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Vasculitis

FRI0303 THE IGG4:IGG RNA RATIO IS A NEW AND PROMISING DISEASE ACTIVITY MARKER IN GRANULOMATOSIS WITH POLYANGIITIS

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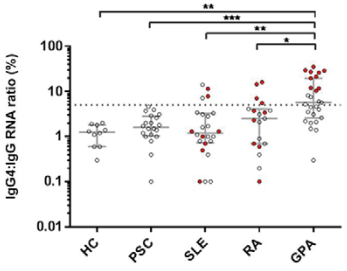
Background: Granulomatosis with Polyangiitis (GPA) is a form of vasculitis characterized by inflammation of blood vessels in lungs, kidneys and the ear, nose and throat region. Regular monitoring and treatment adjustments are common, as the disease activity tends to fluctuate over time. Unfortunately, good markers for disease activity are lacking. This leads to both over- and undertreatment. Immunoglobulin G4 positive (IgG4+) B-cells and plasma cells are implicated in the pathogenesis of GPA, but the level of serum IgG4 does not seem to be a good disease activity marker. Recently we developed a test that indirectly measures the presence of IgG4+ B-cells/plasma cells by measuring the IgG4:IgG RNA ratio[1]. We hypothesized that this test could be used as disease activity marker.
Objectives: To test the IgG4:IgG RNA ratio in peripheral blood as a disease activity marker in GPA.
Methods: 27 PR3+ ANCA+ positive GPA patients were included in this cross-sectional study. Mean age was 52 years, 56% were female, and 39% had active disease. For each patient the ESR, CRP, BVAS, and ANCA titre were measured and peripheral blood samples were obtained. Patients were defined as having active disease if the BVAS was ≥3. In addition we included 10 healthy controls, and 63 patients with other immune mediated inflammatory diseases (systemic lupus erythematosus (SLE) (n=24), rheumatoid arthritis (RA) (n=19), primary sclerosing cholangitis (PSC) (n=20)). A validated qPCR test was performed in all groups to measure the IgG4:IgG RNA ratio in peripheral blood samples [1]
Results: The median IgG4:IgG RNA ratio was significantly higher in the GPA cohort (5.7, IQR 2.6 – 19.7) compared to all control groups: 1.2 in SLE (0.7 - 3.3; $p<0.01$), 2.5 in RA (0.7 - 4.1; $p<0.05$), 1.6 in PSC (1.0 - 2.8; $p<0.001$) and 1.3 in HC (0.6 - 1.8, $p<0.01$). In addition, the median IgG4:IgG RNA ratio was significantly higher in patients with active disease (23.8; IQR 12.1 – 29.1) compared to patients in remission (3.5; IQR 2.0 – 5.5) ($p<0.0001$). The height of the IgG4:IgG RNA ratio significantly correlated with height of the BVAS (r^2 =0.76, $p<0.0001$), while the ESR, CRP and ANCA titre did not. Interestingly, IgG4/IgG RNA ratios among patients with active disease were consistently above 9.3, and among patients in remission they were below this threshold.



IgG4:IgG RNA ratio (%) in healthy controls (HC), primary sclerosing cholangitis (PSC), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and granulomatosis with polyangiitis (GPA). Red dots represent patients with active disease (resp. SLEDAI, DAS28 and BVAS). * <0.05, **<0.01, *<0.001**

Conclusions: The IgG4:IgG RNA ratio distinguishes active GPA from GPA in remission with excellent specificity and sensitivity. Moreover the ratio shows a significant correlation with disease severity, in contrast to ESR, CRP and ANCA titre. Retesting in another, prospective study is indicated to validate the IgG4:IgG ratio as a novel, highly sensitive and specific marker of disease activity in GPA.
References:
[1] Doorenspleet ME et al. Hepatology 2016; 64(2): 501–7.
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FRI0304 THE UTILITY OF 18F FDG-PET/CT IN DISTINGUISHING BENIGN FROM MALIGNANT RETROPERITONEAL FIBROSIS

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Background: Retroperitoneal fibrosis (RPF) could be idiopathic or secondary to various factors including malignancy. Pathology remains the most reliable diagnostic approach. However, the pathological features have yet been well defined and the feasibility of biopsy procedure depends on several factors such as the proximity of the lesions to abdominal aorta. ^{18}F FDG-PET/CT may help exclude malignancy by assessing FDG-uptake and mapping the whole body, especially when biopsy procedure is inaccessible.
Objectives: To evaluate the utility of PET/CT in distinguishing benign from malignant RPF.
Methods: Patients with benign or malignant RPF diagnosed between September 2011 and June 2016 were included. Morphologic features, FDG-uptake of retroperitoneal lesions and lymph nodes (LNs) were compared. FDG-uptake of retroperitoneal lesions was assessed visually with the referrence of liver and assessed semiquantitatively with SUVmax. LNs were regarded as specific LNs if frequencies of LNs with high FDG-uptake were observed differently between two forms of RPF. ROC analyses were performed to evaluate the diagnostic accuracy.
Results: Seventy-one cases with benign RPF and 21 cases with malignant RPF secondary to lymphoma (15) or metastatic carcinoma (6) with primary sites of pancreas (2), colon (2), stomach (1) and kidney (1) were included. The craniocaudal length, axial width, and distances between anterior or posterior

Table 1. Morphologic features, FDG-uptake of retroperitoneal lesions and lymph nodes (LNs)

Parameters	Benign RPF (71)	Malignant RPF (21)	*p* value
Morphologic features			
Craniocaudal length, median (IQR), mm	107.0 (80.5,136.4)	164.9 (104.7,229.2)	0.001
Axial width, median (IQR), mm	41.0 (32.3,52.0)	85.0 (62.3,98.5)	<0.001
Aorta lumen to anterior limit, median (IQR), mm	8.9 (6.0,12.0)	20.7 (13.9,45.3)	<0.001
Aorta lumen to posterior limit, median (IQR), mm	2.8 (2.2,4.4)	7.4 (4.5,14.5)	<0.001
FDG-uptake of retroperitoneal lesions			
High FDG-uptake, n (%)	55 (77.5)	21 (100.0)	0.017
SUV max, mean (S.D.)	4.8 (1.7)	12.2 (7.1)	<0.001
LNs with high FDG-uptake, n (%)			
Hilar/Mediastinal	27 (38.0)	13 (61.9)	0.054
Cervical	6 (8.5)	5 (23.8)	0.058
Axillary	4 (5.6)	6 (28.6)	0.003
Retroperitoneal	3 (4.2)	16 (76.2)	<0.001
Supraclavicular	2 (2.8)	8 (38.1)	<0.001
Inguinal	1 (1.4)	5 (23.8)	<0.001
Peritoneal	0 (0.0)	10 (47.6)	<0.001
Number of specific LNs, n (%)	0 (0,0)	2 (1,3)	<0.001

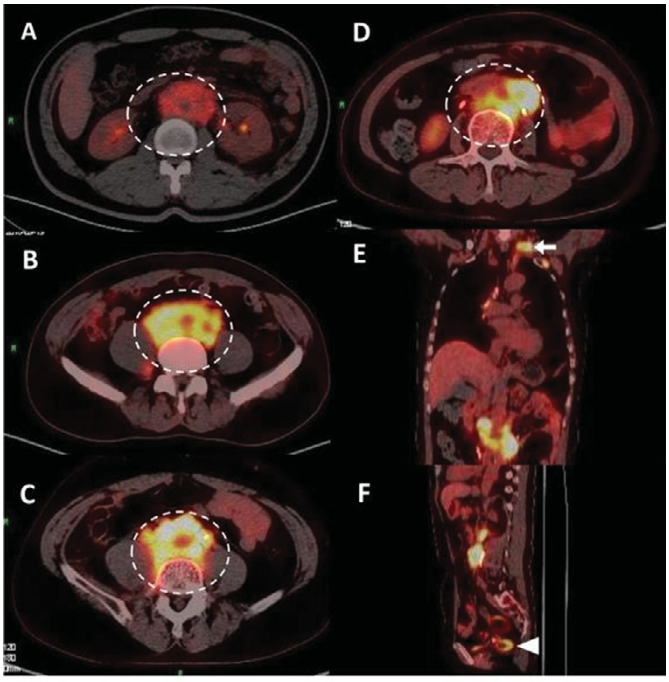

Figure 1. Representative ^{18}F fluorodeoxyglucose positron emission tomograph images for benign retroperitoneal fibrosis (**A**) and malignant retroperitoneal fibrosis secondary to lymphoma (**B, C**) and metastatic carcinoma (**D**). The retroperitoneal process are encircled by circles in the same size with different level of FDG-uptake. **D-F** are images from one patient with histological diagnosis of colon cancer. FDG-uptake is accumulated in left supraclavicular lymph node pointed by the arrow (**E**) and in sigmoid colon pointed by the arrow head (**F**).

limits and aorta were less in benign RPF, however, significant differences were only observed when comparing with lymphoma (p values: all <0.001) but not with metastatic carcinoma (p value: 0.396, 0.181, 0.112 and 0.64). A greater frequency of retroperitoneal lesions with high FDG-uptake (100% vs 77.5%, p value: 0.017) and a higher mean SUVmax (12.2 vs 4.8, p value: <0.001) were observed in malignant RPF. The frequencies of LNs with high FDG-uptake were greater with significance in malignant RPF except for hilar/mediastinal and cervical LNs, hence the rest LNs were regarded as specific LNs. At ROC analyses, the AUCs of SUVmax and specific LNs were 0.893 and 0.947. The sensitivity and specificity were 85.7% and 81.4% when the SUVmax was 6.23. The AUC of logistic regression model combining SUVmax and specific LNs was 0.974 with sensitivity of 90.5% and specificity of 90.1%.

Conclusions: PET/CT could help distinguish benign from malignant RPF, especially when taking into account the FDG-uptake of retroperitoneal process and LNs.

Disclosure of Interest: None declared

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FRI0305 RELATIVE FDG ACCUMULATION OF THE AORTIC WALL LESIONS TO AORTIC BLOOD POOL IN 18F-FDG-PET AND PET/CT COULD BE A USEFUL PARAMETER FOR THE PREDICTION OF DISEASE RELAPSE AFTER SUCCESSFUL TREATMEN IN TAKAYASU ARTERITIS

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Background: The assessment of disease activity of Takayasu arteritis (TA) is difficult if symptoms and serum inflammatory marker were not detected. Even in those conditions, relapses were frequently observed during the dose reduction of corticosteroid and immunosuppressant. There is accumulating evidence that 18F-fluolodeoxyglucose-positron emission tomography (FDG-PET) and PET/computed tomography (PET/CT) is useful for monitoring patients with TA when TA was clinically active. However, it is not clear the significance of FDG accumulations when TA was inactive.

Objectives: To investigate a quantitative predictor in FDG-PET or PET/CT scans for the relapse of TA.

Methods: We retrospectively investigated 76 FDG-PET or PET/CT scans and extracted 37 scans which were performed in inactive status. These scans were divided in two groups according to relapse of TA for 5years. The relapse was defined the increase of CRP and steroid dose or addition of immunosuppressant. FDG accumulations in aortic wall lesions of TA was evaluated by semi-quantitative index; the standardized uptake value (SUV). In addition to SUVmax in the aortic wall, we also calculated SUV ratio of maximum aortic wall uptake to mean lung uptake (ratio Lu), SUV ratio of maximum aortic wall uptake to mean liver uptake (ratio Li), and SUV ratio of maximum aortic wall uptake to mean aortic blood pool uptake (ratio BP). We compared groups using these parameters. We also determined the cutoff levels, sensitivity, and specificity of 4 sets of SUVs (SUVmax, ratio Lu, ratio Li, and ratio BP) for the prediction of relapse using Receiver Operating Characteristic (ROC) analysis. Moreover, Kaplan-Mayer analysis for the long-term relapse-free survival was performed to assess the reliability of these cutoff levels.

Results:

Table 1. Characteristics of two groups

Relapse	(–)	(+)
#	17	20
Age (yr)	47 [30–72]	28.5 [14–68]
CRP (mg/dl)	0.13±0.03	0.13±0.03
Steroid dose (mg/d equivalent to prednisolone)	15.6±2.4	17.7±3.6
Immunosuppressant	2/17	7/35
Duration until relapse (Days)		702.5 [4–1769]

In 37 total PET and PET/CT scan examinations, non-relapse and relapse groups included 17 and 20 scans, respectively. Relapse group had more immunosuppressant users than non-relapse group. Although CRP level and SUVmax were equivalent, ratio of SUV, especially ratio BP of relapse group was higher than that of non-relapse group (p=0.09) (Figure top panel). The cut-off level of these parameters was calculated as follows; SUVmax 1.4, ratio Lu 5.31, ratio Li 1.01, and ratio BP 1.41, respectively. Using these cut-off level, relapse rates of below and over cut-off level were as follows; SUVmax 50% vs 54%, ratio Lu 43% vs 62%, ratio Li 43% vs 69%, and ratio BP 31% vs 67%, respectively (Figure middle panel). Using Kaplan-Mayer analysis, relapse rate of these two groups divided by ratio BP was not significantly different (p=0.268) though these two curves looked different (Figure bottom panel).

Conclusions: Our data suggest that ratio BP at stable condition, which represents relative FDG accumulation of the aortic wall lesions to aortic blood pool, could be a promising predictor to assess the relapse after successful treatment.

Disclosure of Interest: None declared

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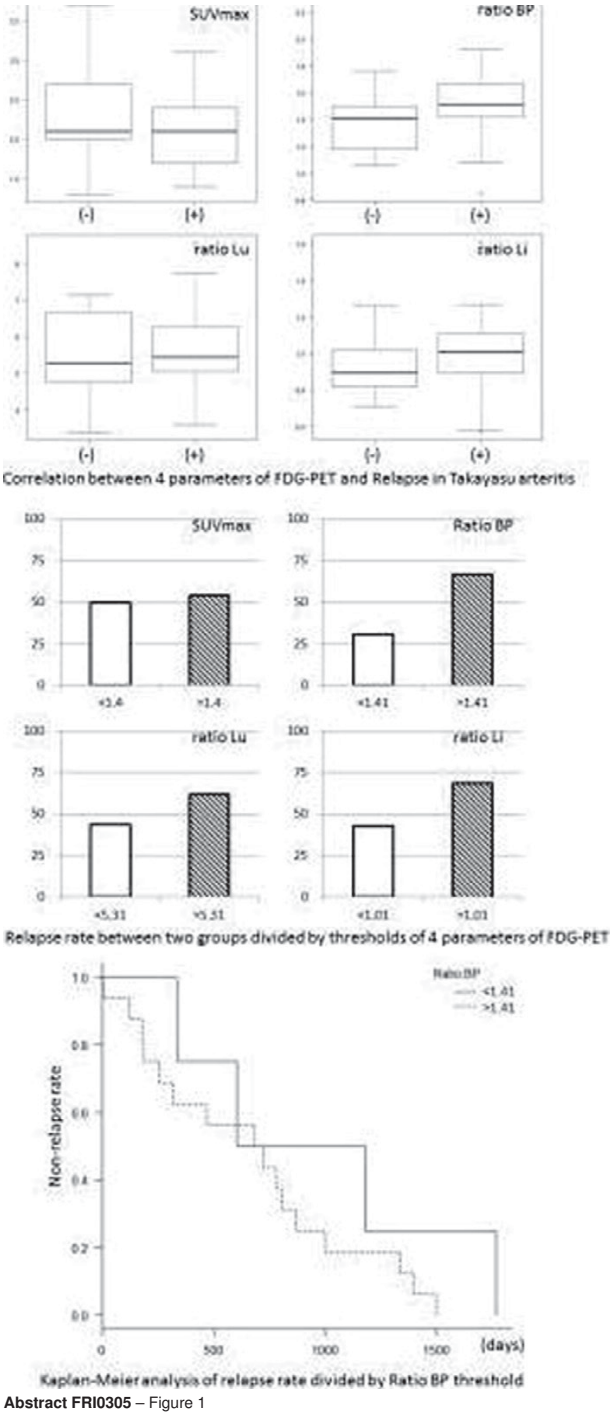

Abstract FRI0305 – Figure 1

FRI0306 LONG TERM DRUG-FREE REMISSION IS FEASIBLE IN SEVERE BEHCET'S DISEASE AFTER CESSATION OF SUCCESSFUL ANTI-TNF TREATMENT: A SINGLE CENTER, RETROSPECTIVE LONGITUDINAL OUTCOME STUDY

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Background: The efficacy of anti-TNF treatment for patients with severe forms of Behcet's disease (BD) is well established (ref), but long term data on the outcome after cessation of such treatment are lacking.

Objectives: To examine whether sustained long term remission of severe BD is feasible after cessation of successful anti-TNF treatment.

Methods: This retrospective longitudinal outcome study was conducted in December 2016 and included all patients with severe BD refractory to conventional immunosuppressive therapy who were considered complete responders to continuous anti-TNF treatment in our center, the first being treated in 2000.