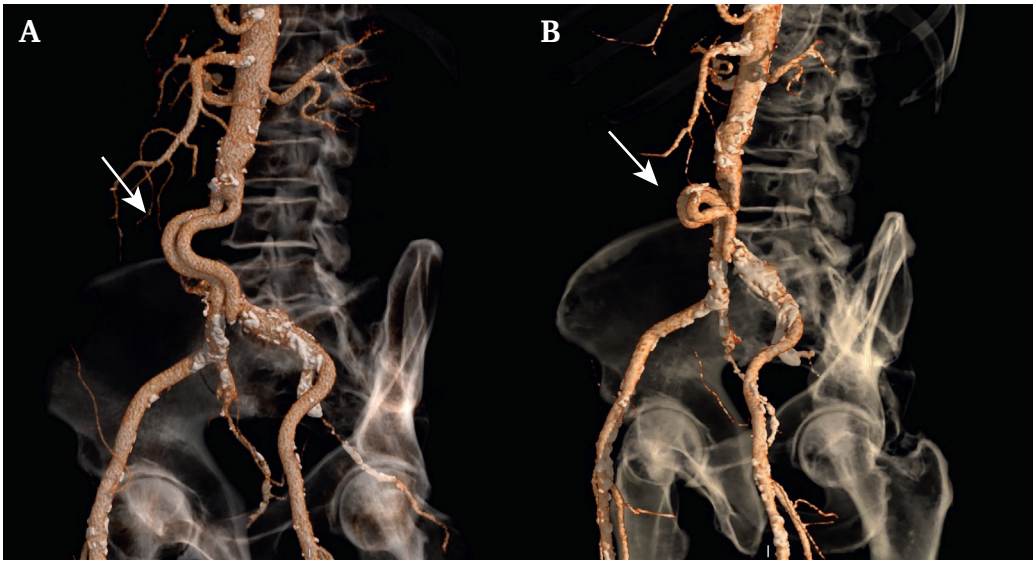

In 2010, a 77 year old patient was treated for ruptured abdominal aortic aneurysm with an 80 mm maximum diameter. He underwent emergency aortobi-iliac bypass (white arrows). The post-operative course was uneventful. He progressively developed an asymptomatic stenosis of the left limb screened by ultrasound. Panel A shows the early post-operative computed tomography angiography image, and panel B shows the legs' folding 12 years later. Shrinkage of the residual aneurysm sac caused the folding of the legs. The patient successfully underwent redo surgery with shortening of both legs and direct anastomosis. Grafts need to be pulled as much as possible to avoid future kinking!

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