



Assessment of disease activity in Takayasu arteritis: A quantitative study with computed tomography angiography☆



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ABSTRACT

Background: Identifying disease activity in Takayasu arteritis (TAK) is challenging. This study aimed to investigate the value of quantitative characterization with computed tomography angiography in the assessment of disease activity in patients with TAK.

Methods: We retrospectively analysed the data on 162 aortic CT angiography from 140 TAK patients. Patients were categorized based on disease activity according to the National Institutes of Health criteria into two groups: active disease group ($n = 65$) and inactive disease group ($n = 97$).

Results: Patients with active TAK had a thicker wall compared with patients with inactive TAK (5.2 ± 2.4 mm vs. 2.5 ± 0.8 mm, $p < 0.001$). The relative post-contrast enhancement ratio of the thickened wall was higher in active TAK than in inactive TAK (1.5 ± 0.3 vs. 1.1 ± 0.2 , $p < 0.001$). Given a thickness cutoff of 3.3 mm, sensitivity for active-phase TAK was 83.1%, specificity 89.7%, positive predictive value 84.4%, and negative predictive value 88.8%. With a relative post-contrast enhancement ratio cutoff of 1.2, sensitivity for active-phase TAK was 89.2%, specificity 76.3%, positive predictive value 71.6%, and negative predictive value 91.3%. In receiver-operating characteristic curves comparison, maximal wall thickness and relative post-contrast enhancement ratio were superior to C-reactive protein and erythrocyte sedimentation rate for determining active phase disease ($p < 0.05$).

Conclusions: Quantitative characterization with CT angiography was a useful tool to assess disease activity in TAK patients. Maximal wall thickness and relative post-contrast enhancement ratio have a high sensitivity and specificity for detecting TAK activity.

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1. Introduction

Takayasu arteritis (TAK) is a chronic, primary granulomatous large vessel vasculitis of unknown origin that commonly affects the aorta and its immediate branches as well as pulmonary artery [1]. The disease course extends over many years with variable degrees of activity [2].

Abbreviations: CRP, C-reactive protein; CI, confidence interval; CTA, computed tomography angiography; ESR, erythrocyte sedimentation rate; MRI, Magnetic resonance imaging; NPV, negative predictive value; NIH, National Institutes of Health; PPV, positive predictive value; ROC, Receiver-operating characteristic; SE, sensitivity; SP, specificity; TAK, Takayasu arteritis.

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Even in patients receiving corticosteroid treatment, recurrences are frequent. The assessment of disease activity is crucial in the management of TAK as appropriate therapy can relieve vascular inflammation, slow down the disease progression and reduce the risk of vascular complications [3]. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are important markers generally used to assess disease activity in TAK patients. However, ESR and CRP do not correlate well with vascular inflammation [4]. There are currently no specific biomarkers for diagnosing TAK.

Conventional angiography has been traditionally used as the gold standard for the diagnosis and assessment of TAK. However, this invasive approach is limited by its defect in observation of the vessel wall [5]. Multidetector computed tomography has an excellent spatial resolution. CT angiography (CTA) depicts both the luminal and mural changes in the aorta and its major branches [6]. Wall thickening and enhancement, low-attenuation ring and calcification are distinctive wall changes in TAK patients reported in previous studies [7–10]. However, no larger sample size studies have investigated the efficiency of these

markers in differentiation between active and inactive TAK. The diagnostic utility of quantitative measurement has not been established. Thus, the purpose of this study was to investigate the value of quantitative characterization with CTA in the assessment of disease activity in TAK patients.

2. Material and methods

2.1. Patient population

The diagnostic criterion of TAK was the classification criteria of the American College of Rheumatology (1990) [11]. A total of 140 patients with TAK underwent 162 aortic CTA examinations in Fuwai hospital from January 2017 to January 2019 were enrolled in this retrospective study. They were divided into an active group ($n = 65$) and an inactive group ($n = 97$) according to the National Institutes of Health (NIH) criteria, which define clinical status on the basis of 4 elements: systemic features, elevated ESR or CRP, vascular ischemia, and new arterial lesion or worsening of pre-existing lesions on imaging. The active phase is defined as the new onset or worsening of 2 or more of these features [1]. The NIH criteria were scored within one month before or after CTA. Personal information was protected and kept anonymous. Institutional Review Board approval was obtained (CRFH20180070).

2.2. Clinical data

Clinical characteristics (sex, onset age, age at diagnosis, disease duration and body mass index), symptoms, information from a physical examination were recorded. Disease duration was defined as the onset of corresponding symptoms, such as pulselessness, claudication, hypertension, amaurosis or dizziness to the data of CTA. Laboratory tests included CRP and ESR (the interval time between laboratory testing and CT examination was <1 week). The local laboratory normal standard ranges were 1–20 mm/h for ESR and <8 mg/L for CRP.

2.3. CT techniques

All aortic CTA was performed using a dual-source CT (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany). CT parameters were as follows: tuber voltage, 100–120 kV, tuber current determined by Care Dose 4D (Siemens), range from 113 to 394 mAs, rotation time of 0.28 s, pitch of 1.2; collimation, $2 \times 128 \times 0.6$ mm. Aortic CTA was performed in craniocaudal direction from the thoracic inlet to the femoral head. All patients were asked to elevate and place arms on the table and hold their breath after deep inspiration during the examination.

Iodinated contrast medium (iopromide [Ultravist] 370 mg iodine/ml, Bayer Healthcare, Berlin, Germany) was injected via peripheral veins at a volume of 1.5 ml/kg body weight with a saline chaser of 30 ml at a rate of 4–5 ml/s. Automated bolus tracking was applied with a circular ROI positioned at the heart level of the descending aorta. Data acquisition was started 6 s after the contrast media reached a threshold of 100 HU. Venous phase was performed 90 s after the contrast medium injection.

2.4. CT data post-processing and analysis

Images were reconstructed as follows: contiguous 0.625 mm thickness and increment of 0.4 mm using a medium smooth-tissue (B26f). All images were anonymous and transferred to an external workstation (syngo.via, version VB10A, clinical application: CT vascular, Siemens Healthcare, Erlangen, Germany) for further analysis. Multiple planar reconstruction, curved planar reformation, maximum intensity projection, and volume rendering were applied for image interpretation.

CT analysis was focused on the evaluation of imaging in the following parameters. Involved segments include ascending aorta, aortic arch, descending thoracic aorta, abdominal aorta, innominate artery, proximal common carotid artery, subclavian artery, celiac trunk, superior mesenteric artery, renal artery, coronary artery and pulmonary artery, maximal wall thickness and relative post-contrast enhancement ratio. Maximal wall thickness was measured by the arterial phase cross-sectional images. The thickest segment was determined jointly by the two observers subjectively. The measurement was performed by the two observers independently. CT attenuation was measured on post-contrast cross-sectional images. The position of circular ROI was same as that of maximal wall thickness measurement on the same slide. The dimension of ROI was manually defined by the observers according to the wall thickness to include the entire thickened arterial wall. Paravertebral muscle attenuation was measured in a 0.2 cm^2 circular ROI on the same image. Relative post-contrast enhancement ratio was defined as the ratio of mural attenuation to paravertebral muscle attenuation. Luminal abnormalities include stenosis, occlusion lesions, and dilatation. Stenosis >50% was considered as significant stenosis. The lumen was deemed to be dilated if it was >4 cm in the ascending aorta and >3 cm in the descending aorta [10]. Positive remodelling and low-attenuation ring (Online supplement Fig. E1). Positive remodelling was defined as an increased lesion vessel area (resulted by the thickened wall) compared with the adjacent or contralateral normal-caliber arterial segment [12]. Low-attenuation ring was defined as a concentric, poorly enhanced, low-density ring along the inner surface of the wall [10].

Two cardiovascular radiologists (Gao Y, with ten years of experience in cardiovascular imaging, and Yin W, with eight years of experience in cardiovascular imaging) who were blinded to clinical history and status of disease activity independently analysed the data. The inter-observer variability for the two observers was tested and is expressed by using Cohen k values and Bland–Altman plots. Any disagreement between the two observers was resolved by consensus. The mean values of maximal wall thickness and CT attenuation measured by two observers were used for analysis.

2.5. Statistical analysis

Statistical analysis was performed by SPSS 20.0 software (SPSS, Chicago, IL, USA). Continuous variables were expressed as the mean \pm standard error of mean or median with 25–75% inter-quartile range (IQR), as appropriate. Categorical variables were expressed as absolute numbers and percentages. Normally distributed variables were compared with the independent samples t -test. Non-normally distributed variables were compared with the Mann–Whitney U test for two groups. Categorical variables were compared using a Chi-squared test. Inter-observer agreements of positive remodelling, low-attenuation ring and calcification were expressed in Cohen k values. Bland–Altman analysis was performed to test the difference of maximal wall thickness and CT attenuation between the two observers. Receiver-operating characteristic (ROC) analysis was performed to compare diagnostic performance and determine cut-off values of continuous variables. The best cutoff values were determined by the Youden index, the maximum sum of sensitivity and specificity at ROC curve analysis. The areas under the ROC curves along with the corresponding 95% confidence intervals (CI) were calculated in MedCalc for Windows (version 15.2.2, MedCalc Software, Ostend, Belgium) and compared using the method described by DeLong et al. [13]. A p -value < 0.05 was considered to indicate a significant difference.

3. Results

3.1. Patient characteristics

The main clinical characteristics of the overall cohort and active vs. inactive cases are summarized in Table 1. Patients with active TAK were younger than those patients with stable disease and had a shorter disease duration (median 2 years) compared with the inactive group (median 12 years). Patients in the active phase had a smaller BMI than patients with inactive TAK. ESR and CRP were significantly higher in active than in inactive cases. There was no significant difference in onset age and gender between the two groups.

With regards to the clinical features, hypertension was the most common presenting feature (51.9%) and followed by systolic pressure difference (45.7%), dyspnea on exertion (43.2%) and vascular murmur (43.8%). Diminished pulse or pulselessness (24.7%), amaurosis or dizziness (22.8%), claudication (25.6%), upper limb numbness (7.4%) and hemoptysis (6.8%) were less common features of presentation in this cohort. Hypertension was more common seen in inactive TAK (30.7% vs. 66%, $p < 0.001$). Unexplained fever and pain (including carotidynia, myalgia, periumbilical pain and back pain) were only presented in patients with active TAK.

3.2. Arterial luminal changes

The involvement of aorta and its main branches and frequency of lumen stenosis, occlusion and dilatation are presented in Table E1. Left subclavian artery was the most frequent involved segment, presented in 61.7% of patients, and followed by descending thoracic aorta (60.5%), aortic arch (59.3%), left common carotid artery (58%), abdominal aorta (58%), innominate artery (52.5%), right common carotid artery (55.6%) and right subclavian artery (36.4%). Involvement of renal artery, celiac trunk, and superior mesenteric artery was less commonly, presenting in 30.9% (right renal artery), 30.2% (left renal artery), 25.9% and 19.1% of patients, respectively. Pulmonary artery and coronary artery involvement were identified in 6.2% and 20.4% of the patients respectively. Results revealed that luminal narrowing and occlusion were the two most frequent luminal changes in TAK patients. Dilatation or aneurysm was less common seen compared with stenosis and occlusion lesions.

3.3. Arterial wall abnormalities

Wall thickening was presented in all TAK patients. However, the intensity of vessel wall thickening in patients with active and inactive disease was different. Maximal wall thickness in active TAK was thicker than that in inactive TAK (5.2 ± 2.4 mm vs. 2.5 ± 0.8 mm, $p < 0.001$). The relative post-contrast enhancement ratio was also higher in active TAK compared with patients with inactive disease (1.5 ± 0.3 vs. 1.1 ± 0.2 , $p < 0.001$) (Fig. 1). Of the 22 patients who had a follow-up CT evaluation, wall thickening relieved in 20 patients (Fig. E2). Two patients who suspected to have a relapsed TAK were found to have new lesions. Aortic positive remodelling, low-attenuation ring and mural calcification were also recorded and were showed in Table 2. Of 162 TAK, aortic positive remodelling was identified in 44 patients, 40 in an active stage and 4 in the inactive stage. Low-attenuation ring was found in 36 patients with active TAK and 7 with inactive TAK. Aortic positive remodelling and low-attenuation ring were more commonly found in patients with active TAK. Mural calcification was noted in 75 patients and more commonly seen in patients with inactive TAK (13.8% vs. 68%, $p < 0.001$).

The inter-observer agreement was excellent, 0.87 for aortic positive remodelling, 0.91 for low-attenuation ring and 0.96 for mural calcification. The Bland–Altman analysis showed good agreement between two observers as to maximal wall thickness and CT attenuation. The mean difference was 0.01 (95% CI: 0.63 to -0.62) for mural thickness and 0.4 (95% CI: 13.3 to -12.4) for mural CT attenuation.

3.4. Comparisons among utilities of maximal wall thickness, relative post-contrast enhancement ratio, CRP, and ESR for determining active phase TAK

With ROC curve, we determined the cutoff value for these markers (maximal wall thickness ≥ 3.3 mm, relative post-contrast enhancement ratio ≥ 1.2 , CRP ≥ 9.23 and ESR ≥ 21). With this cutoff for maximal wall thickness, sensitivity (SE) for active-phase TAK was 83.1%, specificity (SP) was 89.7%, positive predictive value (PPV) was 84.4%, and negative predictive value (NPV) was 88.8%. As for relative post-contrast enhancement ratio, SE for active-phase TAK was 89.2%, SP was 76.3%, PPV was 71.6%, and NPV was 91.3%. As for CRP, SE for active-phase TAK was 49.2%, SP was 88.7%, PPV was 74.5%, and NPV was 72.3%. As for ESR,

SE for active-phase TAK was 53.9%, SP was 87.6%, PPV was 74.4%, and NPV was 73.9%.

Comparisons of ROC curves showed area under the curve to be 0.906 (95% CI: 0.850 to 0.946) for maximal wall thickness, 0.876 (95% CI: 0.815 to 0.923) for relative post-contrast enhancement ratio, 0.718 (95% CI: 0.642 to 0.786) for CRP, and 0.763 (95% CI: 0.690 to 0.826) for ESR (Fig. 2). Maximal wall thickness and relative post-contrast enhancement ratio were superior to CRP and ESR ($p < 0.05$) in terms of ROC curve analysis for determining active phase disease with statistical significance.

4. Discussion

The present study investigated the value of quantitative characterization with CTA in the assessment of disease activity in 162 cases with TAK. Our study suggested that arterial wall was thicker and had a higher enhancement in patients with active TAK than in patients with inactive TAK. Quantitative observation on the mural thickness and enhancement provided valid means of comparing patients with active and inactive TAK, providing high sensitivity and specificity for detecting TAK activity. Low-attenuation ring and aortic positive remodelling were sensitive indicators of active disease.

TAK is a chronic, nonspecific inflammatory disease that the course extends over many years with variable degrees of activity. Assessment of disease activity in TAK remains a clinical challenge. Recently, multiple imaging modalities are used in the activity assessment of TAK [14]. Every technique has its strengths and weaknesses. Ultrasound demonstrates important diagnostic value in the assessment of carotid [15,16]. Lottspeich et al. reported that with a maximum intima-media thickness cutoff of >2.7 mm, the sensitivity and specificity for active TAK was 69.2% and 88.9%, respectively [15]. Huang et al. found that carotid vascularization by carotid contrast-enhanced ultrasound, as a sole inflammatory marker, had a high predictive value for disease activity in Type I TA [16]. However, the inadequacies in ultrasonography make it challenging to detect lesions in thoracic aorta and pulmonary artery [17]. Magnetic resonance imaging (MRI) with superior soft tissue characterization and multiple dedicated sequence protocols has been widely used in the diagnosis and activity assessment of TAK [18–20]. It was able to detect mural oedema and fibrosis, providing valuable information regarding disease activity. It could also be used in the evaluation of

Table 1
Baseline characteristics of study participants.

Variables	Total (n = 162)	Active group (n = 65)	Inactive group (n = 97)	p-Value
<i>Demographics</i>				
Female, n (%)	132 (81.5)	54 (83.1)	78 (80.4)	0.72
Age (y), median (IQR)	37 (27–47)	29 (22–42)	41 (32–52)	0.004
Onset age (y), median (IQR)	27 (21–33)	26 (18–35)	27 (23–33)	0.929
Disease duration (y), median (IQR)	5.5 (1–17)	2 (0.5–5)	12 (4–20)	<0.001
BMI (kg/m ²), mean	21.9 (20.0–24.2)	21.1 (19.7–23.2)	22.7 (20.1–25.0)	0.003
ESR (mm/h), median (IQR)	14 (6–27.5)	26 (12–48.5)	8 (5–17)	<0.001
CRP (mg/L), median (IQR)	6.0 (3.0–10.2)	8.4 (5.1–25.8)	4.1 (2.8–7.0)	<0.001
<i>Symptom at presentation, n (%)</i>				
Fever (temperature > 38 °C), n (%)	11 (6.8)	11 (16.9)	0	<0.001
Pain	13 (8.0)	13 (20.0)	0	<0.001
Amaurosis or dizziness	37 (22.8)	18 (27.7)	19 (19.6)	0.116
Upper limb numbness	12 (7.4)	7 (10.8)	5 (5.2)	0.181
Limb claudication (upper)	26 (16.0)	11 (16.9)	15 (15.5)	0.804
Limb claudication (lower)	17 (10.5)	10 (15.4)	7 (7.2)	0.096
Dyspnea on exertion	70 (43.2)	27 (41.5)	43 (44.3)	0.725
Hemoptysis	11 (6.8)	5 (7.7)	6 (6.2)	0.709
<i>Examination abnormalities, n (%)</i>				
Hypertension	84 (51.9)	20 (30.7)	64 (66.0)	<0.001
Diminished pulse/pulselessness	43 (26.5)	16 (24.6)	27 (27.8)	0.649
UBPD ≥ 10 mmHg	74 (45.7)	28 (43.1)	46 (47.4)	0.586
Vascular murmur	71 (43.8)	29 (44.6)	42 (43.3)	0.869

BMI: body mass index, IQR: interquartile range; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; UBPD: upper extremity blood pressure discrepancy.

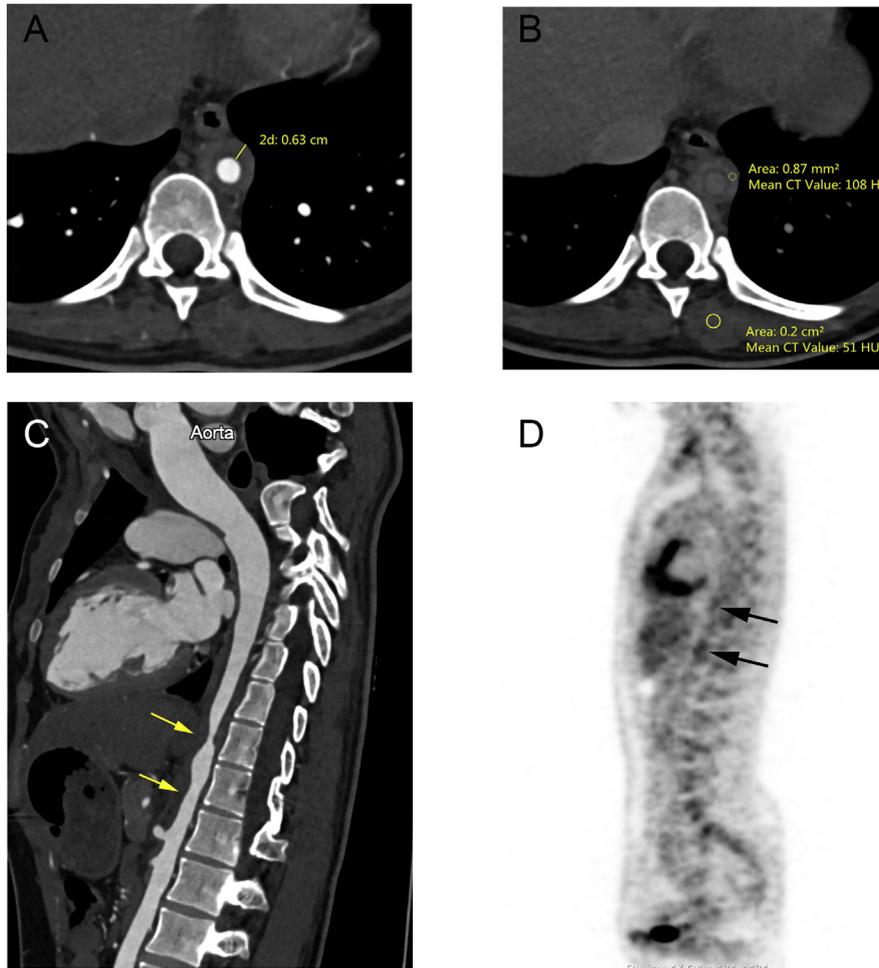


Fig. 1. Representative case #1 (an active Takayasu arteritis). An 18-year-old female complained of a lower limb claudication and hypertension for 3 months. The CRP and ESR were normal, 2.29 mg/dl and 12 mm/h, respectively. CTA axial images showed maximal wall thickness was 6.3 mm, relative post-contrast enhancement ratio was 2.1 and an active Takayasu arteritis was diagnosed by CTA (A, B). Curved planar reformation showed stenosis in the thoracic artery (C). 18F-fluorodeoxyglucose-PET showed abnormal uptake in the diseased thoracic artery (D).

myocardial function and aortic regurgitation. Besides, release from ionizing radiation renders MRI an indispensable component of TAK follow-up and identification of relapse. The drawbacks of MRI were time-consuming, artefacts, limited in calcification depiction and false-positive diagnoses of occlusion lesions [18]. PET/CT as a functional imaging technique was useful in the assessment of local inflammatory and vascular remodelling events during follow-up [21]. It could provide information about vascular inflammation that is complementary to, and unique from, clinical assessment [22]. The drawback of PET/CT is that it shows variant specificity in the evaluation of disease activity [23]. Besides, it is costly and has a relatively low spatial resolution [5].

CTA was particularly attractive for imaging aortitis and branch vessel arteritis due to unparalleled spatial resolution and scan time generally

<1 min, requiring only a single breath hold. It has been widely used in the depiction of mural and luminal changes in TAK patients [7–10]. Zhu et al. summarized that circumferential wall thickening and enhancement, concentric, low-attenuation ring and a circumferential type of calcification were distinctive mural changes of TAK [24,25]. However, the efficiency of CTA in the assessment of disease activity remains to further study and practice [6]. Niranjana et al. reported that the wall thickness of the aorta was increased in all these nine patients including 6 active and 3 inactive TAK [8]. However, the intensity of mural thickening was not clarified in their study. Kim et al. evaluated the mural changes by CTA on follow-up examinations of 18 patients with active TAK [25]. They showed a decrement in mean mural thickness with treatment. This was consistent with our finding that wall thickening relieved with a treatment in 20 of the 22 patients who had a follow-up CT evaluation. Although these preliminary studies illustrate the potential that CTA provides for the assessment of disease activity and progression of TAK, the evidence is restricted to small sample analysis. The diagnostic utility of quantitative measurement has not been established. In this study, we described the quantitative efficiency of maximal wall thickness and enhancement in the discrimination of active and inactive disease in 162 TAK. Herein, we propose a cutoff of 3.3 mm for maximal wall thickness and 1.2 for relative post-contrast enhancement ratio based on our clinical study, providing a quantitative reference, thereby aiding the decision to the management of TAK.

Low-attenuation ring was another sign of TAK reported by previous studies [25,26]. It was defined as an inner, concentric, poorly enhanced,

Table 2
Comparison of CTA characteristics in patients with active and inactive Takayasu arteries.

Characteristics on CT angiography	Active group (n = 65)	Inactive group (n = 97)	p-Value
Maximal wall thickness (mm), mean	5.2 ± 2.4	2.5 ± 0.8	<0.001
Relative post-contrast enhancement ratio, mean	1.5 ± 0.3	1.1 ± 0.2	<0.001
Positive remodelling, n (%)	40 (61.5)	4 (4.1)	<0.001
Low-attenuation ring, n (%)	36 (55.4)	7 (7.2)	<0.001
Calcification, n (%)	9 (13.8)	66 (68.0)	<0.001

Relative post-contrast enhancement ratio = CT attenuation of thickened wall/CT attenuation of paravertebral muscle.

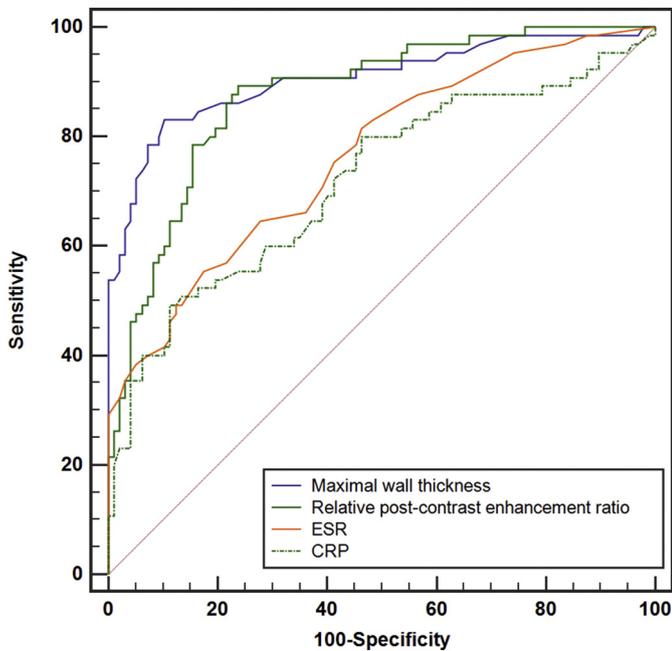


Fig. 2. ROC curve showed the performance of maximal wall thickness, relative post-contrast enhancement ratio, CRP and ESR. Area under the curve was 0.906 (95% CI: 0.850 to 0.946) for maximal wall thickness, 0.876 (95% CI: 0.815 to 0.923) for relative post-contrast enhancement ratio, 0.718 (95% CI: 0.642 to 0.786) for CRP, and 0.763 (95% CI: 0.690 to 0.826) for ESR. Maximal wall thickness and enhancement were superior to CRP and ESR ($p < 0.05$).

low density ring seen on the axial images. Histologically, it was due to thickened intima, while the enhancing outer ring is believed to represent the florid active inflammation in the media and adventitia of the vessel wall [8]. In our study, low-attenuation ring was detected in 43 patients and 36 of them were in an active stage. Therefore, low-attenuation ring may be considered as an indicator of active inflammation. Positive remodelling was referred to as an increased lesion vessel area. However, it was different from the localized extension in dilatation or an aneurysm. The increased diseased vessel area in positive remodelling was accompanied by apparently thickened and enhanced wall. In this study, positive remodelling was observed in 60.5% of the active TAK and 4.1% of inactive TAK. So positive remodelling may be considered as a manifestation of active TAK. Therefore, low attenuation ring and positive remodelling could be used as indicative markers of active disease in TAK patients.

Luminal narrowing and occlusion were the two most frequent luminal changes in TAK patients in this study. This was consistent with previous findings reported by Enrico et al. [27]. They found that TAK had more stenosis and occlusion lesions and less dilation lesions than large-vessel giant cell arteritis. Besides, they provided a standardized, qualitative and quantitative definition of arterial involvement in large-vessel vasculitis by using the three new imaging-based scores. The novel angiographic scores mirrored arterial disease evolution, reflecting both progressive injury and lesion improvement in TAK follow-up. This is valuable in the management and outcome measurement of TAK. Calcification is another manifestation of TAK. The luminal changes were usually accompanied by severe wall calcification especially for patients with long TAK history. The frequency of artery calcification was significantly increased among patients with TAK, presented in 45% of patients, reported by Emire et al. [9]. Nevertheless, the difference in calcified lesions between active and inactive TAK patients was not referred to in their study. In our research, calcification was observed in 46.3% of the TAK patients, present in 13.8% of active and 68% of inactive TAK. Calcification was more commonly seen in inactive TAK. The pathogenesis and influence factors of the calcification lesions need further researches in the future [28]. Besides, the condition of mural

calcification was one of the main factors to be considered in the management of symptomatic artery stenosis caused by TAK. CTA is valuable in the depiction of wall calcification and aortic luminal changes, providing accurate anatomy information in pretreatment assessment.

ESR and CRP were the traditional laboratory markers of active disease in vasculitis. However, the evidence based on histopathology of operative patients has shown that a normal range ESR does not indicate the cessation or regression of the inflammation [29]. Kerr et al. found that the traditional laboratory markers were inaccurate in about 50% of cases [1]. In a substantial number of patients who have appear to have active TAK, serum levels of acute phase reactants are not increased; whereas in some others who appear to have no signs and symptoms of active disease, there is evidence of laboratory inflammation. In our study, the efficiency of ESR and CRP were inferior in the discrimination of active and inactive disease, although the level of ESR and CRP were higher in active TAK compared with these inactive cases. This was corresponded with the previous studies.

There are limitations to our study. Firstly, it had a retrospective design, which has inherent limitations. Only the proximal segment of common carotid artery was analysed in this study. The images of middle and distal segments of common carotid artery were not obtained because the scan range was from the thoracic inlet to the femoral head. Secondly, NIH criteria were adopted to diagnose disease activity in this study, not on histopathological findings. This has always been a limitation in all TAK studies because the histopathological examination was not usually possible unless the surgery was performed. Finally, ionizing radiation and iodinated contrast media are the drawbacks of CTA. Fortunately, the recent rapid developments in multi-detector CT is moving toward minimization of radiation exposure and iodinated contrast media.

In conclusion, our findings suggest that quantitative characterization with CTA was a useful tool to assess disease activity in TAK patients. Maximal wall thickness and enhancement have a high sensitivity and specificity for detecting TAK activity.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2019.04.086>.

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Conflict of interest

All authors declared that they have no conflicts of interest to this work.

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References

- [1] G.S. Kerr, C.W. Hallahan, J. Giordano, et al., Takayasu arteritis, *Ann. Intern. Med.* 120 (1994) 919–929.
- [2] E.S.H. Kim, J. Beckman, Takayasu arteritis: challenges in diagnosis and management, *Heart.* 104 (2018) 558–565.
- [3] H. Ohgashi, G. Haraguchi, M. Konishi, et al., Improved prognosis of Takayasu arteritis over the past decade—comprehensive analysis of 106 patients, *Circ J* 76 (2012) 1004–1011.
- [4] S. Seth, N.K. Goyal, P. Jagia, et al., Carotid intima-medial thickness as a marker of disease activity in Takayasu's arteritis, *Int. J. Cardiol.* 108 (2006) 385–390.

- [5] S. Mavrogeni, T. Dimitroulas, S.N. Chatziioannou, G. Kitis, The role of multimodality imaging in the evaluation of Takayasu arteritis, *Semin. Arthritis Rheum.* 42 (2013) 401–412.
- [6] C. DeJaco, S. Ramiro, C. Duftner, et al., EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice, *Ann. Rheum. Dis.* 77 (2018) 636–643.
- [7] I. Yamada, T. Nakagawa, Y. Himeno, F. Numano, H. Shibuya, Takayasu arteritis: evaluation of the thoracic aorta with CT angiography, *Radiology.* 209 (1998) 103–109.
- [8] N. Khandelwal, N. Kalra, M.K. Garg, et al., Multidetector CT angiography in Takayasu arteritis, *Eur. J. Radiol.* 77 (2011) 369–374.
- [9] E. Seyahi, A. Ucgul, D. Cebi Olgun, et al., Aortic and coronary calcifications in Takayasu arteritis, *Semin. Arthritis Rheum.* 43 (2013) 96–104.
- [10] S. Sharma, S. Sharma, K. Taneja, A.K. Gupta, M. Rajani, Morphologic mural changes in the aorta revealed by CT in patients with nonspecific aortoarteritis (Takayasu's arteritis), *AJR Am. J. Roentgenol.* 167 (1996) 1321–1325.
- [11] W.P. Arend, B.A. Michel, D.A. Bloch, et al., The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis, *Arthritis Rheum.* 33 (1990) 1129–1134.
- [12] P. Maurovich-Horvat, M. Ferencik, S. Voros, B. Merkely, U. Hoffmann, Comprehensive plaque assessment by coronary CT angiography, *Nat. Rev. Cardiol.* 11 (2014) 390–402.
- [13] A. Hata, M. Noda, R. Moriwaki, F. Numano, Angiographic findings of Takayasu arteritis: new classification, *Int. J. Cardiol.* 54 (1996) S155–S163 Suppl.
- [14] L. Barra, T. Kanji, J. Malette, C. Pagnoux, *CanVasc. Imaging modalities for the diagnosis and disease activity assessment of Takayasu's arteritis: a systematic review and meta-analysis, Autoimmun. Rev.* 17 (2018) 175–187.
- [15] C. Lottspeich, C. Dechant, A. Kohler, et al., Assessment of disease activity in Takayasu arteritis: potential role of contrast-enhanced ultrasound, *Ultraschall Med.* (2019) <https://doi.org/10.1055/a-0817-5423>.
- [16] Y. Huang, X. Ma, M. Li, H. Dong, Y. Wan, J. Zhu, Carotid contrast-enhanced ultrasonographic assessment of disease activity in Takayasu arteritis, *Eur. Heart J. Cardiovasc. Imaging* (2018) 1–7.
- [17] D. Wen, X. Du, C.S. Ma, Takayasu arteritis: diagnosis, treatment and prognosis, *Int. Rev. Immunol.* 31 (2012) 462–473.
- [18] S.K. Garg, S. Mohan, S. Kumar, Diagnostic value of 3D contrast-enhanced magnetic resonance angiography in Takayasu's arteritis—a comparative study with digital subtraction angiography, *Eur. Radiol.* 21 (2011) 1658–1666.
- [19] Y.H. Choe, B.K. Han, E.M. Koh, D.K. Kim, Y.S. Do, W.R. Lee, Takayasu's arteritis: assessment of disease activity with contrast-enhanced MR imaging, *AJR Am. J. Roentgenol.* 175 (2000) 505–511.
- [20] L. Jiang, D. Li, F. Yan, X. Dai, Y. Li, L. Ma, Evaluation of Takayasu arteritis activity by delayed contrast-enhanced magnetic resonance imaging, *Int. J. Cardiol.* 155 (2012) 262–267.
- [21] E. Incerti, E. Tombetti, F. Fallana, et al., (18)F-FDG PET reveals unique features of large vessel inflammation in patients with Takayasu's arteritis, *Eur. J. Nucl. Med. Mol. Imaging* 44 (2017) 1109–1118.
- [22] P.C. Grayson, S. Alehashemi, A.A. Bagheri, et al., (18) F-Fluorodeoxyglucose-positron emission tomography as an imaging biomarker in a prospective, longitudinal cohort of patients with large vessel vasculitis, *Arthritis & rheumatology.* 70 (2018) 439–449.
- [23] G.R. Hartlage, J. Palios, B.J. Barron, et al., Multimodality imaging of aortitis, *J. Am. Coll. Cardiol. Img.* 7 (2014) 605–619.
- [24] F.P. Zhu, S. Luo, Z.J. Wang, Z.Y. Jin, L.J. Zhang, G.M. Lu, Takayasu arteritis: imaging spectrum at multidetector CT angiography, *Br. J. Radiol.* 85 (2012) e1282–e1292.
- [25] S.Y. Kim, J.H. Park, J.W. Chung, et al., Follow-up CT evaluation of the mural changes in active Takayasu arteritis, *Korean J. Radiol.* 8 (2007) 286–294.
- [26] C.S. Restrepo, D. Ocazonez, R. Suri, D. Vargas, Aortitis: imaging spectrum of the infectious and inflammatory conditions of the aorta, *Radiographics: a review publication of the Radiological Society of North America, Inc.* 31 (2011) 435–451.
- [27] E. Tombetti, C. Godi, A. Ambrosi, et al., Novel angiographic scores for evaluation of large vessel Vasculitis, *Sci. Rep.* 8 (2018), 15979.
- [28] O.D. Argyropoulou, A.D. Protogerou, P.P. Sfikakis, Accelerated atheromatosis and arteriosclerosis in primary systemic vasculitides: current evidence and future perspectives, *Curr. Opin. Rheumatol.* 30 (2018) 36–43.
- [29] G.S. Hoffman, Takayasu arteritis: lessons from the American National Institutes of Health experience, *Int. J. Cardiol.* 54 (1996) S99–102 Suppl.