Study on the association of serum pentraxin-3 and lysosomal-associated membrane protein-2 levels with disease activity in Chinese Takayasu's arteritis patients

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ABSTRACT

Objective. *To evaluate the association between disease activity and serum levels of pentraxin-3 (PTX-3) and lysosomal-associated membrane protein-2 (LAMP-2) as well as the acute reactants in Chinese Takayasu's arteritis (TAK) patients.*

Methods. *The serum PTX-3 and LAMP-2 levels were tested in 98 TAK patients and 40 age- and gender-matched healthy controls. The disease activity of these TAK patients was assessed according to the National Institute of Health (NIH) and Abatacept in giant cell arteritis and Takayasu's arteritis (AGATA) criteria, respectively.*

Results. *Among the 98 TAK patients, 45 and 52 patients had active disease according to the NIH criteria and AGATA criteria respectively. The total agreement rate between these two criteria was 90.82% (κ=0.817, p<0.001). Both serum PTX-3 and LAMP-2 levels were elevated in TAK patients compared with those in healthy controls (PTX-3: 0.32±0.03 ng/ml vs. 0.18±0.02 ng/ml, p=0.001; LAMP-2: 4.40±0.14 ng/ml vs. 3.30±0.20 ng/ml, p<0.001). TAK patients with active disease had higher serum PTX-3 levels compared with those who had inactive disease (NIH criteria: 0.42±0.06 ng/ml vs. 0.25±0.02 ng/ml, p=0.004; AGATA criteria: 0.38±0.05 ng/ml vs. 0.27±0.02 ng/ml, p=0.049). However, serum LAMP-2 levels did not differ between patients with active and inactive disease according to both NIH and AGATA criteria. A cutoff value of PTX-3 with 0.30 ng/ml maximised the ability of disease activity assessment with a sensitivity/specificity of 57.10%/73.10% and 47.90%/71.10% according to the NIH and AGATA criteria, respectively.*

Conclusion. *Serum PTX-3 and LAMP-2 levels are elevated in Chinese TAK patients. However, serum PTX-3 but not LAMP-2 level is associated with active disease.*

Introduction

Takayasu's arteritis (TAK) is an uncommon systemic vasculitis that primarily affects the aorta and its major branches. Vascular inflammation always results in organ and tissue ischaemia supplied by the involved arteries (1). Coronary artery disease, stroke and visual loss may present in some TAK patients as part of active disease, but it can also be the sequelae of chronic vascular ischaemia (2). When the disease is in an active stage, aggressive treatment is mandatory to prevent these vital organ involvements, while prevention of complications is the mainstay in managing stable diseases. However, reliable disease activity assessment is a big challenge in the management of TAK. Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) are conventional biomarkers for TAK disease activity, but ESR and CRP may be affected by various conditions, and elevation is observed in only about half of the TAK patients with active disease (3). Therefore, the value of ESR and CRP in reflecting disease activity is strongly limited by the lack of specificity.

Serum PTX-3 was reported to be related to disease activity in the literature, but there are limited studies in Chinese TAK patients. LAMP-2 was reported to play a crucial role in the pathogenesis of anti-neutrophil cytoplasmic antibody associated vasculitis (AAV). However, its association with disease activity in TAK patients has not been studied yet. In this study, we tested serum PTX-3 and LAMP-2 levels in Chinese TAK patients and aimed to explore their roles in the evaluation of disease activity.

Methods

Patients and samples

This was a cross-sectional study carried out in the Department of Rheumatology of Peking Union Medical College Hospital (PUMCH), a Chinese nationwide referral centre, from April 2013 to November 2015. A total of 98 TAK patients and 40 healthy controls were enrolled. Blood samples of TAK patients and healthy controls were collected and stored at -80°C until tested. Their clinical data were recorded at the visit when the blood samples were taken. This study was approved by the Institution Review Board (IRB) of PUMCH and written informed consent was obtained from each patient.

All patients fulfilled the TAK classification criteria defined by the American College of Rheumatology (ACR) in 1990 (4). Disease activity was assessed based on two independent criteria, *i.e.* the National Institutes of Health (NIH) criteria (1) proposed by Kerr *et al*. and the AGATA (Abatacept in giant cell arteritis and TAK) criteria developed by the Vasculitis Clinical Research Consortium (VCRC) (5).

The artery involvement patterns were classified as I, IIa, IIb, III, IV and V according to the Numano criteria by catheterised angiography or computed tomography angiography (CTA) (6, 7). The demographic data, clinical manifestations and physical examinations were collected and stored in the Chinese Rheumatism Data centre (CRDC) database (8). In addition, blood white cell counts, haemoglobulin (Hb), platelet (PLT) counts, serum creatinine (Scr), ESR and hypersensitive C-reactive protein (hsCRP) levels were measured at the same visit when the blood samples were taken. The upper normal limit for ESR and hsCRP was 20 mm/h and 3 mg/L, respectively.

Furthermore, serum from 40 age- and gender-matched healthy controls (HCs) was collected. Commercial enzyme-linked immune sorbent assays (ELISAs) were used to measure the serum PTX-3 (Sigma-Aldrich) and LAMP-2 (RayBiotech) levels under the manufacturers' protocols.

Colour Doppler ultrasonography was used as a measurement to track vascular inflammation and disease progression. The mural thickness and lumen diameter of bilateral common carotid artery (CCA), subclavian artery (SCA), renal artery, abdominal aorta, mesenteric artery and coeliac trunk were examined to monitor artery inflammation progression every 6-month during regular follow-ups. Artery inflammation aggravation was defined as appearance of new lesions or aggravation of lumen narrowness. These colour Doppler ultrasonography examinations were conducted by two specialised examiners who were blind to the blood tests and treatment.

Statistical analysis

Statistical analyses were conducted by the SPSS software (v. 13.0). Numerical data with normality were expressed as mean±SEM (standard error of mean), while numerical data without normality were expressed as median (25% quantile, 75% quantile); categorical data were expressed as percentages or numbers. The numerical data were first analysed by the One-Sample Kolmogorov-Smirnov Test to verify the normality and homoscedasticity of the parameters. For parameters with normality and homoscedasticity, they were further compared with the independent sample *t*-test. While those without normality and homoscedasticity were further analysed by the Mann-Whitney test. Categorical data were compared with the Chi-square test or Fisher's exact test, where appropriate. The agreement between the NIH and AGATA criteria was estimated using κ statistics. Pearson's correlation test was used to test the relationship between serum PTX-3/LAMP-2 levels and ESR/hsCRP. We determined the cut-off values for serum PTX-3, LAMP-2, ESR and hsCRP levels by receiver operating characteristics (ROC) curves with the MedCalc software (v. 11.2) to compare the accuracies of these markers with disease activity identification. The cut-off points of PTX-2 and LAMP-2 were determined when the Youden's Index (sensitivity + specificity - 1) was at the highest. All probabilities were two-sided, and a p-value <0.05 was considered to be statistically significant.

Results

Of these 98 TAK patients, 88 were female. Forty-five and fifty-two patients had active disease based on the NIH criteria and AGATA criteria, respectively (Table I). The total agreement between these two criteria was 90.82% (κ=0.817, p<0.001). In our study, more TAK patients had active disease according to the AGATA criteria (Table II) than the NIH criteria.

Patients with stable disease had longer disease duration (Table I). Malaise (62/98) followed by weight loss (27/98) and fever (22/98) were the three most common constitutional symptoms. The prevalence of hypertension did not differ between TAK patients with active and stable disease. The artery involvement patterns were different between patients with active and stable disease according to both the NIH criteria and the AGATA criteria (p=0.007 and p=0.023, respectively). Numano subtype I and IIa were more common among patients with active disease; while Numano subtype V was more common among those with inactive disease.

Compared with healthy controls, patients with Takayasu arteritis had higher levels of WBC and PLT counts. Meanwhile, ESR, serum hsCRP, PTX-3 and LAMP-2 levels were also elevated in TAK patients compared with those in healthy controls (Table I). Furthermore, compared with patients who had inactive disease, those patients with active disease had higher levels of serum PTX-3 based on both criteria (Table I). Similarly, ESR and hsCRP were higher in patients with active disease. Nevertheless, serum LAMP-2 levels did not differ between patients with active and inactive disease. The median disease duration in our study was 26 months. Serum PTX-3 and LAMP-2 did not differ between patients with early (disease duration y ≤26 months, n=52) and late disease (disease duration >26 months, n=46) ($PTX_{early\ vs.\ late}$, 0.35±0.05 ng/ml *vs*. 0.30±0.03 ng/ml, P=0.401; $LAMP\text{-}2_{early\ vs.\ late}$, 4.37±0.21 ng/ml *vs*. 4.45±0.17 ng/ml, p=0.779). The treatment naïve patients (n=17) had similar serum PTX-3 and LAMP-2 levels compared with those who had always been treated by corticosteroids or at least

Table I. Demographic, clinical characteristics and laboratory findings between TAK patients with active and inactive disease.

				NIH Criteria			AGATA Criteria		
	Healthy Controls (Mean±SEM/ n)/ Median (25%, 75%Q)	Total Patients (Mean±SEM/ n) / Median (25%, 75%Q)	*p*-value	Active (Mean±SEM/n)/ Median (25%, 75%Q)	Inactive (Mean±SEM/n)/ Median (25%, 75%Q)	*p*-value	Active (Mean±SEM/n)/ Median (25%, 75%Q)	Inactive (Mean±SEM/n)/ Median (25%, 75%Q)	*p*-value
Female	34/40	88/98	0.425	41/45	47/53	0.750	48/52	40/46	0.508
Age at disease onset (years)	/	27.12±0.95/98	/	27.28±1.45/45	26.98±1.26/53	0.877	27.68±1.33/52	26.52±1.36/46	0.544
Disease duration (months)	/	26.00(9.00,67.00)	/	16.00(4.00,45.00)	35.50(12.25,69.75)	***0.002****	16.00(4.00,39.00)	41.00(14.50,75.50)	***0.021****
Constitutional symptoms									
Fever	/	22/98	/	9/45	13/53	0.631	11/52	11/46	0.812
Malaise	/	62/98	/	35/45	27/53	***0.011***	38/52	24/46	***0.022***
Weight loss	/	27/98	/	14/45	13/53	0.650	17/52	10/46	0.203
Arthralgia/ Arthritis	/	18/98	/	5/45	13/53	0.116	7/52	11/46	0.197
Headache	/	37/98	/	16/45	21/53	0.679	20/52	17/46	0.819
Carotidynia	/	23/98	/	13/45	10/53	0.340	15/52	8/46	0.165
Vascular findings									
Upper limb claudication	/	21/98	/	9/45	12/53	0.807	12/52	9/46	0.636
Lower limb claudication	/	16/98	/	5/45	11/53	0.273	8/52	8/46	0.821
Pulse deficit	/	31/98	/	22/45	9/53	***0.001***	23/52	8/46	***0.004***
Asymmetric BP	/	35/98	/	20/45	15/53	0.138	23/52	12/46	0.061
Hypertension	/	31/98	/	11/45	20/53	0.194	13/52	18/46	0.133
Laboratory data									
WBC ($\times10^9$/L)	6.74±0.23/40	8.93±0.28/98	***<0.001***	8.82±0.46/45	9.04±0.58/53	0.764	9.04±0.51/52	8.81±0.57/46	0.756
Hb (g/L)	127.93±1.40/40	123.20±1.42/98	0.120	118.65±2.71/45	127.46±2.64/53	***0.024***	120.06±2.51/52	127.05±2.94/46	0.076
PLT($\times10^9$/L)	232.0(198.0,272.5)	260.5(222.5,307.5)	***<0.001****	307.5(252.5,385.5)	267.5(221.5,304.0)	0.104*	285.5(247.5,376.5)	271.0(227.5,309.0)	0.107*
Scr (umol/L)	60.50(55.50,65.00)	60.50(54.00,68.00)	0.584*	58.50(50.75,69.00)	64.00(53.75,74.25)	0.102*	58.00(51.00,69.00)	64.00(53.50,78.50)	0.187*
ESR (mm/h)	8.50(4.25,11.00)	12.50(7.00,28.00)	***<0.001****	31.50(14.00,66.50)	12.50(5.75,23.25)	***0.019****	19.50(10.00,55.25)	14.00(7.00,27.50)	***<0.001****
hsCRP (mg/L)	1.40(0.63,1.91)	2.51(0.88,13.62)	***<0.001****	17.68(5.67,57.93)	3.98(0.70,12.98)	***0.019****	10.52(3.12,53.50)	5.56(0.73,13.82)	***<0.001****
PTX-3(ng/ml)	0.19±0.02/40	0.32±0.02/98	***0.006***	0.42±0.06/45	0.25±0.02/53	***0.004***	0.38±0.05/52	0.27±0.02/46	***0.049***
LAMP-2(ng/ml)	3.31±0.20/40	4.40±0.12/98	***<0.001***	4.29±0.21/45	4.51±0.18/53	0.435	4.38±0.18/52	4.44±0.21/46	0.827
Numano subtypes									
I	/	33/98	/	13/45	20/53	***0.007***	16/52	17/46	***0.023***
IIa	/	21/98		15/45	6/53		16/52	5/46	
IIb	/	7/98		6/45	1/53		6/52	1/46	
III	/	2/98		0/45	2/53		0/52	2/46	
IV	/	5/98		1/45	4/53		1/52	4/46	
V	/	29/98		10/45	19/53		12/52	17/46	

NIH: National Institutes of Health; AGATA: Abatacept in giant cell arthritis (GCA) and Takayasu's arteritis (TAK); SEM: standard error of mean; BP: blood pressure; WBC: white blood cell; Hb: haemoglobulin; PLT: platelet; Scr: serum creatinine; ESR: erythrocyte sedimentation rate; hsCRP: hypersensitive C-reactive protein; PTX-3: pentraxin-3; LAMP-2: lysosomal-associated membrane protein-2. *parameters were analysed by the Mann-Whitney test; Median (25% quantile, 75% quantile).

Table II. The AGATA criteria compared with the NIH criteria according to disease activity in TAK patients.

Activity by indices		NIH criteria	
		Active (n)	Inactive (n)
AGATA criteria	Active (n)	44	8
	Inactive (n)	1	45

AGATA: Abatacept in giant cell arthritis (GCA) and Takayasu's arteritis (TAK); NIH: National Institutes of Health; TAK: Takayasu's arteritis.

one immunosuppressant (n=81) (PTX-3: 0.25±0.04 ng/ml *vs*. 0.34±0.04 ng/ml, *p*=0.270; LAMP-2: 4.71±0.28 ng/ml *vs*. 4.34±0.16 ng/ml, *p*=0.316).

We further analysed the relationship between serum PTX-3/LAMP-2 levels and ESR/hsCRP levels with the Pearson correlation test. We found that neither serum PTX-3 nor LAMP-2 level was significantly correlated with ESR/hsCRP level in our TAK patients (Fig. 1 A-D). TAK patients with vascular inflammation aggravation had higher serum PTX-3 levels than those without (0.48±0.08 ng/ml *vs*. 0.25±0.02 ng/ml, *p*<0.001). However, serum LAMP-2 levels were similar between TAK patients with and without vascular inflammation aggravation (4.45±0.23 ng/ml *vs*. 4.38±0.17 ng/ml, *p*=0.832).

The area under the ROC curve (AUC) for PTX-3, LAMP-2, ESR and hsCRP were not statistically different from each other (Fig. 2-3). A serum cut-off value 0.30 ng/ml of PTX-3 maximised the ability of disease activity assessment with a sensitivity/specificity of 57.10%/73.10% and 47.90%/71.10% according to the NIH and AGATA criteria, respectively. A serum cut-off value 3.36 ng/ml of LAMP-2 maximised the ability of disease activity assessment with a sensitivity/specificity of 27.50%/82.20% and 31.10%/84.30% according to the NIH and AGATA criteria. With established ESR and hsCRP thresholds in our centre, ESR and hsCRP were able to identify disease activity with a sensitivity/specificity of 59.09%/68.00% and 85.00%/42.00% according to the NIH criteria and of 48.98%/60.00% and 75%/43.48% according to the AGATA criteria, re-

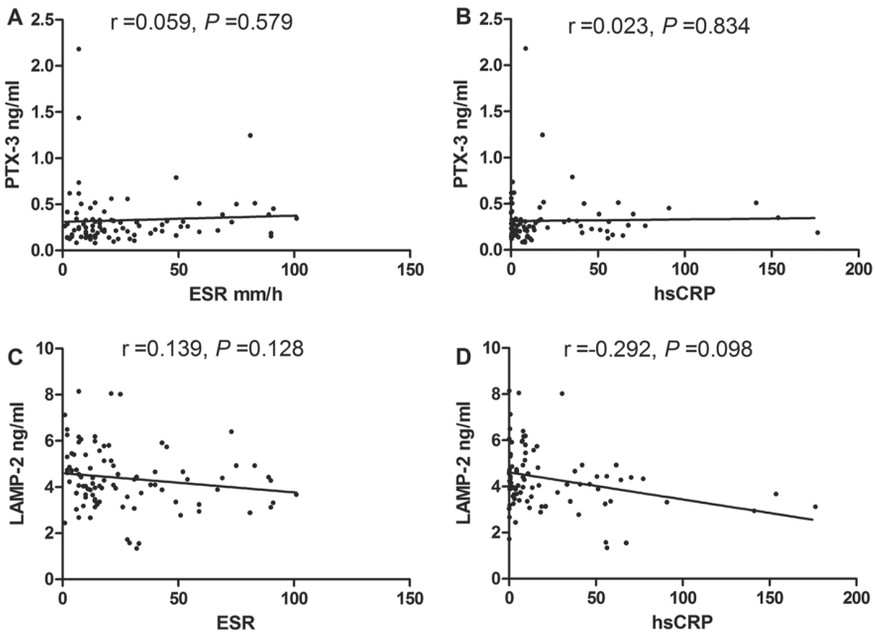

Fig. 1. Correlation between serum PTX-3/ LAMP-2 levels and ESR/ hsCRP in patients with TAK. (**A**-**D**) Serum PTX-3/LAMP-2 levels did not correlate with ESR/hsCRP levels in TAK patients.
PTX-3: pentraxin-3; LAMP-2: lysosomal-associated membrane protein-2; ESR: erythrocyte sedimentation rate; hsCRP: hypersensitivity C-reactive protein; TAK: Takayasu's arteritis.

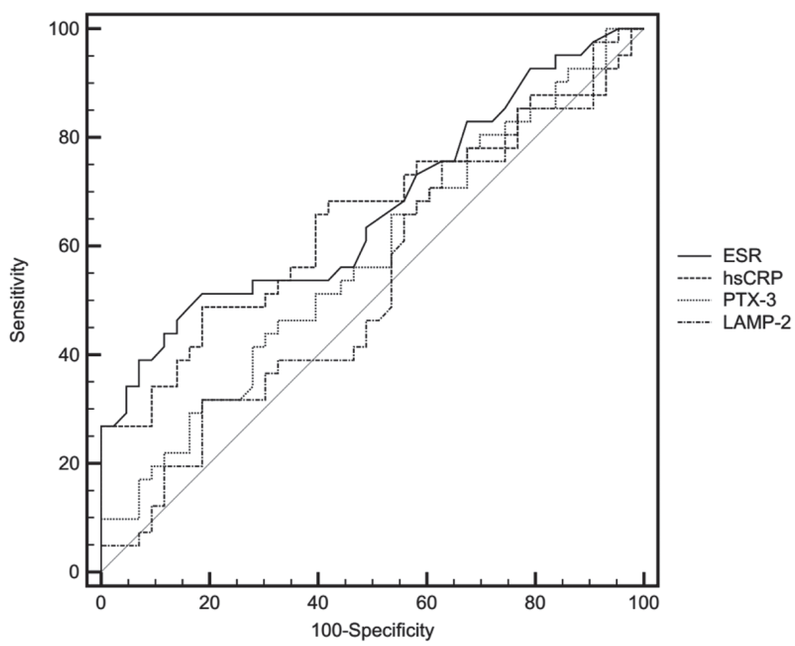

Fig. 2. The ROC curves for ESR, hsCRP, PTX-3 and LAMP-2 in 98 TAK patients according to the NIH criteria. The AUC for ESR, hsCRP, PTX-3 and LAMP-2 were 0.75 (95% CI 0.65-0.84), 0.72 (95% CI 0.61-0.81), 0.64 (95% CI 0.52-0.74) and 0.50 (95% CI 0.39-0.61), respectively. The AUC of ESR and hsCRP was higher than that of LAMP-2 according to the NIH criteria.
ROC: receiver operating characteristics; AUC: the area under the ROC curve; ESR: erythrocyte sedimentation rate; hsCRP: hypersensitivity C-reactive protein; PTX-3: pentraxin-3; LAMP-2: lysosomal-associated membrane protein-2; TAK: Takayasu's arteritis; NIH: National Institutes of Health; CI: credit interval.

spectively. Thus, hsCRP levels were more sensitive than specific to disease activity assessment compared with PTX-3 levels. Therefore, we further analysed the ability of PTX-3 (cut-off value 0.30 ng/ml) for disease activity assessment among TAK patients who had elevated hsCRP levels. Among this specific group of TAK patients (n=61), the specificity of PTX-3 levels for disease activity assessment increased to 81.48% according to both criteria. However, in the multivariate analysis, the AUCs for hsCRP and serum PTX-3 levels combination were 0.73 (95% CI 0.62–0.84) and 0.64 (95% CI 0.51–0.76) according to the NIH and AGATA criteria, which were not different from the AUCs for hsCRP/serum PTX-3 levels alone.

Discussion

Disease activity assessment is quite important for optimal management of TAK, including medication therapy, intervention and surgery (9). However, disease activity assessment in TAK is a big challenge.

The NIH criteria is the most commonly used and widely accepted disease activity assessment tool in TAK (10). Recently, the steering committee of VCRC developed the AGATA criteria which focuses on the effectiveness of Abatacept for the treatment of GCA and TAK (5, 11). Researchers have found that the characteristics of disease flares are fully consistent with clinical and imaging parameters set-up in the definitions. The results imply that the AGATA criteria are reliable for disease activity assessment. Moreover, most of the parameters listed in the AGATA criteria are accepted by rheumatologists of the International Delphi on Disease Activity Assessment in Large-vessel Vasculitis (12). Our study has shown that NIH and AGATA criteria are highly consistent for TAK disease activity assessment. Compared with the NIH criteria, the AGATA criteria were able to assess disease activity only in TAK patients who have localised and asymptomatic vascular disease. However, all the clinical and imaging parameter-based criteria, including AGATA, are "subjective" to some extent. Serum biomarkers may be the most promising objective indicators for disease activity assessment. Unfortunately, so far, no reliable serum biomarkers are available for disease activity assessment in TAK patients.

Pentraxin-3 (PTX-3) is a member of the pentraxin family. Unlike other pen-

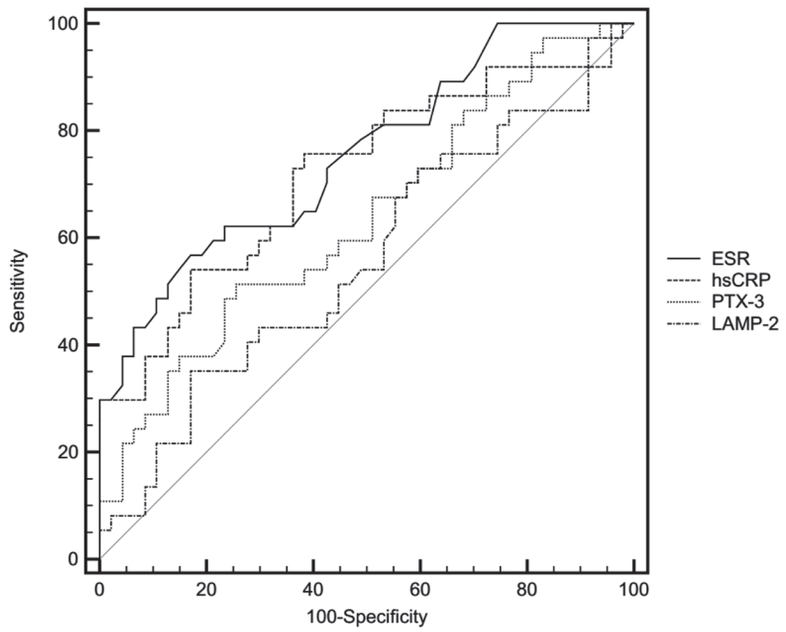

Fig. 3. The ROC curves for ESR, hsCRP, PTX-3 and LAMP-2 in 98 TAK patients according to the AGATA criteria. The AUC for ESR, hsCRP, PTX-3 and LAMP-2 were 0.66 (95% CI 0.54-0.76), 0.63 (95% CI 0.52-0.73), 0.59 (95% CI 0.48-0.70) and 0.53 (95% CI 0.42-0.64), respectively.
No statistical significance was observed between each group.
ROC: receiver operating characteristics; AUC: the area under the ROC curve; ESR: erythrocyte sedimentation rate; hsCRP: hypersensitivity C-reactive protein; PTX-3: pentraxin-3; LAMP-2: lysosomal-associated membrane protein-2; TAK: Takayasu's arteritis; AGATA: Abatacept in giant cell arthritis (GCA) and Takayasu's arteritis; CI: credit interval.

traxin family members, such as CRP and amyloid protein which are produced by the liver, PTX-3 is secreted by local monocytes and macrophage lineage cells residing in situ in vascular inflammation sites and are seldom changed by systemic inflammation (13, 14). Previous studies indicated that PTX-3 could enhance local inflammation by promoting complement deposition and by facilitating endothelium and monocytes secreting tissue factor (13). Furthermore, PTX-3 is a humoral arm of innate immunity by promoting opsonisation, facilitating phagocytosis and it also promotes the production of pro-inflammatory cytokines. Higher serum PTX-3 levels predicted worsening vascular lesions during follow-ups and serum PTX-3 levels decreased after vascular inflammation was relieved (3, 15). Thus, PTX-3 may be a potential candidate for TAK activity assessment. To date, five studies have analysed the relationship between serum PTX-3 level and disease activity worldwide. However, the results vary between the different studies and populations (3, 16-19).

Dagna *et al*. first reported that PTX-3 was a marker of disease activity in Italian TAK patients (13). They found that serum PTX-3 level was higher in TAK patients and even higher in patients with active disease. Serum PTX-3 was more specific than ESR/CRP in distinguishing active and inactive disease in TAK at the threshold of 1.0 ng/ml. Thereafter, Ishikara *et al*. reported that serum PTX-3 level was markedly increased in TAK patients with active disease in Japanese TAK patients (19). However, PTX-3 was not superior to hsCRP in assessing disease activity. Sun *et al*. also reported that serum PTX-3 levels were elevated in TAK patients with active disease (17). In the present study, we found that serum PTX-3 level was significantly elevated in TAK patients with active disease and that PTX-3 had a similar ability in reflecting active disease as ESR/hsCRP. Meanwhile, the specificity of PTX-3 for disease activity was increased in patients with activity disease and high hsCRP levels. In our study, PTX-3 level higher than 0.30 ng/ml combined with elevated hsCRP level increased the specificity for predicting active disease from 70% to 80%.

However, not all studies found that PTX-3 levels were elevated in TAK patients with activity disease. In the Turkish TAK patients, Alibaz-Oner *et al*. found that although TAK patients had higher serum PTX-3 levels compared with healthy controls, serum PTX-3 levels did not differ between patients with active disease and stable disease (18). In another study in the Italian population, Tombetti *et al*. also reported that serum PTX-3 levels were similar between TAK patients with and without active disease (3).

In Dagna's research, serum PTX-3 levels were elevated in TAK patients with active disease and PTX-3 had been shown to be superior to ESR/hsCRP in reflecting active disease (13). In Sun's study, they found that serum PTX-3 levels were positively correlated with quantitative magnetic resonance scores in aspects of luminal stenosis and mural thickening (17). We also found that TAK patients with deteriorated vascular inflammation had higher serum PTX-3 levels. These results implied that serum PTX-3 elevation might be an indicator for vascular inflammation. A novel biomarker must have much higher sensitivity and specificity than those provided by the routinely used CRP and ESR. In the present study, we found that the AUC for PTX-3, LAMP-2, ESR and hsCRP were not statistically different from each other. Thus, PTX-3 alone was not superior to ESR/hsCRP for disease activity evaluation. However, PTX-3 together with hsCRP might be a promising evaluation index for the evaluation of disease activity.

Lysosomal-associated membrane protein-2 (LAMP-2) is a heavily glycosylated type 1 membrane protein which distributes on lysosomal membrane and vascular endothelia cells (20). LAMP-2 plays important roles in many pathophysiology processes, including cell adhesion, autophagocytosis and antigen presentation (21). Kain *et al*. first reported that LAMP-2 was a kind of target antigen of anti-neutrophil cytoplasmic antibodies (ANCA) (22). Anti-LAMP-2 auto-antibodies always present as the p-ANCA pattern in

indirect immunofluorescence (23). The prevalence of anti-LAMP-2 autoantibodies in patients with AAV and pauci-immune focal necrotising glomerulonephritis ranged from 80–90% (24). In contrast to anti-myeloperoxidase (MPO) and anti-proteinase 3 (PR3) ANCA, anti-LAMP-2 autoantibodies disappeared rapidly after initiation of immunosuppressive therapy (25). However, anti-LAMP-2 autoantibodies re-appeared when clinical relapse occurred (25). Thus, serum anti-LAMP-2 autoantibody levels might be a promising disease activity indicator in AAV patients. In addition, Kawakami *et al*. showed that anti-LAMP-2 auto-antibodies were elevated in patients with cutaneous polyarteritis nodosa (CPN) and Henoch-Schönlein purpura (HSP) where anti-MPO and anti-PR3 ANCA were always negative (23). Takeuchi and colleagues found that LAMP-2/anti-LAMP-2 autoantibodies played essential roles in the pathogenesis of CPN and HSP in rat models (26). However, to the best of our knowledge, no study has tested LAMP-2/anti-LAMP-2 autoantibody levels in patients with TAK. Vascularisation is a potential marker for disease activity assessment in TAK (27). Since LAMP-2 abundantly locates on the vascular endothelium, it is the basic element for vascularisation (28). Thus, we hypothesised that serum LAMP-2 levels might be changed in TAK and have the potential to be used for disease assessment in TAK patients. We found that serum LAMP-2 levels were markedly increased in TAK patients compared with healthy controls. However, no statistically significant difference was detected between patients with active and stable disease. Nor did we find any correlation between serum LAMP-2 and ESR/hsCRP level.

There are several limitations to our study. First, we did not follow the time course changes of serum PTX-3 and LAMP-2 levels, so we do not know whether the increased serum PTX-3 level might change with treatment and time course. Second, we did not analyse the atherosclerosis in our TAK patients. Because PTX-3 is elevated in both atherosclerosis and TAK, we could not evaluate the influence of atherosclerosis in our TAK patients. Third, colour Doppler ultrasonography cannot be used for vascular inflammation tracking in thoracic artery.

Conclusion

Both serum PTX-3 and LAMP-2 levels are elevated in TAK patients. The total agreement for disease activity assessment between the NIH and the AGATA criteria was high. Serum PTX-3 level is associated with active disease and can be used as an indicator for active TAK disease. However, PTX-3 is not superior to ESR/hsCRP for disease activity assessment in Chinese TAK patients. Nevertheless, the combination of CRP and PTX-3 could further increase the sensitivity and specificity for reflecting active TAK disease. LAMP-2 is elevated in TAK patients but not associated with disease activity.

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