

GUIDELINE

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2025 Chinese guideline for the imaging diagnosis and evaluation of Takayasu arteritis

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Abstract

Background Takayasu arteritis (TAK) presents as systemic vasculitis. Imaging is crucial for the diagnosis and evaluation of TAK, but the rational selection of imaging methods and interpretation of imaging results are major challenges in clinical practice, which can affect treatment decisions. This guideline aims to establish standardized protocols for selecting imaging modalities (as well as interpreting their findings) in TAK.

Methods Relevant clinical questions were formulated by an expert panel. Systematic reviews of evidence published from database establishment to 31 October 2023 were done. The grading system set by the Oxford University Evidence-Based Medicine Center was employed to assess the quality of evidence. Recommendations were developed through consensus using the Delphi method.

Results Seventeen recommendation statements were developed based on evidence summaries and consensus. The first four recommendations focused on overarching principles. Recommendations 5 to 14 covered the advantages and disadvantages of different imaging modalities, as well as the selection of imaging modalities in the diagnosis and evaluation of TAK, including ultrasound (three statements), magnetic resonance angiography (two), computed tomography angiography (two), positron emission tomography/computed tomography (two), and digital subtraction angiography (one). Recommendations 15 to 17 focused on the selection of imaging methods for special populations and organ perfusion.

Conclusion These recommendations could help to standardize the use of imaging modalities by clinicians in the diagnosis and evaluation of TAK.

Clinical trial number Not applicable.

Keywords Takayasu arteritis, Imaging method, Guideline, Diagnosis, Assessment

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Introduction

Takayasu arteritis (TAK) is a primary large-vessel vasculitis. It mainly affects the aorta and its branches. TAK is more common in young Asian women under the age of 30. There is a lack of clinical serological biomarkers to assess disease activity. Therapeutic agents such as glucocorticoids and inhibitors of the interleukin-6 receptor affect the clinical evaluation of inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) for TAK activity, and obtaining histopathological specimens is difficult [1]. Therefore, imaging is crucial to diagnose and evaluate TAK.

Previously, digital subtraction angiography (DSA) was the “gold standard” for an imaging diagnosis of TAK, but it is invasive [2]. The rapid development of imaging technology has enabled sensitive detection of vascular lesions and evaluation of wall inflammation. Therefore, non-invasive imaging methods have replaced DSA gradually, and are helpful for the diagnosis and evaluation of patients with TAK during follow-up.

In the updated European League Against Rheumatism (EULAR) recommendations for the use of imaging examinations in clinical practice for large-vessel vasculitis in 2023 [3], only five articles related to TAK were included, and most of the recommendations were applicable to giant-cell arteritis. Therefore, establishing imaging guidelines for TAK is important to facilitate the rational and standardized selection of imaging modalities as well as interpreting their findings.

The purpose of this guideline is to provide evidence-based information on the use of imaging modalities to diagnose, evaluate and monitor patients with TAK. This strategy could help to guide the diagnosis and treatment of TAK in clinical practice.

Guideline development methods

Guideline working group and management of conflict of interest

This guideline was supported by the Chinese Rheumatology Association and Rheumatology Committee of Primary Health Care Foundation of China. It was launched on 13 September 2023. The Guideline Working Group members consisted of rheumatologists, radiologists, specialists in nuclear medicine, ultrasound experts, and methodologists. All members disclosed their potential conflicts of interest before starting this process. This guideline has been registered on the International Practice Guide Registration and Transparency Platform (www.guidelines-registry.org) with registration number PREPARA-2023CN702.

Target users and population

This guideline is intended for rheumatologists, cardiologists, vascular surgeons, neurologists, radiologists,

ultrasound specialists, nuclear-medicine specialists, and other specialists in medicine at all levels of medical institutions. It is also intended for professionals involved in the diagnosis, treatment, and management of rheumatic diseases. The target population for the guideline is patients aged ≥ 18 years who are suspected of having or who have been diagnosed with TAK.

Determination of clinical issues

The Secretary Group formed 50 clinical issues preliminarily. This task was achieved by reviewing relevant guidelines, management recommendations, consensus, as well as diagnostic and treatment standards for the imaging of rheumatic diseases in China and overseas, combined with clinical practice and extensive expert consultation within China. The Delphi method was used to solicit expert opinions in the form of questionnaire scoring. Finally, 16 clinical questions to be solved by this guideline have been selected according to their importance ranking and expert opinions.

Evidence retrieval

The Evidence Evaluation Team deconstructed data based on the principles of population, intervention, comparison, outcome (PICO). They searched: (1) Chinese databases, including CNKI, Wanfang Database, and China Biomedical Literature Database; (2) English databases, including Embase, Web of Science, PubMed, and The Cochrane Library; (3) Guideline-related websites, including those of authoritative academic organizations such as the American College of Rheumatology, European League Against Rheumatism (EULAR), Asia Pacific League Against Rheumatism, and Chinese Medical Association, that have published guidelines and consensus on rheumatology and immunology. The search terms were “Takayasu arteritis”, “diagnosis”, “evaluation”, “imaging”, as well as the various imaging techniques including “ultrasound”, “computed tomography angiography”, “magnetic resonance angiography”, “positron emission tomography”, “digital subtraction angiography”. The search period was from database establishment to 31 October 2023, and included clinical studies with a sample size of ≥ 20 suspected and/or confirmed cases of TAK.

Evaluation and grading of evidence

Tools for assessing the quality of evidence included: AGREE II for clinical guidelines and expert consensus; AMSTAR2 for systematic review and meta-analysis; Cochrane Collaboration Tool for Assessing Risk of Bias for methodological quality evaluation of randomized controlled trials [4]; Newcastle Ottawa Scale for cohort and case-control studies [5]; Institute of Health Economics for case series reports [6]. The grading system set by the Oxford University Centre for Evidence Based

Table 1 Evidence grading by Oxford centre for Evidence-Based medicine (2011 edition)

Level of evidence	Description
Level 1	Randomized trials or systematic reviews of randomized trials
Level 2	Randomized trial or (exceptionally) observational study with a dramatic effect
Level 3	Non-randomized controlled cohort/follow-up study
Level 4	Case series, case-control study, or historically controlled studies
Level 5	Mechanism research

Note: Grading can be downgraded based on the quality of evidence, inaccuracy, indirectness (the PICO of the cited research does not match the PICO involved in the recommended guidelines), and small effect size. Upgrades can also be made based on the dramatic effect

RCT: Randomized controlled trial; PICO: population, intervention, comparison, outcome (population, intervention, control, outcome)

Table 2 Recommended standards of the Oxford centre for Evidence-Based medicine (2011 edition)

Levels of recommendation	Description
A	Consistent research with evidence level 1
B	Consistent studies with evidence levels of 2 and 3; indirect research with evidence level 1
C	Consistent research with evidence level 4; indirect studies with evidence levels of 2 and 3
D	Research with evidence level 4 or inconsistent or uncertain research at any level

Note: The recommended strength is based on the grading system set in 2011, but in the process of forming some recommended strengths, specific clinical practices were considered to determine the final grade

Medicine in 2011 was used to classify the body of evidence and recommendations [7] (Tables 1 and 2).

Formation of guideline recommendations

The Evidence Evaluation Team organized the evidence of various clinical issues, presented the types and quality of evidence, and formed preliminary recommendations

based on comprehensive consideration of factors. The latter included the balance between advantages and disadvantages, the cost of imaging modalities, and patient preferences. An online discussion meeting was held on 17 July 2024 to collect expert opinions on the recommendation strength of each item in the form of a questionnaire. After external expert review, the consensus was accepted if >70% of the members were in favor of the recommendation.

Implementation and update of our guideline

After the release of this guideline, the Working Group will organize promotion and dissemination through academic journals, websites, and academic conferences to ensure that physicians and other stakeholders understand it fully and use it correctly. This guideline will be updated in the future based on demand and evidence updates.

Definitions

To reduce confusion in the literature, we proposed consensus definitions for imaging vascular lesions in TAK (Table 3).

Results

Overall principle

Early diagnosis and treatment are necessary for TAK to prevent irreversible damage to blood vessels. Therefore, appropriate imaging examinations are important (Fig. 1). A summary of the recommendations, level of evidence and degree of agreement for each elaborated clinical question is presented in Table 4.

Clinical question 1: Imaging selection for patients suspected of having TAK

Recommendation 1: DSA was the radiological gold standard for diagnosing TAK, but it has been replaced gradually by non-invasive and equally efficient imaging

Table 3 Definition of vascular lesions according to imaging

Vascular lesion	Definition
Vasculitis	Vasculitis is manifested histologically as infiltration by inflammatory cells in the vascular wall and surrounding areas, accompanied by fibrinoid necrosis. Upon imaging, it manifests as thickening and unevenness of the vessel wall, narrowing or dilation of the lumen, and leakage around the tube. Specifically, intima thickening with reduced echo in ultrasound, neovascularization in CEUS, edema, concentric thickening, delayed gadolinium enhancement in MRA, concentric low-density rings in CTA and increased ¹⁸ F-FDG uptake of vascular wall in PET/CT.
Degree of stenosis and dilation	Using the NASCET method [8], the degree of stenosis is $(1 - DS/DN) \times 100$, where DS is the diameter of the narrowest lumen of the blood vessel, and DN is the lumen diameter of the normal vascular site before and after vascular stenosis. According to the degree of vascular stenosis, it can be divided into grade 1 (mild stenosis, < 50%); grade 2 (moderate stenosis, ≥ 50–80%); grade 3 (severe stenosis, ≥ 80% to < 100%); grade 4 (blocked). Vascular dilation = $(DD - DN/DN) \times 100$, where DD is the diameter of the widest lumen of the blood vessel. If the dilation of blood vessels is > 50% of the normal diameter, it is called an "aneurysm".
Irreversible damage	After standardized treatment, vascular structural abnormalities identified by imaging persist, including stenosis, occlusion, dilation, aneurysm, arteriosclerosis, thrombosis, or fibrosis.

Abbreviations: CEUS, contrast-enhanced ultrasound; MRA, magnetic resonance angiography; CTA, computed tomography angiography; FDG, fluorodeoxyglucose; PET/CT, positron emission tomography/computed tomography; NASCET, North American Symptomatic Carotid Endarterectomy Trial; DS, the diameter of the narrowest lumen of the blood vessel; DN, the lumen diameter of the normal vascular site before and after vascular stenosis; DD, the diameter of the widest lumen of the blood vessel.

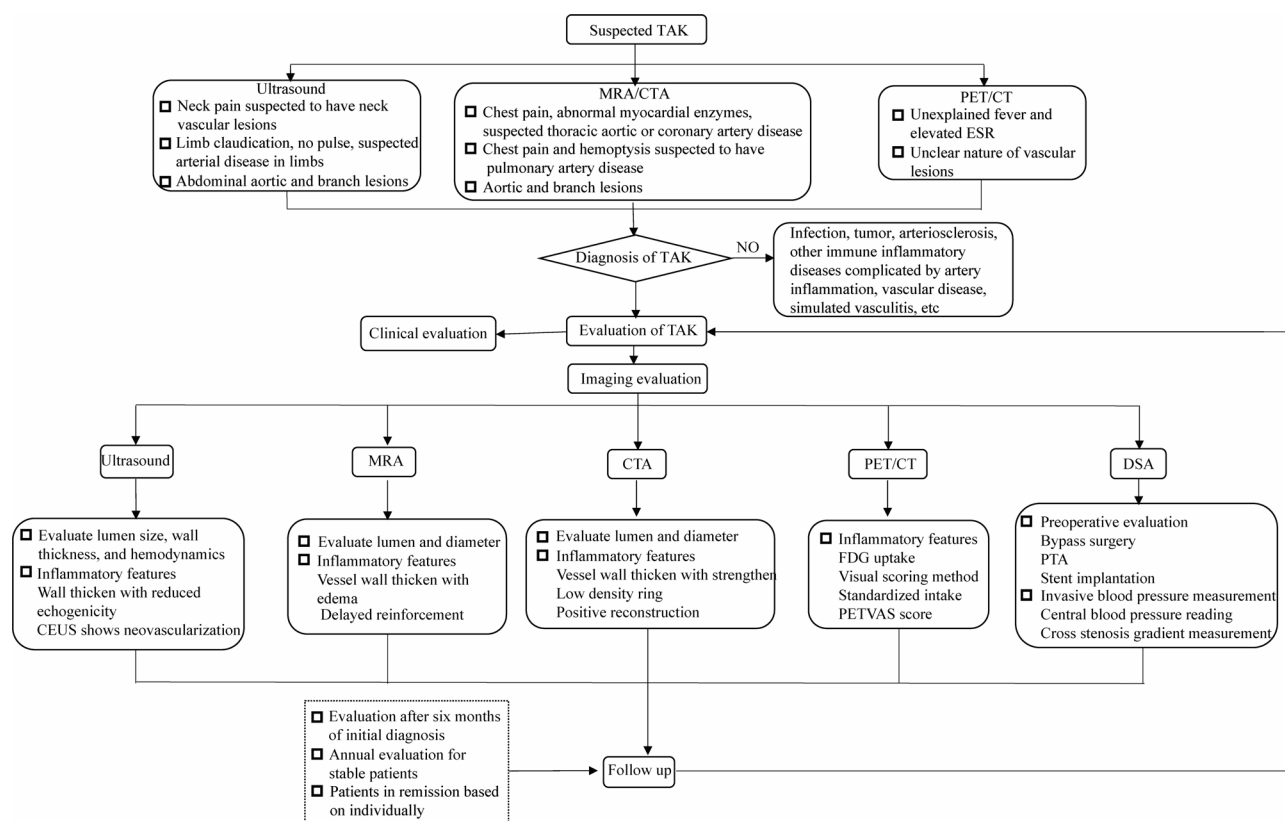


Fig. 1 Flowchart for the imaging diagnosis and evaluation of Takayasu arteritis

methods. Ultrasound is valuable for carotid artery (CA) and arteries in the upper and/or lower limbs and is therefore the first choice for screening patients with neck pain and limb claudication. For the aorta and its branches, computed tomography angiography (CTA) or magnetic resonance angiography (MRA) is recommended. If the patient presents with systemic symptoms such as fever and fatigue, positron emission tomography/computed tomography (PET/CT) can be used to detect vascular-wall inflammation and affected areas, and clarify if tumors or infections are present (2 B).

The characteristics of vascular lesions in TAK include involvement of the aorta and its branches, multiple vascular lesions, thickening of the circumferential wall of the annulus, inflammation of the vessel wall, and narrowing or dilation of the lumen. DSA is not sensitive to early wall lesions of the aorta or its branches (which may delay the diagnosis of TAK) and is invasive. Ultrasound has been used widely in the clinical diagnosis of TAK. Ultrasound can be selected if the patient has neck pain, cold hands, numbness, lack of pulse, limb claudication, or other suspected arterial lesions in the neck and limbs. The descending thoracic aorta is often involved in patients with TAK, but conventional ultrasound cannot be used to detect it. For patients suspected of having thoracic and abdominal aortic involvement, a comprehensive analysis

of clinical manifestations, physical signs, and ankle-brachial index of blood pressure in limbs is needed [9], and CTA or MRA can be selected. For patients with chest pain and abnormal levels of myocardial enzymes, coronary CTA is recommended. For patients with chest pain, hemoptysis, and suspected involvement of pulmonary arteries on CT of the chest, then CTA of the pulmonary arteries is recommended. During the acute phase of TAK, CTA and MRA can be employed to detect wall thickening of the aorta and its branches before the appearance of abnormal luminal structures. For patients with non-specific manifestations, such as unexplained fever, increased ESR, and lack of vascular inflammation, PET/CT can be used to detect inflammation and lesions in the aortic wall, as well as infections or tumors. Adili et al. found that, during delayed PET/CT, the blood-pool activity of the inflamed lesions in the vascular wall was lower, and the uptake of ^{18}F -fluorodeoxyglucose (FDG) was higher, thereby improving contrast of the lesions-to-blood pool and helping to detect wall inflammation [10].

Clinical question 2: Evaluation of systemic vascular imaging is required for patients with newly diagnosed TAK

Recommendation 2: TAK causes multiple vascular lesions. The pathologic changes during the same period are diverse, including inflammation, scar repair, and

Table 4 Recommendations for the imaging diagnosis and evaluation of Takayasu arteritis

Clinical question	Recommendation	Level of evidence	Strength of recommendation	Degree of agreement (%)
Imaging selection for patients suspected of having TAK	DSA was the radiological gold standard for diagnosing TAK, but it has been replaced gradually by non-invasive and equally efficient imaging methods. Ultrasound is valuable for carotid artery (CA) and arteries in the upper and/or lower limbs and is therefore the first choice for screening patients with neck pain and limb claudication. For the aorta and its branches, tomography angiography (CTA) or magnetic resonance angiography (MRA) is recommended. If the patient presents with systemic symptoms such as fever and fatigue, positron emission tomography/computed tomography (PET/CT) can be used to detect vascular-wall inflammation and affected areas, and clarify if tumors or infections are present	2	B	98.2
Evaluation of systemic vascular imaging is required for patients with newly diagnosed TAK	TAK causes multiple vascular lesions. The pathologic changes during the same period are diverse, including inflammation, scar repair, and thrombosis. Imaging can detect them in a timely manner. Therefore, comprehensive evaluation of imaging is important for diagnosis and comprehensive treatment	5	D	92.2
Timing and frequency of image evaluation during follow-up of TAK	In general, newly diagnosed patients should undergo imaging follow-up after 6 months of treatment. Patients with stable conditions should undergo imaging follow-up annually. For patients who require repeat examinations, ultrasound and MRA are recommended as first choices. For patients in clinical remission, the screening frequency and imaging methods used should be determined based on individual needs	5	D	91.2
Imaging selection during the follow-up of TAK	MRA, CTA, PET/CT, or vascular ultrasound can be used to evaluate vascular inflammation and monitor chronic structural changes at the site of vascular inflammation during follow-up. PET/CT is a sensitive form of imaging for monitoring vasculitis, but it is not recommended as the preferred method or for frequent short-term examinations	2	B	90.8
Ultrasound operators should receive professional training	Vascular ultrasound should be undertaken by experienced ultrasound physicians or trained physicians. Standardizing instrument parameter settings and operating methods can help reduce the risk of operators deviating from standardized protocols	5	D	95.4
Ultrasound diagnosis and characteristic manifestations of TAK	Ultrasound images of TAK are characterized by diffuse circumferential thickening of the vessel wall, with or without changes in the lumen, and the characteristic feature is the “macaroni sign”	2	B	92.6
Ultrasound follow-up of changes in vessel-wall inflammation and lumen	Diffused thickening of the vessel wall, reduced echo in the thickened area, and formation of neovascularization within the wall observed by CEUS are signs of vessel-wall inflammation. Thickening of the intima is a sensitive indicator of inflammation. Intramural neovascularization is a specific manifestation of inflammation, and its efficacy in inflammatory evaluation is equivalent to that of PET/CT	2	B	89.6
Diagnosis of TAK by MRA	The diagnostic efficiency of MRA is comparable with that of DSA. MRA can be an effective alternative imaging modality to DSA. In patients who cannot use contrast agents, MRI can also clearly display aortic lesions	2	B	89.8
Evaluation of inflammation in the vessel wall by MRA	Thickening, edema, and wall enhancement around the circumference of the vessel on MRA are manifestations of active inflammation of the vessel wall	2	B	92.2
Diagnosis of TAK by CTA	CTA has diagnostic efficiency comparable with that of DSA. CTA can serve as an effective alternative imaging modality to DSA	2	B	89.8
Evaluation of vessel-wall inflammation by CTA	Thickening and enhancement of the vessel wall in the arterial phase, and concentric low-density rings surrounding the vessel on the delayed phase of CTA, indicate active lesions	2	B	80.4

Table 4 (continued)

Clinical question	Recommendation	Level of evidence	Strength of recommendation	Degree of agreement (%)
Diagnosis of TAK by PET/CT	PET/CT is not the preferred diagnostic method. If the nature of vascular lesions is unclear, or if an increase in the ¹⁸ F-FDG uptake of the vessel wall is detected before morphological changes occur, it has certain value for the early diagnosis of TAK	4	C	86.6
Evaluation of disease activity by PET/CT	PET/CT can use semiquantitative methods to evaluate vascular inflammation. The PET Vascular Activity Score (PETVAS) can reflect systemic vascular inflammation and serve as a reference index for predicting recurrence and for monitoring the treatment response	2	B	87.6
Diagnosis of TAK by DSA	It is not recommended to use DSA routinely for the diagnosis of TAK. DSA can be used for preoperative evaluation, endovascular surgery, and invasive measurement of blood pressure	2	B	80.08
Selection of imaging examination for special populations	Patients who have undergone implantation of a vascular stent can choose CTA and intravascular ultrasound (IVUS) for the diagnosis and follow-up. Patients undergoing vascular graft are recommended to choose aortic CTA examination. PET/CT is recommended if further investigation of vasculitis is needed	2	B	93.8
	Ultrasound examination of blood vessels is preferred during pregnancy. MRI examination shows no evidence of adverse effects on the fetus, but should be used with caution	2	B	93.8
Imaging evaluation methods for organ perfusion	For moderate-to-severe vascular stenosis, corresponding evaluation of organ perfusion is necessary because it can help predict adverse events and optimize comprehensive treatment plans	5	D	94.2

thrombosis. Imaging can detect them in a timely manner. Therefore, comprehensive evaluation of imaging is important for diagnosis and comprehensive treatment. (5 D)

Patients with treatment-naïve TAK may have mild or limited clinical manifestations, which can lead to a missed diagnosis and inaccurate evaluation. Patients suffering from TAK have multivessel lesions, with type V being the most common in the 1996 Numano classification [11]. The vascular pathologic changes of TAK are complex and diverse, and imaging can detect vascular-wall inflammation and luminal lesions intuitively, which is an important basis for comprehensive treatment. Therefore, the Expert Group recommends that ultrasound, MRA, and CTA can be selected for systemic evaluation of vascular imaging for patients with treatment-naïve TAK.

Ultrasound has advantages for detection of the branches of the aortic arch, abdominal aorta and its branches, and limb arteries. MRA and CTA can image multiple parts of the chest and abdomen simultaneously, and can detect structural lesions in the walls and lumina of the aorta and its branches. Compared with ultrasound, the advantages of MRA and CTA are higher standardization of data acquisition, and MRA does not involve ionizing radiation. The speed of CTA is fast, but involves ionizing radiation. Hospitals with adequate facilities can carry out whole-body vascular examinations such as MRA or CTA. For hospitals that do not have adequate facilities, ultrasound can be used, or they can be evaluated at a higher-level hospital. Different imaging methods

have their own advantages and disadvantages, and can be combined (if necessary) to optimize the diagnosis. Vascular assessment includes location, scope, structure (intimal, wall, perivascular tissues), nature (stenosis, occlusion, dilation, thrombus), severity, presence of inflammation, and hemodynamics [12].

Clinical question 3: Timing and frequency of image evaluation during follow-up of TAK

Recommendation 3: In general, newly diagnosed patients should undergo imaging follow-up after 6 months of treatment. Patients with stable conditions should undergo imaging follow-up annually. For patients who require repeat examinations, ultrasound and MRA are recommended as first choices. For patients in clinical remission, the screening frequency and imaging methods used should be determined based on individual needs (5 D).

TAK is a difficult-to-treat disease. Therefore, through a series of imaging follow-ups and image comparisons before and after treatment, one can clarify the outcome of the original vascular lesions (lesion progression, unchanged or improved), whether there are new lesions, understand disease progression, treatment efficacy, or provide imaging evidence if clinical recurrence is suspected.

In many clinical studies evaluating the efficacy of drug treatments for TAK, MRA, CTA, or PET/CT were used to observe changes in vascular imaging from 6 months to 12 months after treatment [13, 16].

It is recommended to undergo imaging examinations in four main situations: (1) increased serum levels of inflammatory markers without specific manifestations; (2) new ischemic events; (3) if disease-related ischemic manifestations worsen; (4) suspected clinical recurrence. Studies had found that positive imaging findings were more sensitive than clinical symptoms and detection of acute reaction protein [17, 18]. If clinical and laboratory test results are uncertain, imaging examinations can clarify clinical evaluation.

Clinical question 4: Imaging selection during the follow-up of TAK

Recommendation 4: MRA, CTA, PET/CT, or vascular ultrasound can be used to evaluate vascular inflammation and monitor chronic structural changes at the site of vascular inflammation during follow-up. PET/CT is a sensitive form of imaging for monitoring vasculitis, but it is not recommended as the preferred method or for frequent short-term examinations (2 B).

The methods for imaging evaluation include ultrasound, CTA, MRA, and PET/CT, which are commonly used for assessing TAK activity and can distinguish disease activity from irreversible vascular damage [3]. One study involving 106 patients with TAK, with a median follow-up of 16 months, found that half of patients had recurrence according to the Kerr score [18]. However, the disease response rate was lower if evaluated by contrast-enhanced ultrasound (CEUS) of the CA, indicating that imaging assessment is more sensitive than clinical assessment. Two PET/CT studies showed that, after treatment relief from TAK, ^{18}F -FDG uptake in the vascular wall improved, which could have reflected changes in disease activity during follow-up [19, 20]. One study involving 28 patients with TAK suggested that patients with high vascular uptake of ^{18}F -FDG (maximum standardized uptake value (SUV_{max}) ≥ 1.3) had an increased risk of recurrence in the future [21]. Thickening of the vessel wall and narrowing of the lumen are common imaging manifestations of TAK, which may be manifestations of inflammation or post-inflammation repair, increased extracellular volume during scar formation, or diffused fibrosis [22, 23]. Therefore, disease activity cannot be evaluated based solely on these two manifestations. Hence, comprehensive evaluation of the clinical and imaging findings of inflammation is needed.

Diagnosis of TAK using ultrasound

Clinical question 5: Ultrasound operators should receive professional training

Recommendation 5: Vascular ultrasound should be undertaken by experienced ultrasound physicians or trained physicians. Standardizing instrument parameter

settings and operating methods can help reduce the risk of operators deviating from standardized protocols (5 D).

Clinical question 6: Ultrasound diagnosis and characteristic manifestations of TAK

Recommendation 6: Ultrasound images of TAK are characterized by diffuse circumferential thickening of the vessel wall, with or without changes in the lumen, and the characteristic feature is the “macaroni sign” (2 B).

Ultrasound two-dimensional imaging can detect changes in the arterial lumen and intima-media thickness (IMT), especially in the CA. Maeda was the first to describe the characteristic image of CA in TAK displayed by ultrasound, with diffuse circumferential thickening of the vessel wall, known as the macaroni sign [24]. One meta-analysis showed that, compared with clinical standards, the overall sensitivity and specificity for diagnosing TAK using carotid ultrasound IMT with a cutoff of 1 mm were 81% and 100%, respectively [25]. One study in 2023 found that arterial-wall thickening in patients with TAK led to increased arterial stiffness [26]. The sensitivity and specificity of shear-wave elastography (which uses the shear-wave velocity of ultrasound to evaluate the elasticity of biological tissues) for diagnosing TAK were 91.8% and 96.5%, respectively.

Clinical question 7: Ultrasound follow-up of changes in vessel-wall inflammation and lumen

Recommendation 7: Diffused thickening of the vessel wall, reduced echo in the thickened area, and formation of neovascularization within the wall observed by contrast-enhanced ultrasound (CEUS) are signs of vessel-wall inflammation. Thickening of the intima is a sensitive indicator of inflammation. Intramural neovascularization is a specific manifestation of inflammation, and its efficacy in inflammatory evaluation is equivalent to that of PET/CT (2 B).

The IMT of the CA increases in patients with active TAK and decreases after treatment [16]. One meta-analysis showed that, using the Kerr score or physician's global assessment (PGA) as the gold standard, the sensitivity and specificity of carotid IMT in diagnosing active TAK were 70% and 71%, respectively [17, 27, 29]. Using the Kerr score as the gold standard, Seth et al. found that the sensitivity and specificity of diagnosing CA activity using IMT with a cutoff of 0.8 mm were 82% and 60%, respectively [28]. Dong et al. reported that IMT had a sensitivity and specificity of 53% and 77%, with a cutoff of 2.5 mm [29].

CEUS can quantitatively observe the newly formed nourishing blood vessels in the thickened vessel wall. Most studies have focused on CA assessment. Ma et al. found neovascularization in the wall of patients with active TAK to be located in the center of the wall [30].

The semiquantitative scoring employed in CEUS is: grade 0 (no angiogenesis, i.e., microbubble contrast agent is not found in the wall of the CA lesion); grade 1 (mild vascular formation, with a limited amount of mobile microbubble contrast agent observed in the wall of the CA lesion); grade 2 (moderate vascular formation, with a moderate amount of mobile microbubble contrast agent observed in the wall of the CA lesion); grade 3 (severe vascular formation, i.e., extensive vascular-wall formation, with clearly visible microbubble contrast agent). A CEUS semiquantitative score of ≥ 2 is used as the standard for active inflammation of the vessel wall. One meta-analysis showed that, using the Kerr score or PGA as the gold standard, the sensitivity and specificity of the CEUS semiquantitative score in diagnosing CA activity were 84% and 79%, respectively [17, 18, 29, 31]. The sensitivity and specificity of the CEUS semiquantitative score ≥ 2 were 95.5% and 69.2% [18], respectively, whereas the sensitivity and specificity of a CEUS semiquantitative score ≥ 3 were 59.5% and 96.1%, respectively [29, 31]. Two studies used PET/CT visual scoring as the gold standard. Authors found that the sensitivity of CEUS for diagnosing CA activity was 100%, and the specificity were 80% and 80.4%, respectively [32, 33], indicating that the diagnostic efficiency was comparable with that of PET/CT.

Diagnosis of TAK by MRA

Clinical question 8: Diagnosis of TAK by MRA

Recommendation 8: The diagnostic efficiency of MRA is comparable with that of DSA. MRA can be an effective alternative imaging modality to DSA. In patients who cannot use contrast agents, MRI can also clearly display aortic lesions (2 B).

Using DSA as the gold standard, Yamada et al. found that MRA had a diagnostic sensitivity and specificity of 100% for 20 patients with confirmed TAK and 10 patients with suspected TAK [34]. The sensitivity and specificity of three-dimensional contrast-enhanced magnetic resonance angiography (3D-CEMRA) for detecting stenosis and occluded lesions were 93.58% and 87.80%, respectively [35]. The sensitivity and specificity of 3D-CEMRA for detecting obvious stenosis lesions ($>50\%$) were 98.33% and 97.25%, respectively. Without the use of contrast agents, MRI can also be employed to describe systemic vascular lesions (including those in pulmonary arteries) in large-vessel vasculitis, making it a diagnostic method for patients who cannot tolerate contrast agents [36].

Clinical question 9: Evaluation of inflammation in the vessel wall by MRA

Recommendation 9: Thickening, edema, and wall enhancement around the circumference of the vessel on

MRA are manifestations of active inflammation of the vessel wall (2 B).

Through short-tau inversion recovery (STIR), T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI) of MRA, edema and delayed enhancement of the arterial wall can be observed in active TAK [37, 39]. Using Indian Takayasu Clinical Activity Score (ITAS) as the gold standard, two studies found that the sensitivity and specificity of wall thickening with enhancement in the diagnosis of disease activity were 66.7–100% and 85.7–89%, respectively [40, 41]. Zhang et al. reported the sensitivity and specificity of diagnosing disease activity through wall edema to be 66.7% and 84%, respectively [42].

Diagnosis of TAK using CTA

Clinical question 10: Diagnosis of TAK by CTA

Recommendation 10: CTA has diagnostic efficiency comparable with that of DSA. CTA can serve as an effective alternative imaging modality to DSA (2 B).

CTA can apply post-processing methods such as maximum intensity projection, curved projection reconstruction, and volume rendering to assist in displaying lesions in the wall and lumen of blood vessels. One small study included 25 patients with suspected TAK [43]. In that study, DSA was used as the gold standard for diagnosing TAK, and the sensitivity and specificity of diagnosing TAK by luminal lesions displayed by CTA were 95% and 100%, respectively. The sensitivity and specificity of diagnosing TAK with the lumen and wall lesions displayed by CTA were both 100%.

Clinical question 11: Evaluation of vessel-wall inflammation by CTA

Recommendation 11: Thickening and enhancement of the vessel wall in the arterial phase, and concentric low-density rings surrounding the vessel on the delayed phase of CTA, indicate active lesions (2 B).

One study evaluated 140 patients indicated that the sensitivity and specificity of assessing disease activity by using a maximum wall thickness of 3.3 mm on CTA were 83.1% and 89.7%, respectively, using the Kerr score as the gold standard [44]. A meta-analysis using the Kerr score or PGA as the gold standard showed that the sensitivity and specificity of CTA in diagnosing disease activity were 65% and 97%, respectively [44, 46].

Diagnosis of TAK using PET/CT

Clinical question 12: Diagnosis of TAK by PET/CT

Recommendation 12: PET/CT is not the preferred diagnostic method. If the nature of vascular lesions is unclear, or if an increase in the ^{18}F -FDG uptake of the vessel wall is detected before morphological changes occur, it has certain value for the early diagnosis of TAK (4 C).

There is no direct evidence for using PET/CT in the diagnosis of TAK. The increased ^{18}F -FDG uptake of the vessel wall on PET/CT is of reference value for the diagnosis of TAK. Several other diseases, such as inflammation of non-TAK and an unstable plaque in atherosclerotic regions, can also have an increased ^{18}F -FDG uptake, and which may be misdiagnosed as TAK. These diseases should be differentiated in clinical practice [47].

Clinical question 13: Evaluation of disease activity by PET/CT

Recommendation 13: PET/CT can use semiquantitative methods to evaluate vascular inflammation. The PET Vascular Activity Score (PETVAS) can reflect systemic vascular inflammation and serve as a reference index for predicting recurrence and for monitoring the treatment response (2 B).

The visual scoring method for PET/CT is: grade 0 (no uptake); grade 1 (intake lower than liver intake); grade 2 (ingestion equals that of the liver); grade 3 (higher intake than that in the liver). Grades 2 and 3 are considered significant manifestations of vascular uptake of ^{18}F -FDG. Based on vascular uptake of ^{18}F -FDG, the literature proposes different indicators, such as SUV_{max} , SUV_{mean} , and target-to-background ratio. According to different research reports, the cutoff of SUV_{max} for diagnosing TAK activity is 1.3–2.3, with sensitivity and specificity of 62.1–92.7% and 50–100%, respectively, using the Kerr score or PGA as the gold standard [19, 20, 47, 51]. Two meta-analyses showed that the pooled sensitivity and specificity of ^{18}F -FDG PET/CT for detecting TAK activity were 81% and 83%, respectively [52, 53]. These indicators arise from ^{18}F -FDG uptake in a few lesion areas, and cannot reflect systemic inflammatory status or be used to evaluate the response to treatment. In 2018, Grayson et al. proposed PETVAS [54]. Based on ^{18}F -FDG uptake, nine arterial regions (ascending aorta, aortic arch, descending thoracic aorta, abdominal aorta, right CA artery, left CA, brachiocephalic trunk, right subclavian artery, and left subclavian artery) were scored with visual scores ranging from 0 points to 3 points for each vessel, resulting in a total score of 0–27 points. In recent studies, PETVAS with a cutoff between 5.5 and 8 has been used to diagnose active TAK with a sensitivity range from 50 to 76.5%, and specificity range from 75.9 to 100%, using the Kerr score or PGA as the gold standard [50, 51, 55, 56].

The value of PET/CT in diagnosing TAK activity during immunosuppressive therapy is controversial. Grayson et al. found that ~60% of patients with clinically inactive TAK showed active signs of TAK upon PET/CT, which indicated subclinical vasculitis [54]. However, there is a lack of long-term follow-up data for vessels with signs of active TAK on PET/CT. Due to the unclear clinical importance of persistent imaging abnormalities, routine

PET/CT examination is not recommended during the stable phase of TAK [20, 21, 56]. Other studies have shown that the intensity of ^{18}F -FDG uptake of patients during remission can be used to predict disease recurrence [19, 48, 57].

Diagnosis of TAK using DSA

Clinical question 14: Diagnosis of TAK by DSA

Recommendation 14: It is not recommended to use DSA routinely for the diagnosis of TAK. DSA can be used for preoperative evaluation, endovascular surgery, and invasive measurement of blood pressure (2 B).

DSA can provide a detailed description of changes in luminal structure, but it cannot provide information about the morphology of the vessel wall. The main indications for DSA in TAK are as part of surgical vascular intervention, such as preoperative evaluation for bypass surgery, percutaneous transluminal balloon angioplasty, or stent implantation [36]. DSA can be used for invasive measurement of blood pressure. It can be employed to measure the central blood pressure and cross-stenosis pressure gradient of patients with vascular stenosis [58].

Imaging diagnosis of TAK in special populations

Clinical question 15: Selection of imaging examination for special populations

Recommendation 15: Patients who have undergone implantation of a vascular stent can choose CTA and intravascular ultrasound (IVUS) for the diagnosis and follow-up. Patients undergoing vascular graft are recommended to choose aortic CTA examination. PET/CT is recommended if further investigation of vasculitis is needed (2 B).

CTA is the preferred imaging modality for patients undergoing vascular graft or endograft, and is not affected by implantation of a vascular stent [59, 60]. However, if undertaking MRA, the implant material must be clarified. Titanium alloy and biological valve materials are applicable. Coronary arteries can also be examined using IVUS and optical coherence tomography. IVUS and optical coherence tomography have a higher detection rate for poor adhesion of a stent, incomplete dilation, and intimal hyperplasia after implantation of a coronary stent, but they are invasive examinations [61].

Due to foreign-body reactions of the graft material, most transplants have a mild increase in uptake of ^{18}F -FDG, which does not represent disease activity [62]. Youngstein et al. found that 88% (23/26) of patients had high uptake of ^{18}F -FDG around the graft, which remained unchanged for 116 months [63]. Therefore, it is not recommended to change the treatment plan based solely on the results of this examination.

Recommendation 16: Ultrasound examination of blood vessels is preferred during pregnancy. MRI

examination shows no evidence of adverse effects on the fetus, but should be used with caution (2 B).

Evidence for the application of MRI during pregnancy has arisen from retrospective studies [64, 67]. Gadolinium-based contrast agents can cross the placenta and increase the risk of adverse events such as fetal death and neonatal death. Hence, the use of gadolinium-based contrast agents should be restricted [64, 68].

Exposure of pregnant women and fetuses to radiation may increase the risk of congenital malformations, developmental delays, or intellectual disabilities. Experts in the application of radiographic imaging during pregnancy have suggested that the risk of adverse outcomes is dependent upon the gestational age and exposure dose to the fetus. The minimum dose of radiation exposure that can cause adverse outcomes in the fetus is usually 50–200 mGy. In theory, the use of iodine-based contrast agents in CTA can affect fetal thyroid function, but this has not been confirmed in clinical studies.

One study involving six women between 5 weeks and 7 months of pregnancy who underwent PET, PET/CT, or PET/MRI found that fetal radiation doses were higher in early pregnancy and exhibited individual variability [69]. Among these three types of examination, PET/MRI is recommended as the most suitable. A PET/MRI study was conducted on 11 pregnant women with cervical cancer at different gestational weeks. Authors found that the dose of ^{18}F -FDG absorbed by the fetus was very low (between 2.21×10^{-2} mGy/MBq to $7.38 \pm 0.25 \times 10^{-3}$ mGy/MBq) [70]. That study suggested that pregnant women with cancer can choose PET/MRI. However, relevant research reports on patients with TAK are lacking.

The general principles of using radiographic imaging during pregnancy are: (1) the diagnostic benefits outweigh the risks for patients; (2) minimizing the dose as much as possible; (3) informing patients and their families of the importance of the examination and potential risks of fetal injury before the examination, and respect their right to informed consent [64, 69].

Clinical question 16: Imaging evaluation methods for organ perfusion

Recommendation 17: For moderate-to-severe vascular stenosis, corresponding evaluation of organ perfusion is necessary because it can help predict adverse events and optimize comprehensive treatment plans (5 D).

Multiple vascular lesions and moderate-to-severe luminal stenosis can lead to decreased perfusion in the corresponding organs, resulting in functional impairment. Therefore, perfusion evaluations of the corresponding organ can assist in predicting adverse events and optimizing treatment, especially for the heart, brain, and kidneys. Computed tomography perfusion (CTP) and MR perfusion weighted imaging (PWI) with iodine or

gadolinium as contrast agent can be used to evaluate the blood flow and perfusion in the brain. Nuclide renal dynamic imaging with $^{99\text{m}}\text{Tc}$ -diethylenetriamine penta-acetic acid (DTPA) and $^{99\text{m}}\text{Tc}$ -dimercaptosuccinic acid (DMSA) as radio tracers can simultaneously observe perfusion of renal blood flow, renal parenchyma, and renal excretion, thereby providing a comprehensive evaluation of renal function and morphology. Myocardial radio-nuclide imaging with $^{99\text{m}}\text{Tc}$ -methoxyisobutylisonitrile (MIBI) as radio tracers can reflect the blood supply and functional status of myocardial tissue.

New methods of inspection

Gadolinium-labeled-fibroblast activating protein inhibitor ([69] Ga-FAPI) is a new PET tracer for FAP. [69] Ga-FAPI is applied to fibrosis caused by wound healing, inflammation, or atherosclerotic plaques [71]. One study suggested that FAPI-PET may help distinguish inflammation or fibrosis at the lesion site. In a case report of TAK, PET/CT did not detect ^{18}F -FDG uptake in the vessel wall [72]. Two days later, [69] Ga-FAPI PET/CT revealed an increase in [69] Ga-FAPI uptake in the affected vessel. [69] Ga-FAPI PET/CT could become a promising imaging modality for TAK. In addition, a combination of ^{19}F -sodium fluoride (^{18}F -NaF), chemokine receptor 4 (CXCR4), and other tracers has been applied for the imaging of atherosclerosis [73]. PET/MRI can be used to distinguish active and inactive vasculitis by combining with somatostatin receptors [74].

Discussion

There is an urgent need to establish validated, efficient, and feasible indicators for imaging evaluation. Long-term follow-up of vessel lesions is required. Artificial intelligence could be used for the diagnosis and evaluation of TAK. Accurately distinguishing between vascular active inflammation and irreversible structural damage using imaging is important.

Five recommendations were related to TAK in the 2023 EULAR recommendations [3] on the use of imaging examinations for large-vessel vasculitis in clinical practice. If diagnosing suspected TAK, DSA is not recommended, and MRA is preferred for examining wall inflammation and changes in luminal structure. Similarly, our guideline recommends using other non-invasive imaging methods with equivalent diagnostic value to replace DSA for diagnosing TAK. According to the conditions in China, it is recommended to first use vascular ultrasound to diagnose individuals suspected of having TAK. During follow-up, our guideline provides 6 months and annual imaging follow-up recommendations for patients with newly diagnosed TAK to detect the progression of vascular lesions promptly.

Given the important role of imaging in management of the entire course of TAK and its potential wider application in the future, our guideline will be updated with relevant content in a timely manner. Our guideline is based on evidence-based medicine, and aims to standardize the imaging diagnosis and evaluation of TAK. It is only for reference and application by clinical staff or researchers, and does not have legal repercussions.

Abbreviations

TAK	Takayasu arteritis
ESR	Erythrocyte sedimentation rate
CRP	C-reactive protein
DSA	Digital subtraction angiography
EULAR	European League Against Rheumatism
PICO	Population, intervention, comparison, outcome
CA	Carotid artery
CTA	Computed tomography angiography
MRA	Magnetic resonance angiography
PET/CT	Positron emission tomography/computed tomography
IMT	Intima-media thickness
CEUS	Contrast-enhanced ultrasound
PGA	Physician's global assessment
3D-CEMRA	Three-dimensional contrast-enhanced magnetic resonance angiography
STIR	Short-tau inversion recovery
T2WI	Through T2-weighted imaging
DWI	Diffusion-weighted imaging
ITAS	Indian Takayasu Clinical Activity Score
PETVAS	PET Vascular Activity Score
FDG	Fluorodeoxyglucose
SUV	Standard uptake value
IVUS	Intravascular ultrasound
CTP	Computed tomography perfusion
PWI	Perfusion weighted imaging
DTPA	Diethylenetriamine pentaacetic acid
DMSA	Dimercaptosuccinic acid
MIBI	Methoxyisobutylisonitrile
FAPI	Fibroblast activating protein inhibitor
CXCR4	Chemokine receptor 4

Supplementary Information

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Supplementary Material 1

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Author contributions

YL and LYM contributed to writing the manuscript. LDJ initiated, conceived and designed the study. YL and LDJ revised the manuscript. All authors provided clinical expertise and critical review in formulating the recommendations. In addition, all authors have read and approved the final version of this manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

The study was approved by the Institutional Review Board of Zhongshan Hospital.

Human ethics and consent to participate declarations

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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