The Establishment and Validation of Reference Intervals for Plasma Pentraxin-3 in Healthy Volunteers and Patients with Takayasu's Arteritis

Xiang Zhou
Fourth Military Medical University

Qing Han
Fourth Military Medical University

Xiqing Wang
Fourth Military Medical University

Ming Zhang
Fourth Military Medical University

Xiang Li
Fourth Military Medical University

Wenhui Ma
Fourth Military Medical University

Xueying Wang
Fourth Military Medical University

Weidong Yang
Fourth Military Medical University

Ping Zhu
Fourth Military Medical University

Jing Wang
Fourth Military Medical University

Fei Kang (✉ fmmukf@qq.com)
Fourth Military Medical University

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Abstract

Objective

To establish reference intervals (RIs) for PTX-3 and to validate the performance of these RIs in a population including healthy volunteers and Takayasu's arteritis (TAK) patients.

Methods

Enzyme-linked immunosorbent assays were used to determine the plasma PTX-3 levels of 166 healthy volunteers and 63 TAK patients. RIs were established in healthy volunteers according to guidelines from the Clinical and Laboratory Standards Institute (CLSI, C28-A3). Global assessment was used to quantitatively diagnose active/non-active TAK patients. PTX-3 cut-off values and RI-derived values were calculated as candidate standards for quantitative diagnosis. Screening and monitoring performances were validated by identifying active TAK patients from the whole population or diagnosed TAK patients. Traditional inflammatory markers C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were included in the comparison.

Results

PTX-3 level increased with age but were not significantly different among different age or gender groups (p > 0.05). The PTX-3 RI was calculated to be 0.87–2.78 ng/mL (RI median: 1.66 ng/mL). For screening purposes, the cut-off value (1.55 ng/mL) had a high sensitivity of 90.32% and the RI upper limit (2.78 ng/mL) had a high specificity of 97.94%. For monitoring purposes, the sensitivity/speciﬁcity of the cut-off value (1.55 ng/mL) and RI median were 90.32%/90.63% and 80.85%/90.63%, respectively. These screening and monitoring performances of PTX-3 were superior to those of CRP and ESR.

Conclusion

The distribution of serum PTX-3 levels was stable and uniform across the population. The screening and monitoring performances of the cut-off value and RI-derived values of PTX-3 were higher than CRP and ESR.

Introduction

Takayasu's arteritis (TAK) is a type of autoimmune disease that is characterized by large vessel granulomatous vasculitis with massive intimal fibrosis and vascular narrowing (1, 2). Due to continuous inflammatory damage incurred by the main arteries, TAK has a high rate of mortality (5%-33%) and disability (23%-74%) after diagnosis (3). The high relapse and progression rate associated with this condition makes the long-term clinical management of TAK very difficult (4–6). Therefore, precise inflammatory activity assessment is needed to make appropriate therapeutic decisions (7).

The current diagnostic methods for inflammatory activity include clinical standards, imaging standards, and serum markers. Proposed criteria, such as the National Institutes of Health (NIH) criteria, have limited accuracy and do not consider inflammation within the vessel walls; therefore, non-active patients diagnosed by these
criteria often undergo vascular progression (1, 8, 9). Invasive histological diagnosis is only possible during revascularization procedures; therefore, this option is rarely available and cannot reflect the burden created by whole-body inflammation (10). Although imaging diagnostic methods, such as ultrasound, computed tomography angiography, magnetic resonance angiography, and $^{18}$F-fluorodeoxyglucose-positron emission tomography ($^{18}$F-FDG PET), have been applied in TAK patients, the high costs, radiation exposure, or incomplete establishment of quantitative diagnosis criteria, restrict their routine use (11). Therefore, in the latest clinical guideline, inflammatory biomarkers considered as conventional and convenient tools for the routine follow-up of patients with TAK (12).

Biomarkers have two main clinical tasks: firstly, screening active TAK patients from the whole population with high levels of sensitivity. Secondly, monitoring active patients in diagnosed TAK patients with high levels of accuracy. However, commonly used inflammatory biomarkers, such as ESR and serum marker CRP, are not able to accurately discriminate active and inactive disease, thus resulting in a severe mismatch in the levels of these biomarkers and the clinical features in as high as 50% of all TAK patients (1, 8, 13). Further research and clinical validation on new biomarkers are urgently needed to achieve more precise diagnosis and to help guide treatment decisions in TAK patients (14).

Pentraxin-3 (PTX-3) is a key player in innate immunity and is locally excreted by inflammatory cells and intrinsic cells. Compared with non-specific ESR and CRP, PTX-3 is theoretically directly related to the degree of inflammation. It has been reported that PTX-3 is a potentially better biomarker for quantifying the inflammatory activity of TAK patients (15–17), although we have yet to develop qualitative diagnostic standards for application in the clinic. Furthermore, whether such standards represent universal options for different populations remains unclear (18).

In the present study, we investigated the distribution characteristics and reference intervals (RIs) of PTX-3 in a population of healthy volunteers and TAK patients, and further validate the performance of PTX-3 RI-derived values (upper limit, median), the PTX-3 cut-off value, and traditional biomarkers, for the screening and monitoring of patients with TAK.

**Materials And Methods**

1. Volunteers and patients

Blood samples were provided by volunteers and TAK patients with informed and signed consent. In total, we enrolled 166 healthy volunteers, including 82 males and 84 females (aged 18–78 years; 39.7 ± 16.4 years), who came to Xijing Hospital to receive annual physical examination between January 2017 and January 2018. These subjects were selected by a negative medical history and physical examination results relating to infections, autoimmune diseases, hematological diseases, neurological diseases, hepatobiliary diseases, acute or chronic kidney disease, asthma, genetic metabolic diseases, tumors, pregnancy, history of surgery or blood transfusion. These volunteers were divided into four groups according to their age (< 20, 21–40, 41–60, > 60 years). The gender ratio was 1:1 in each group to ensure that the sampling was representative, as previously reported (19). Minors (< 18 years) were not selected for ethical considerations. In addition, we enrolled 63 patients, including 10 males and 53 females (aged 19–74 years; 37.4 ± 15.1 years), with a diagnosis of TAK according to the 1990 American College of Rheumatology Classification Criteria (20). None of the patients had any other specific
diseases. Female volunteers or patients during their ovulation period were excluded because of the association between estrogen excretion and arteritis (21).

2. Sample collection and the measurement of inflammatory markers

According to the instructions of the relevant kit, all volunteers and patients underwent fasting blood sample collection. Whole blood samples of 3–5 mL were collected from the median cubital vein using a separator tube containing EDTA (EDTA-2K, 5mL, Kangjian, China) and separation gel (5mL, Improve medical, China). Blood samples were centrifuged for 15 minutes at 1000 g within 30 minutes of collection for PTX-3 and CRP detection. Plasma and serum samples were aliquoted and stored at -20°C. We made every effort to avoid repeated freeze-thaw cycles. Tubes containing sodium citrate (5mL, BD, American) were used to detect ESR.

An enzyme linked immunosorbent assay (ELISA) kit (R&D, USA) was used to detect the plasma levels of PTX-3. The level of serum C-reactive protein (CRP) was measured by using an immunoturbidimetric assay (BN2, SIEMENS). Erythrocyte sedimentation rate (ESR) was detected using the Westergren method (VITAL MONITOR 100, ELECTA LAB). According to the latest recommendations and the verified laboratory's range, the normal reference range for screening CRP and ESR are set as < 6.0 mg/L and 0–20mm/h, respectively (16, 22). All detection methods were calibrated and quality controlled according to the manufacturer's instructions.

3. Determination of RIs

The number of volunteers met the sample size (n = 120) recommended by CLSI C28-A3 and previous studies (23, 24). A previous study noted that a robust estimate of the 90% confidence intervals of the reference limit can be obtained from this sample size (25). The RIs were determined under the guidance of CLSI C28-A3 (19). Volunteers of different age from the medical examination center were used as the reference population, and reference individuals were selected from the reference population who met the required age group by a direct sampling method: a total of 211 subjects (106 males, 105 females) were identified. The reference individuals were screened by investigation and physical examination according to the aforementioned criteria, and 45 subjects (24 males, 21 females) were excluded. Specimen collection and testing were performed on reference individuals. Quality control procedures were carried out throughout the process and the quality objectives provided by laboratories and suppliers were reached. The obtained test data constituted a reference sample, which was analyzed to obtain the reference values (distribution, upper and lower limits, reference intervals); these reference values were verified, evaluated and applied in clinical patients.

4. The evaluation of inflammatory activity in TAK patients

The qualitative determination of inflammatory activity (active/non-active) is carried out by the physician's global assessment (PGA) method (16). This represents the normal gold standard at present (26). Two experienced rheumatologists conducted a comprehensive assessment based on the syndrome, physical examination, clinical history, and computed tomography (CT) angiography results (16). Acute phase reactants were not incorporated into clinical response monitoring to ensure an unbiased comparison. The assessment results of 18F-FDG PET/CT were also used as one of the criteria for determining inflammatory activity (27–29). All diagnosed TAK patients underwent whole body 18F-FDG PET/CT (Biograph 40, SIEMENS) scans by following standard clinical protocols (30). Any site of focal or diffuse increased FDG uptake detected on the PET component of the PET/CT study as compared to the physiological tracer activity in adjacent structures was defined as higher activity. The degree of
\[^{18}\text{F-FDG}\] uptake in the target lesion was assessed visually by two nuclear medicine physicians (31). The interior of the liver and the increased FDG uptake lesions (usually the aorta) were circled with an oval and the mean standard uptake value (SUV) was determined by software supplied by the vendor. The SUV ratio (artery/liver) was also determined as one of the standards for PGA in accordance with previous clinical studies (32, 33). Comparisons of quantitative inflammatory activity between SUV ratio data and PTX-3 levels was also performed, and then compared with ESR and CRP.

5. Statistics

First, 95% CIs were calculated for the endpoints of the RI. Data are presented as mean ± standard deviation (SD) or as medians (X25%~X75%). Two-tailed Mann-Whitney U tests and Chi-squared tests were used to compare intervals and categorical variables across the four groups of 166 volunteers. The Newman-Keuls test was used for multiple comparisons between the four age groups. The D’Agostino & Pearson omnibus normality test was used to determine if data conformed to the Gaussian distribution. A p value < 0.05 was considered statistically significant. ROC (receiver operating characteristic) curves were used to determine the diagnostic efficiency of the indicators. The area under the ROC curve (AUC) and Youden index (YI=sensitivity + specificity-1) were calculated to evaluate the discriminatory ability of each criterion and to determine the cut-off value. GraphPad Prism software version 9.0.0 (GraphPad Software, San Diego, California) was used for calculations.

Results

1. Baseline characteristics of the study population

Population information and distribution are shown in Table 1. The volunteer population included 82 males and 84 females with a mean age of 39.7 ± 16.4 years (range 18–78 years). The TAK patient population included 10 males and 53 females, with a mean age of 37.4 ± 15.1 years (range 19–74 years). Among the TAK patients, 31 were diagnosed as active and the other 32 were non-active. There were no significant differences in terms of age and gender (p > 0.05).
Table 1
Population information and PTX-3 levels

<table>
<thead>
<tr>
<th>Population</th>
<th>Gender</th>
<th>Number</th>
<th>Number</th>
<th>Number</th>
<th>Number</th>
<th>PTX-3 level (ng/mL)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>82</td>
<td>18</td>
<td>22</td>
<td>31</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Volunteers</td>
<td>Male</td>
<td>82</td>
<td>18</td>
<td>22</td>
<td>31</td>
<td>14</td>
<td>41.8 ± 17.3</td>
</tr>
<tr>
<td>Volunteers</td>
<td>Female</td>
<td>84</td>
<td>14</td>
<td>24</td>
<td>32</td>
<td>11</td>
<td>37.8 ± 15.2</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td>166</td>
<td>32</td>
<td>46</td>
<td>63</td>
<td>25</td>
<td>39.7 ± 16.4</td>
</tr>
<tr>
<td>Activity Diagnosis</td>
<td>Male</td>
<td>31</td>
<td>5</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takayasu's arteritis (TAK) patients</td>
<td>Female</td>
<td>5</td>
<td>26</td>
<td>39.6 ± 15.8</td>
<td>3.56 ± 0.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-active</td>
<td>32</td>
<td>5</td>
<td>27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td>63</td>
<td>10</td>
<td>53</td>
<td></td>
<td></td>
<td>37.4 ± 15.1</td>
</tr>
</tbody>
</table>

2. Establishment of PTX-3 Reference intervals (RI)

As shown in Fig. 1 and Table S1, the PTX-3 levels of all 166 healthy volunteers, as well as the male and female subgroups, were normally distributed according to graphical and statistical verification. The mean and median levels of PTX-3 for all volunteers/males/females were 1.73/1.70/1.76 ng/mL and 1.66/1.56/1.68 ng/mL, respectively (Table 2). Further analysis of the differences between different genders and age groups showed there was no significant difference in the PTX-3 levels when compared between genders (p = 0.92). The data were normally distributed in each group according to graphical and statistical verification; there was a small gradual increase in PTX-3 levels with age although there was no statistically significant difference (p = 0.94) between the groups according to one-way analysis of variance (ANOVA). PTX-3 had clinical discriminative value at both high and low levels. Therefore, the 2.5th (lower limit) to 97.5th (upper limit) percentiles were defined as a biological RI by applying the percentile method. After calculation, the PTX-3 RI for the normal PTX-3 level, as detected by the ELISA kit (R&D, USA), was defined as 0.87–2.78 ng/mL and the median of the RI was defined as 1.66 ng/mL.
Table 2
Distribution of PTX-3 levels across genders

<table>
<thead>
<tr>
<th>Gender</th>
<th>95% CIs (ng/mL)</th>
<th>Mean (ng/mL)</th>
<th>M(X25% - X75%) (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>1.57 ~ 1.83</td>
<td>1.70</td>
<td>1.56(1.25–2.19)</td>
</tr>
<tr>
<td>F</td>
<td>1.63 ~ 1.89</td>
<td>1.76</td>
<td>1.68(1.25–2.26)</td>
</tr>
<tr>
<td>All</td>
<td>1.64 ~ 1.82</td>
<td>1.73</td>
<td>1.66(1.26–2.21)</td>
</tr>
</tbody>
</table>

3. Validation of the PTX-3 RI in TAK patients and volunteers

The circulatory levels of PTX-3, CRP and ESR were measured in 31 active patients, 32 non-active patients and all healthy volunteers. As shown in Fig. 2A, active TAK patients had significantly higher levels of PTX-3 than healthy volunteers (p<0.001) and non-active TAK patients (p<0.001). Furthermore, the levels of PTX-3 in non-active TAK patients was significantly lower than normal volunteers (p<0.001).

The efficacy of the upper limit of the RI, the median RI, and the cut-off values for PTX-3, CRP and ESR for screening active TAK patients from the entire population are given in Table S2. The cut-off value for PTX-3 had a higher AUC (0.82) and Youden index (0.45) than those for CRP (0.81, 0.30) and ESR (0.67, 0.27) (Fig. 2B). Furthermore, PRX-3 could sensitively identify 90.32% active patients. The upper limit of the RI had a high specificity as 97.94%, and 51.61% of active patients were specifically identified by applying this standard. Moreover, the median RI had a screening sensitivity of 80.65%, although the sensitivity and Youden index (0.38) were not as good as the cut-off value.

The efficacy of the upper limit of the RI, the median RI, as well as the cut-off values for PTX-3, CRP and ESR when monitoring active patients from diagnosed TAK patients are given in Table S3. As with PTX-3, the levels of CRP and ESR in active patients were significantly higher than those in non-active TAK patients (p<0.001) (Fig. 3A, B, Table S4). The cut-off value for PTX-3 had a much higher AUC (0.96) and Youden index (0.81) than those of CRP (0.72, 0.23) and ESR (0.69, 0.23) (Fig. 3C). PTX-3 could sensitively and specifically identify 90.32% of active and 90.63% of non-active patients. The median RI had a screening sensitivity of 80.65%, although the sensitivity and Youden index (0.38) were not as good as the cut-off value. The diagnostic performance of the median RI was close to the cut-off value for PTX-3; the sensitivity (80.65%), specificity (90.63%) and Youden index (0.71) were all higher than the traditional indicators CRP (51.61%, 71.88%, 0.23) and ESR (41.94%, 81.25%, 0.23)

When using the SUV ratio as a parameter, the correlation coefficient between PTX-3 and SUV ratio (Spearman r=0.52) was higher than that for both CRP (0.33) and ESR (0.28) (Table S5, Fig. S1).

Then, we attempted to propose a clinical diagnosis pathway for TAK patients based on PTX-3 (Fig. 4). For screening purposes, the unselected Cohort (the entire population including healthy and TAK cohorts) could be divided into low-risk and medium-risk groups according to the cut-off value (1.55 ng/mL). This could screen out active patients with a high sensitivity of 90.32%. If a patient exceeded the upper limit (2.78ng/mL), then the patient was classified as high-risk; this refers to active TAK patients with 97.94% specificity. The PTX-3 level of medium-risk patients was lower than the upper limit (2.78ng/mL) but higher than the cut-off value (1.55 ng/mL). These particular patients required further differential diagnosis on the basis of imaging vascular
features and systemic symptoms. When diagnosing TAK patients, a PTX-3 level higher than 1.55ng/mL could identify active TAK patients with a sensitivity of 90.32% and a specificity of 90.63%.

Discussion

In this study, we established the RI for PTX-3 in a population of healthy volunteers and validated the performance of this RI for the purpose of screening and monitoring in a mixed population of healthy volunteers and TAK patients. There were three major findings: firstly, the PTX-3 RI was calculated to be 0.87–2.78 ng/mL with an upper limit and median of 2.78 and 1.66 ng/mL, respectively. Secondly, the cut-off value (1.55 ng/mL) for PTX-3 (close to the median) demonstrated high sensitivity (90.32%) for screening active patients from the entire population, and high sensitivity/specificity (90.32%/90.63%) for monitoring active patients from the diagnosed TAK patients. Thirdly, compared with traditional parameters (CRP and ESR), the cut-off and RI-derived values of PTX-3 demonstrated higher diagnostic performance. In addition, we proposed a diagnosis pathway based on PTX-3.

As described previously, PTX-3 has been proven to be an important diagnostic indicator for TAK. However, the diagnostic criteria for PTX-3 remain uncertain, thus meaning that this biomarker has not been established in routine clinical diagnosis according to the latest expert recommendations (22). In several previous studies, the median PTX-3 level varied from 0.11 to 3.9 ng/mL and from 2.1 to 5.5 ng/mL in healthy controls and active TAK patients, respectively; the sample size ranged from 20 to 57 (8, 16). These differences may have been caused by different antibodies, reagents or an insufficient sample size. Therefore, there is an urgent need to investigate the distribution of PTX-3 in a larger healthy population, other than patients for establishing diagnostic criteria (34). In this study, the RI for serum PTX-3 level was calculated in 166 healthy volunteers to lay a foundation for the development of specific diagnostic criteria. We further found that the distribution of PTX-3 levels across different ages and genders was stable and consistent with a normal distribution, thus indicating the universality of fixed diagnostic criteria (16, 24, 35, 36).

There is not always a single diagnostic criterion for laboratory markers; rather, several different diagnostic criteria can exist according to clinical needs and purposes. As with the upper limit of the RI (2.78 ng/mL) and the cut-off value (1.55ng/mL) we set, different prostate specific antigen (PSA) levels can divide a population of patients into low risk (a PSA level < 10 ng/mL), intermediate risk (a PSA level of 10–20 ng/mL) and high risk (a PSA level > 20 ng/mL) (37). However, we cannot ignore that the distribution of PTX-3 levels in healthy volunteers is generally between the active and non-active TAK patients, thus making the RI a relatively broad range. Therefore, when using this standard for screening, some volunteers with high PTX-3 levels may have interfered with the definition of active patients; these non-active patients in the gray area remain an unsolved problem for screening in the future. Thus, the upper limit of the RI (2.78 ng/mL), which excludes almost all negative samples, can be used as a higher diagnostic threshold for screening. Generally, this problem could be improved by narrowing the reference range if data from the 20–60 age group is considered to be more representative (38); however, our results do not show statistical differences between age groups.

However, unlike screening, this standard had a high specificity and sensitivity for monitoring. The reason for this may be that, from the perspective of pathophysiology, PTX-3 will be rapidly elevated due to inflammation-related specific secretion but will also be consumed for tissue repair (39). Furthermore, during the acute phase of inflammation, the expression of PTX-3 is mainly induced by inflammatory cytokines or damage-associated
molecular patterns (DAMPs), and rapidly released by neutrophils, thus making the serum levels of PTX-3 increase rapidly within minutes at specific sites (40). However, after the acute reactive phase, PTX-3 can interact with P-selectin and components of the complement cascade function as an immunoregulatory molecule. PTX-3 can also adhere to apoptotic cells and affect the clearance of apoptotic cells. PTX-3 also recognizes and binds various FGFs (fibroblast growth factors) to inhibit FGF-dependent vascular endothelial injury (41–44). This unique versatility of PTX-3 may result in its plasma concentration decreasing lower than the normal population when inflammation is inactive (45). Our results provide evidence to further elucidate the exact roles and precise mechanisms of PTX-3 in inflammation. Furthermore, our data reduces the gray area for PTX-3 when diagnosing inflammatory activity in TAK patients. This is an important reason for the high diagnostic efficiency of PTX-3. In summary, the establishment of this new PTX-3 standard is expected to provide more sensitive TAK screening tools and more accurate activity monitoring standards for clinical diagnosis and help to develop better laboratory screening methods than ESR and CRP.

The evaluation of TAK inflammatory activity is still a difficult problem in rheumatology immunology. There are currently a variety of quantitative scoring, grading, and diagnostic methods, based on clinical manifestations, imaging manifestations, serum markers, and the cross-mixed use of multiple methods, such as The Birmingham Vasculitis Activity Score (BVAS), Indian Takayasu Clinical Activity Score (ITAS2010), PET vascular activity score (PETVAS), Physician’s Global Assessment (PGA), Disease Extent Index for Takayasu’s arteritis (DEI.Tak), and the four items in the NIH (National Institutes of Health) series (the presence of constitutional symptoms, new bruits, acute-phase response, or new angiographic features)(46, 47). Numerous methods can precisely reflect the challenge, complexity, and controversy of TAK activity assessment. Our previous studies have confirmed that PTX-3 has better consistency with inflammatory markers based on PET functional imaging than other indicators, thus showing superior quantitative inflammatory assessment accuracy (15). Our present study also showed that the levels of PTX-3 had higher quantitative consistency with PET functional imaging. The distribution characteristics and quantitative diagnostic criteria of PTX-3 described in this study will help to establish new and auxiliary diagnostic criteria based on serological markers; this may create a potential supplement to the classical but controversial 1990 NIH criteria (48).

There are some limitations to our study that need to be considered. First, this was a single-center study. Although the sample size exceeds most current studies, it is still limited with regards to yielding accurate and applicable criteria. Our results may also have been affected by environment, lifestyle, and ethnicity; therefore, multicenter and larger sample sizes are now needed to develop more accurate PTX-3 diagnostic criteria. Secondly, although the PGA standard of TAK activity is already a widely used clinical research standard, it still features some subjective factors, which may create certain bias. In addition, the application of the established diagnostic criteria still needs to be verified and revised in future large-scale clinical studies.

Declarations

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Compliance with Ethical Standards
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Conflict of Interest: The authors do not have any possible conflicts of interest.

Informed consent: This study was approved by the Ethics Committee of Xijing Hospital (Approval No. KY20163015-1)

Ethical approval: All procedures performed in studies involving human participants and sample collection were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Figures
Figure 1

A. Frequency distribution of PTX-3 levels with age in all healthy volunteers in the male group and in the female group. The reference interval (RI) for PTX-3 level was 0.87 - 2.78ng/mL (2.5\(^{\text{th}}\) - 97.5\(^{\text{th}}\)). B. Comparative analysis of PTX-3 levels in males and females revealed no significant difference, p=0.92. C. The mean PTX-3 level increased with age; one-way analysis of variance found that there were no significant differences between each pair of these four groups (P=0.94).
Figure 2

The accuracy of PTX-3 for TAK screening. A. Comparative analysis of PTX-3 levels in different TAK groups and volunteers. B. ROC analysis for TAK patients and volunteers when using PTX-3, CRP and ESR as diagnostic markers. C. A comparison of sensitivity and specificity among different screening criteria for biomarkers.
Figure 3

The accuracy of PTX-3 for TAK monitoring. A. B. Comparative analysis of CRP and ESR levels in different TAK groups. C. ROC analysis for TAK patients when using PTX-3, CRP and ESR as diagnostic markers. D. Comparison of sensitivity and specificity among different biomarker monitoring criteria.
Figure 4

The clinical diagnosis pathway for PTX-3 in TAK patients.

Supplementary Files

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- SupplementaryMaterialforReview.docx