# Turkish Society for Rheumatology (Turkish Takayasu Arteritis Study Group) recommendations for the diagnosis, follow-up and the treatment of Takayasu's arteritis

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# **Abstract** Objective

To develop evidence-based and expert opinion guided recommendations for Takayasu's arteritis (TAK) management.

### Methods

A systematic literature review was conducted following the principles outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. To structure the key clinical questions, the task force employed the Population, Intervention, Comparison, and Outcome (PICO) format. The European League Against Rheumatism (EULAR) standardised operating procedures was subsequently applied to grade the quality of the collected evidence and determine the strength of each recommendation.

#### Results

This guideline provides 40 recommendations under the headings: diagnosis, follow-up, medical treatment, pregnancy and surgical interventions. As randomised controlled trials are very limited in number without conclusive results, most data come from case series with low-level evidence. We recommend conventional immunosuppressives as the first choice during remission-induction. Tumour necrosis factor-inhibitors or tocilizumab can be considered in patients with relapsing or refractory disease despite conventional immunosuppressives.

### Conclusion

The first Turkish Takayasu Arteritis Study Group recommendations deriving from a current literature review and large clinical experience, aim to guide clinicians not only in Turkey, but also in other countries who are providing health care to patients with TAK.

### **Key words**

Takayasu's arteritis, recommendations

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#### Introduction

Takayasu's arteritis (TAK) is a rare, chronic granulomatous large-vessel arteritis that predominantly affects aorta and its major branches. Inflammation in the arterial wall may lead to segmental stenosis, occlusion, dilatation, or aneurysm formation. These lesions in the vessel wall lead to various signs and symptoms such as extremity pain, claudication, light-headedness, constitutional features (such as fever, malaise, anorexia and weight-loss), bruits, absent or diminished pulses and loss of blood pressure. TAK generally follows an insidious course at onset, but presentation with atypical or catastrophic disease such as acute visual loss or stroke may also occur (1). In the presence of typical symptoms and physical findings in especially young females such as loss of pulses or decreased arterial blood pressure and elevated acute phase responses, the diagnosis can be confirmed by angiographic imaging modalities such as magnetic resonance imaging (MRI) and computerised tomography (CT) angiographies (MRA and CTA), positron-emission computerised tomography (PET-CT) and ultrasonography (USG).

Correct assessment of the extent of arterial involvement, clinical activity and damage in TAK is essential for management decisions during the disease course (2). However, there are no widely accepted and validated definitions of 'disease activity' or 'response to treatment'. One of the major difficulties is the differentiation between ongoing activity and vascular damage in TAK. Treatment of TAK usually focuses on the prevention of flares. However, disease-related damage should also be prevented and it is critical to differentiate irreversible damage from disease activity, avoiding potential over-treatment with toxic agents such as glucocorticoids (GCs) (3). Although widely used, biomarkers of inflammation [erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)] have limited value for activity assessment in TAK. Among various imaging methods, MRA is the gold standard modality both for the diagnosis and the longitudinal follow-up of the patients with TAK.

GCs are still the mainstay of treatment for remission-induction in TAK. Despite a high early response with GCs in TAK, there is a high relapse rate while gradually tapering the GCs. Current approach is addition of conventional immuno-suppressive (IS) agents while tapering GCs. Tocilizumab (TCZ) or tumour necrosis factor (TNF)-inhibitors (TNFi) can be considered for the refractory patients. Majority of current data on TAK comes from case series and open studies. There are few randomised, double-blind, placebocontrolled trials (RCTs) for the management of TAK. There are also very limited data on some critical management issues such as vascular interventions, pregnancies and comorbidities. Therefore, the level of evidence (LoE) for TAK management is low and expert opinion is still the main determinant while managing TAK patients during daily practice.

Most current global recommendations on TAK are covering both giant cell arteritis (GCA) and TAK, but mainly GCA due to the low prevalence of TAK in Caucasian populations. Despite a lack of clear epidemiological data, TAK is a more frequent large vessel vasculitis (LVV) in Turkey compared to GCA. Turkish Takayasu Arteritis Study group (TTASG) has been working on the pathogenesis, disease outcomes and management of TAK for over 15 years with a large experience and now aimed to conduct a comprehensive guideline including diagnosis, follow-up, treatment, pregnancy, comorbidities and interventional approaches for TAK.

#### Methods

Design

This guideline was developed using an evidence-based framework aligned with the standardised operating procedures (SoPs) recommended by the European League Against Rheumatism (EULAR) (4). A systematic literature review (SLR) was conducted following the principles outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (5). To structure the key clinical questions, the Task Force employed the Population, Intervention, Compari-

competing interests.

son, and Outcome (PICO) format (6). The system proposed in SOPs of EU-LAR was subsequently applied to grade the quality of the collected evidence and determine the strength of each recommendation based on the methodological guidance for formulating or revising EULAR recommendations (4, 7).

# Task Force composition

A task force comprised of 12 rheumatologists, expert in vasculitis, one methodologist (GH), 9 junior researchers, and one patient representative. All physicians were experienced in the diagnosis and management of TAK. Senior researchers were assigned to each group, and the methodologist supervised the groups of two paired junior researchers who reviewed the PICO questions assigned to them. Before initiating the project, all members provided written declarations of potential conflicts of interest.

#### Selection of clinical questions

At the initial meeting, the expert panel convened to determine the scope of the recommendations by generating a comprehensive list of relevant topics. The group reached a consensus on the areas to be addressed: disease definitions related to TAK, diagnosis, follow-up and monitoring strategies, medical and interventional treatment modalities for disease management and exceptional circumstances such as pregnancy. Drawing on these overarching themes, the panel developed 32 clinical questions that would guide the subsequent SLR (Supplementary Table S1).

#### Systematic literature review

PubMed, Turkish National Rheumatology Congress proceedings, Abstract archives of the EULAR and American College of Rheumatology (ACR) congress abstracts were systematically reviewed for relevant studies from database inception through December 2021. Eligible publications included meta-analyses, systematic reviews, randomised clinical trials, cohort studies, and case series with at least five patients. The systematic literature search was carried out by junior researchers (SKT, BI, ECB, TYI, HEO, TS, AO,

ZTD and FY) under the supervision of the methodologist (GH) and experts from the task force members for each group.

Titles and abstracts were examined for each clinical question to determine potential eligibility. Additionally, reference lists of meta-analyses and systematic reviews were reviewed to identify further pertinent articles. Full-text evaluation of eligible papers was then performed jointly by junior and senior Task Force members, and any divergences regarding study selection or data extraction were resolved through discussion and consensus. Further details on the selection of studies and data extraction can be found in the online Supplementary material.

# Development and voting on recommendations

Findings from the SLR were presented to the Task Force for through debate. Preliminary statements were drafted to encapsulate both clinical evidence and expert judgment. Each recommendation was discussed in depth, refined when necessary, and subjected to an internal voting process, requiring a predefined majority (75%) to be approved. A numerical rating scale ranging from 0 (complete disagreement) to 10 (entire agreement) was used to measure the level of consensus within the task force. The proposed EULAR SOPs scale was used to score the level of evidence (LoE) between 1 and 4 and strength of recommendation (SoR) between A and D (4).

#### Ethical considerations

Given that this guideline relies on existing literature and expert opinion, no direct patient or public involvement occurred during its formulation. Ethical principles and institutional standards were adhered to throughout the development process.

#### Results

# **General recommendations**

Recommendation 1: TAK should be considered and expert centers should be contacted when young patients (under the age of <50) and especially females present with the following conditions:

- Unexplained constitutional symptoms and inflammation;
- Presence of findings and symptoms suggestive of arterial ischaemia, such as vascular claudication, lack of pulses, or pulse difference between the extremities; Failure to take a blood pressure measurement or a difference of >20 mmHg between the extremities;
- Auscultating a murmur or palpating a thrill over vascular territories (e.g. carotid, subclavian, renal arteries) during physical examination;
- Secondary hypertension (HT) (especially suggestive of renovascular HT);
- Early age-onset cerebrovascular accident or coronary event;
- Detection of concentric wall thickening, stenosis/occlusion, or aneurysm in large-medium sized vessels suggestive of vasculitis, especially in the aorta and its main branches, by CTA, MRA, USG or PET-CT/MRI.

(LoE evidence: 3; SoR: D)

TAK is a chronic vasculitis of large vessels marked by a strong female predominance – reported in 84–92% of patients and typically presents during the third to fourth decade of life (8-11). TAK is often described as having two distinct phases: an early, pre pulseless systemic phase and a later occlusive phase (12). The active phase may resolve spontaneously within 3-6 months or gradually progress into the chronic phase, marked by inflammatory and obliterative changes in the aorta and its branches (13, 14). TAK exhibits a broad spectrum of clinical presentations at diagnosis, which may include constitutional symptoms in about 8% of cases, carotidynia in 13–15%, other vascular manifestations in 44-57%, major ischaemic events in 28-30%, and an asymptomatic course in 2-6% (15). A study of patients with renovascular HT revealed that TAK was present in 61% of cases, emphasising its role as a notable contributor to this condition (16-19).

Recommendation 2: Patients with pulmonary or coronary artery involvement or a history of cerebrovascular accident should be followed closely in terms of a severe disease course. It should be kept in mind that patients with childhoodonset disease may also have a poor

**Table I.** Definitions for disease activity regarding recommendations.

Active disease	Active disease is defined by the presence of at least one item in two of three domains-clinical, laboratory, and radiological. If only one item is present in one domain, the patient should be closely monitored for signs and findings of active disease or relapse.
Clinical	1- Ischaemic findings due to vascular inflammation, carotidynia/localised pain in large vascular areas; 2- Systemic symptoms such as fever and malaise that cannot be explained by other causes; 3- New murmur, pulselessness, blood pressure difference on physical examination.
Radiological	1- New angiographic abnormalities such as newly developed vessel wall irregularity, thickening, aneurysm, stenosis or occlusion on MRA, CTA, PET-CT or Doppler USG; 2- Extension of previous vascular wall or intraluminal changes.
Laboratory	Increased inflammatory markers (CRP, ESR)
Remission	Remission is defined as the disappearance of clinical findings (vascular, ischaemic, systemic) following medical treatment, acute phase responses within normal limits, absence of new vascular lesions on follow-up imaging and the use of a daily GC dose of less than 5 mg of prednisolone equivalent.
Sustained remission	Sustained remission is defined as maintenance of remission for at least 6 to 12 months.
Refractory disease	Patients without improvement in clinical, laboratory, or radiologic findings within the first 3 to 6 months despite treatment with ISs.

prognosis due to disease extent, higher levels of inflammatory serum biomarkers, and more frequent involvement in mesenteric and renal arteries.

(LoE: 3; SoR: C)

Pulmonary artery involvement (PAI) is common in TAK, affecting 26-31% of patients (20, 21). PAI often leads to pulmonary HT, with 50-62% of PAI patients developing PH (20, 21). Patients with PAI and PH experience more severe symptoms, including dyspnea, haemoptysis and oedema (21). PH significantly worsens prognosis, increasing mortality risk up to 7 times (21). Early detection of PAI is crucial with subpleural wedge-shaped shadows on CT, potentially indicating PAI before PH onset (22). Prognostic factors for poor outcomes include disease duration, New York Heart Association (NYHA) class III/IV, right ventricular dysfunction, and respiratory failure (21). The 6-minute walk distance and PH-targeted therapies are independent predictors of cardiac death and hospital readmissions (23). PAI may also mimic thromboembolic disease (24). Coronary abnormalities, though relatively uncommon, can be fatal and often involve the ostium (25). Coronary involvement is a significant predictor of poor long-term outcomes, including increased mortality, major cardiovascular events and disease relapse (26). Risk factors for coronary involvement include increased age and type V angiographic classification (26). Patients with TAK who exhibit pulmonary or coronary artery involvement or a history of cerebrovascular events require close monitoring due to their association with a more severe disease course (27, 28).

Additionally, childhood-onset TAK (cTAK) often portends a poorer prognosis. (29). Compared to adult-onset, cTAK patients exhibit more frequent abdominal aorta involvement, systemic inflammation and higher remission rates (30-32). However, cTAK carries a significant disease burden, with approximately 50% of patients experiencing flares and a 7% mortality rate within 6 months of diagnosis (33). Prognostic factors associated with poor outcomes include lower body mass index (BMI), younger age at admission, stroke, and elevated CRP (34). Biologic therapies, such as TNFi or tocilizumab, have shown promise in achieving better disease control than non-biologic treatments (29, 33). Despite these advances, cTAK patients often face a guarded prognosis and significant accrued damage (29, 34). Careful and tailored follow-up and management are essential for these high-risk groups to manage complications effectively and improve outcomes (27, 28).

Recommendation 3: MRA is the preferred imaging modality for the diagnosis of TAK, considering the patient's age and disease duration and the need for repeated imaging during follow-up. However, other methods (CTA, PET-CT/ MRI, and USG) can also be used depending on the technical features and adequacy of the devices, the experience of the center and the radiologists, patient characteristics and preferences, and the scope of the vessel planned to be imaged. USG and Doppler evaluation can be preferred in selected conditions such as pregnancy to image easily accessible vessels such as the carotid arteries. (LoE: 3 (MRA and CTA) and 4 (PET and USG); SoR: C (MRA and CTA) and D (PET and USG))

Imaging is crucial in diagnosing and monitoring of TAK. The choice of imaging modality depends on patient characteristics, disease stage, and clinical needs. While CTA or MRA are commonly used for initial diagnosis, MRA is preferred for follow-up due to its lack of radiation exposure (35). MRA, as a non-invasive method, can assess the arterial lumen and wall, making it suitable for follow-up imaging, especially in younger patients. (36). A meta-analysis found high sensitivity and specificity for ultrasound, MRA, and CTA in TAK diagnosis, but their utility in assessing disease activity remains unclear (37). The modalities such as CTA, PET-CT/ MRA, and USG are also valuable in specific contexts. For example, CTA offers excellent spatial resolution for arterial lumen assessment, while PET-CT is highly sensitive to active inflammation and may provide information on arterial wall inflammation before morphological changes appear (28, 38). USG and Doppler imaging are helpful for easily accessible vessels like carotid arteries, particularly in special situations like pregnancy. USG can detect early wall thickening in carotid arteries and differentiate TAK from atherosclerosis (28). The final choice should consider the technical capabilities of the imaging centre, the radiologist's expertise, and the scope of vascular involvement to ensure optimal diagnostic accuracy (19, 37).

Recommendation 4: Considering the frequency of involvement, cross-sectional imaging should be planned to include the common carotid arteries, brachiocephalic and subclavian arteries, ascending aorta, aortic arch, descending thoracic aorta, abdominal arteries, bilateral renal arteries, mesenteric arteries and common iliac arteries. The pulmonary arterial system, coronary arteries, and intracranial vessels can also be visualised based on clinical suspicion in selected cases. (LoE: 3; SoR: D)

Cross-sectional imaging techniques like CTA and MRA effectively diagnose TAK and assess disease activity (19, 39). These methods can demonstrate early signs of inflammation, including vessel wall thickening and enhancement, before developing stenosis and aneurysms (40). CT/MR imaging findings correlate significantly with disease activity markers like elevated ESR and CRP (39). PET/CT excels in identifying active inflammation, whereas MRA offers superior soft-tissue differentiation and visualisation of vascular flow (18, 19, 39, 41).

Recommendation 5: No widely validated diagnostic biomarker can be used in routine practice for differential diagnosis. (LoE: 3; SoR: C)

TAK lacks widely validated diagnostic biomarkers for routine clinical use, making imaging techniques the primary tool for assessment (42, 43). Although various potential biomarkers including acute phase reactants, cytokines and autoantibodies have shown promise in determining disease activity, their clinical utility in TAK diagnosis remain insufficiently explored (44). Emerging biomarkers such as Pentraxin-3 (PTX-3), YKL-40, Chitinase-3-like protein 1 (CHI3L1), interleukin (IL)-6, and tissue inhibitor of metalloproteinases-1 (TIMP-1) are also encouraging, yet their routine application is still limited (44). Genetic and proteomic studies further offer potential diagnostic insights through the identification of proteins like TIMP-1 and various cytokine

profiles (45). However, despite these developments, imaging modalities currently remain the most valid approach for diagnosing TAK (46, 47). Further research is needed to develop reliable biomarkers that complement imaging and enhance disease evaluation and management (27, 48).

Recommendation 6: Patients with TAK should be followed by a multidisciplinary team under the leadership of a rheumatologist. The frequency of followup should be determined according to disease activity, severity of vascular involvement, treatment initiated, duration of remission, and comorbidities of the patient. In the early period (first year), patients with active disease should be monitored at 1–3 month intervals. Patients in remission can be monitored every 3–6 months. (LoE: 4; SoR: C) There are no studies that directly compare the outcome of patients who are

There are no studies that directly compare the outcome of patients who are monitored at different time intervals and with different modalities. The frequency of follow-up of TAK patients, the type and frequency of imaging, and the time of treatment change were determined based on expert opinion.

Recommendation 7: Clinical symptoms, physical examination findings, inflammatory markers (CRP, ESR), imaging modalities (MRI/CT angiography, Doppler USG) and multi-systemic activity scores such as Indian Takayasu Activity Score (ITAS)-A can be used to monitor disease activity. In addition, Vasculitis Damage Index or Takayasu Arteritis Damage Score can be used to detect vasculitis-related damage. It is recommended to use a composite score that includes clinical symptoms and signs, acute phase reactants, and radiological findings to monitor disease activity. (LoE: 3; SoR: C)

The methods of disease activity monitoring and the assessment of disease-related damage were determined based on the activity measurement methods and vascular damage indices used in cohort studies (49, 50). The most commonly used activity scales for disease activity monitoring in cohort studies are National Institutes of Health (NIH)-Kerr activity definition, Physician global as-

sessment (PhGA), ITAS 2010), ITAS-A and vascular damage indices VDI and TADS. The effect of vascular imaging on the assessment of disease activity was evaluated in one study (51). Most of the studies used more than one scale.

Recommendation 8: Since there are no quality of life (QoL) scales developed specifically for TAK, generic QoL scales should be used to assess different aspects such as fatigue, pain, physical and social functioning, mental health, sleep and perception of disease in these patients. The 36-item short form health survey (SF-36) and Multi-dimensional Fatigue Inventory (MFI) can be used. (LoE: 3; SoR: B)

There is no disease-specific scale to assess QoL in TAK. In most of the studies, QoL was evaluated using non-specific scales. SF-36 is one of the most commonly used QoL scales in musculoskeletal diseases and vasculitis and can be used for QoL assessment in patients with TAK (52). MFI is also used to assess fatigue in TAK patients (53, 54).

Recommendation 9: Evaluating serum CRP and ESR alongside clinical findings is recommended for a comprehensive evaluation and monitoring of disease activity. CRP and ESR tests should *be performed every 1–3 months in active* patients and every 3-6 months among those in remission. (LoE: 3; SoR: C) Numerous biomarkers, including CRP, ESR, PTX3, IL-6, matrix metalloproteinase (MMP)-3, and MMP-9, have been studied in various cross-sectional and small-scale studies comparing active and inactive TAK patients. A limited number of studies have assessed sensitivity and specificity. These biomarkers exhibit significantly higher levels in active patients and are considered to have acceptable sensitivity and specificity. CRP and ESR are frequently used, reliable, and cost-effective tests (55-57).

Recommendation 10: We recommend regular non-invasive imaging alongside routine clinical and laboratory evaluation for the follow-up of patients with TAK. We recommend annual imaging for the first two years after re-

mission. The frequency of imaging may be reduced in patients in long-term remission. (LoE: 3, SoR: C)

Clinical and laboratory findings may not always indicate active disease which can be insidious and slowly progressive in TAK (58). In some patients imaging methods can also detect signs of disease activity and progression. Indicators of active disease may include increased vessel wall thickness, oedema and contrast enhancement in the vessel wall, increased 18-fluorodeoxyglucose (FDG) uptake, or new vessel involvement. Stenosis, obstruction, or aneurysm development are considered structural damage.

One or more non-invasive imaging methods that provide information about vascular wall inflammation, such as USG, MRA, and PET-CT, can be selected to assess disease activity during follow-up. The appropriate option may vary based on the clinic's resources and expertise. In regular follow-up, USG can be performed every 3–6 months, and MRA can be performed every 6–12 months, depending on the disease activity. CTA is not recommended for follow-up due to the risk of cumulative radiation exposure (51, 59, 60).

vessels such as the carotid arteries.

Recommendation 11: In patients with TAK who do not have clinical symptoms and signs of active disease but have increased acute-phase reactants, close monitoring should be continued without changing immunosuppressive therapy. (LoE: 4, SoR: D)

ESR and CRP can be affected by a variety of conditions and are not specific for disease activation (61). Therefore, an increase in only acute-phase reactants, without clinical or imaging findings of activity, is not accepted to be sufficient to make changes in management decisions.

Recommendation 12: Patients with TAK who have new or worsening vascular inflammation on imaging (such as new arterial stenosis, vascular oedema, contrast enhancement, increased wall thickness or supraphysiologic 18-FDG uptake in the arterial wall) should be assessed for a change in IS therapy, even if they do not have increased acute-phase reactants and clinical symptoms. (LoE: 3, SoR: B)

Progression in imaging findings can be detected during routine vascular imaging in asymptomatic patients with normal acute-phase reactants (59, 62).

Whether a more aggressive approach for management with these radiological findings should be decided individually according to factors such as the vessel involved, amount of change in lumen stenosis, aneurysms or vessel wall thickness, comorbid diseases and benefit/safety issues of therapeutic agents.

Recommendation 13: Long-term follow-up should be performed in patients with TAK in remission. (LoE: 3, SoR: B) The optimal duration of follow-up in patients with TAK is not known. However, as there is a high risk of relapse in the first 5–10 years of the disease, long-term follow-up is suggested by our expert panel (63).

Recommendation 14: High dose GCs should be used for remission induction in TAK. (LoE: 3, SoR: B)

GCs are the mainstay of treatment for remission induction in TAK. High remission rates can be achieved with high dose (0.5–1 mg/kg/day) GCs (64, 65). Similar complete remission and relapse rates were shown in patients receiving 0.5/mg/kg/d and 1 mg/kg/d as the initial GC dose in a retrospective study (66).

**Table II.** Recommendations for diagnosis, follow-up and medical management.

evaluation can be preferred in selected conditions such as pregnancy to image easily accessible

n.	Recommendation	Level of evidence	External voting	Strength of recommendation
1	TAK should be considered and expert centers should be contacted when young patients (under the age of <50) and especially females present with the following conditions:  - Unexplained constitutional symptoms and inflammation  - Presence of findings and symptoms suggestive of arterial ischaemia, such as vascular claudication, lack of pulses, or pulse difference between the extremities  - Failure to take a blood pressure measurement or a difference of >20 mmHg between the extremities  - Auscultating a murmur or palpating a thrill over vascular territories (e.g. carotid, subclavian, renal arteries) during physical examination.  - Secondary hypertension (HT) (especially suggestive of renovascular HT)  - Early age-onset cerebrovascular accident or coronary event  - Detection of concentric wall thickening, stenosis/occlusion, or aneurysm in large-medium sized vessels suggestive of vasculitis, especially in the aorta and its main branches, by (CT, MRI, USG or PET-CT/MRI.		9.51	D
2	Patients with pulmonary or coronary artery involvement or a history of cerebrovascular accident should be followed closely in terms of a severe disease course. It should be kept in mind that patients with childhood-onset disease may also have a poor prognosis due to disease extent, higher levels of inflammatory serum biomarkers, and more frequent involvement in mesenteric and renal arteries.	3	9.26	С
3	MRA is the preferred imaging modality for the diagnosis of TAK, considering the patient's age and disease duration and the need for repeated imaging during follow-up. However, other methods (CTA, PET-CT/MRI, and USG) can also be used depending on the technical features and adequacy of the devices, the experience of the center and the radiologists, patient characteristics and preferences, and the scope of the vessel planned to be imaged. Ultrasonography and Doppler	3 (MRI and CT) and 4 (PET and USG)	9.57	C (MRI and CT) and D (PET and USG)

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n.	Recommendation	Level of evidence	External voting	Strength of recommendation
4	Considering the frequency of involvement, cross-sectional imaging should be planned to include the common carotid arteries, brachiocephalic and subclavian arteries, ascending aorta, aortic arch, descending thoracic aorta, abdominal arteries, bilateral renal arteries, mesenteric arteries and common iliac arteries. The pulmonary arterial system, coronary arteries, and intracranial vessels can also bevisualised based on clinical suspicion in selected cases.	3	9.31	D
5	No widely validated diagnostic biomarker can be used in routine practice for differential diagnosis.	3	9.5	С
6	Patients with TAK should be followed by a multidisciplinary team under the leadership of a rheumatologist. The frequency of follow-up should be determined according to disease activity, severity of vascular involvement, treatment initiated, duration of remission, and comorbidities of the patient. In the early period (first year), patients with active disease should be monitored at 1-3 month intervals. Patients in remission can be monitored every 3-6 months.	4	9.42	С
7	Clinical symptoms, physical examination findings, inflammatory markers (CRP, ESR), imaging modalities (MRI/CT angiography, Doppler USG) and multi-systemic activity scores such as ITAS-A can be used to monitor disease activity. In addition, VDI or TADS can be used to detect vasculitis-related damage. It is recommended to use a composite score that includes clinical symptoms and signs, acute phase reactants, and radiological findings to monitor disease activity.	3	8.91	С
8	Since there are no quality of life (QoL) scales developed specifically for TAK, generic QoL scales should be used to assess different aspects such as fatigue, pain, physical and social functioning, mental health, sleep and perception of disease in these patients. The 36-item short form health survey SF-36 and Multidimensional Fatigue Inventory (MFI) can be used.	3	8.26	В
9	Evaluating serum CRP and ESR alongside clinical findings is recommended for a comprehensive evaluation and monitoring of disease activity. CRP and ESR tests should be performed every 1-3 months in active patients and every 3-6 months among those in remission.	3	9.2	С
10	We recommend regular non-invasive imaging alongside routine clinical and laboratory evaluation for the follow-up of patients with TAK. We recommend annual imaging for the first two years after remission. The frequency of imaging may be reduced in patients in long-term remission.	3	8.6	С
11	In patients with TAK who do not have clinical symptoms and signs of active disease but have increased acute phase reactants, close monitoring should be continued without changing ISs	4	8.81	D
12	Patients with TAK who have new or worsening vascular inflammation on imaging (such as new arterial stenosis, vascular oedema, contrast enhancement, increased wall thickness or supraphysiologic 18-FDG uptake in the arterial wall) should be assessed for a change in ISs, even if they do not have increased acute phase reactants and clinical symptoms.	3	9.04	В
13	Long-term follow-up should be performed in patients with TAK in remission.	3	9.47	В
14	High dose GCs should be used for remission induction in TAK.	3	9.6	В
15	Although there is no data reporting the superiority of pulse GCs over high dose GCs, pulse GCs may be considered in the presence of severe organ involvement.	4	9.39	D
16	A glucocorticoid dose of 5 mg/day prednisolone equivalent or lower should be targeted at the end of the first year at the latest.	4	8.77	D
17	Since GC monotherapy is associated with high relapse rates, additional ISs should be considered in initial treatment.	3	9.73	В
18	In addition to GCs, methotrexate (MTX), azathioprine (AZA), leflunomide, or mycophenolate mofetil (MMF) may be the first choice for remission induction in TAK.	3	9.21	В
19	Due to its possible side effects, cyclophosphamide (CyP) should only be considered in the presence of system/organ threatening or refractory disease.	3	9.18	D
20	TNFi or TCZ can be considered in patients with relapsing or refractory disease despite conventional ISs.	3	9.52	В
21	Tapering or discontinuation of ISs may be considered for selected cases who have been in sustained remission (6-12 months). Tapering / discontinuation should start with GCs.	4	8.82	D

Recommendation 15: Although there is no data reporting the superiority of pulse glucocorticoid treatment over high dose glucocorticoids, pulse glucocorticoid therapy may be considered in the presence of severe organ involvement. (LoE: 5, SoR: D)

Non-genomic effects of GCs occur more frequently at higher doses, resulting in faster and higher efficacy as well as an increased likelihood of side effects (67). There are no studies comparing the efficacy of high-dose and pulse GCs in TAK. However, open studies show that there is a tendency of clinicians to give pulse GCs in severe or life-threatening disease such as cerebral or mesenteric ischaemia (64-68). The expert panel also felt that similar to other systemic vasculitides, in TAK patients with severe organ involvement, pulse GCs may be preferred.

Recommendation 16: A glucocorticoid dose of 5 mg/day prednisolone equivalent or lower should be targeted, at the latest, at the end of the first year. (LoE: 4, SoR: D)

There is no standard GC dose reduction regimen for TAK. In a prospective cohort, patients received GCs with the initiation dose of 0.8-1 mg/kg/d for 4 weeks and gradually tapered to a 0.1-0.2 mg/kg/d dose within 5 months with the use of concomitant GCs. Complete remission rates were 56-85% and relapse rates 7-17% at 12 months of the treatment (69-71). In an RCT assessing the efficacy of abatacept (ABA) in TAK, patients who achieved remission after 12 weeks of ABA were randomised to ABA and placebo arms and the GC dose was reduced to 20 mg/ day in the 12th week and discontinued at the end of the 28th week (72). The relapse-free survival was 22% and 40% in ABA and placebo groups respectively at the end of 12 months. In the RCT with TCZ, GC dose tapered 10% per week after 4 months of the initial dose. Relapse-free survival rates were 50% in the TCZ and 22% in the placebo group at the end of 24 weeks (73). In the extended follow-up results of this study, 0.1 mg/kg/d GC dose was achieved in 25% of the patients in 48 weeks (74). In line with these data, the majority of our panel members suggested that a lower dose of 5 mg/day GCs should be targeted at the end of the first year. An ongoing need for higher doses of GCs requires the revision of add-on IS regimens.

Recommendation 17: Since GC monotherapy is associated with high relapse rates, additional ISs should be considered in the initial remission-induction phase. (LoE: 3, SoR: B)

Due to the toxicity risk that may occur with long-term GC use and high relapse rates up to 80% during dose reduction with GC monotherapy, additional ISs are needed in the initial treatment of TAK. In a retrospective study, relapsefree survival rates were higher in the IS combination group compared to GC monotherapy, although the difference was not statistically significant (Relapsfree survival with GC monotherapy vs. combination 56% and 82% at 12 months, 56% and 70% at 24 months (HR, 1.20, p=0.77) (75). In open studies in which the treatment was started as GC monotherapy and ISs were added to the treatment in case of a relapse or persistent disease, 44-91% of the patients required immunosuppressives in addition to GCs (76-79).

Recommendation 18: In addition to GCs, methotrexate (MTX), azathioprine (AZA), leflunomide (LEF) or mycophenolate mofetil (MMF) may be the first choice for remission induction in TAK. (LoE: 3, SoR: B)

Efficacy of MTX, AZA, LEF or MMF on induction of remission and prevention of relapses were shown in various observational studies (63, 80-87). Only one study directly compared LEF and MTX prospectively and showed numerically higher number of patients with complete remission at 6th month with LEF, which did not reach statistical significance (29/40 vs. 15/28, p=0.44) (71). Each of these drugs can be used as the first-line ISs in patients with TAK.

Recommendation 19: Due to its possible side effects, cyclophosphamide (CyP) should only be considered in the presence of system/organ-threatening or refractory disease. (LoE 4, SoR: D)

CyP is a cytotoxic agent that has shown efficacy in treatment of patients with refractory TAK (76). Comparative studies with MTX and LEF demonstrated no difference in complete remission rates (69, 70, 88). Although there is paucity of data in TAK patients specifically, CyP has well-known side effects that can be listed as follows: opportunistic infections, myelosuppression, bladder toxicity and gonadal toxicity (89, 90). Because of these adverse effects and no proven superiority against other conventional immunosuppressives, CyP is only recommended for severe system/organ-threatening disease.

Recommendation 20: TNFi or TCZ can be considered in patients with relapsing or refractory disease despite conventional ISs. (LoE: 3, SoR: B)

Efficacy of TNFi on remission-induction and prevention of relapses in TAK was demonstrated in multiple observational studies (91-95). Although a RCT of TCZ vs. placebo failed to meet the primary endpoint for the time to first relapse (p=0.0596) (73), efficacy of TCZ has been suggested in numerous observational studies (96-99).

There is a limited number of studies comparing TNFi and TCZ retrospectively and no clear superiority between them has been shown (100-104). Although statistical significance was not reached, a numerically higher number of patients reached complete remission with TNFi in three studies (100, 103, 104) while two studies from the Mekinian et al. group showed contradictory results (101, 102). The panel favoured TNFi use due to longer-term experience and more extensive safety data in pregnancy for patients with TAK, predominantly consisting of women of reproductive age. TCZ can also be used, but it may influence acute phase reactants and complicate disease activity assessment.

Recommendation 21: Tapering or discontinuation of ISs may be considered for selected cases who have been in sustained remission (6–12 months). Tapering/discontinuation should start with GCs. (LoE: 4, SoR: D)

Optimal duration of ISs is unknown

for TAK. Clinicians should be aware of risks associated with long-term GCs and tapering or discontinuation of GCs should be considered in patients with remission longer than 6–12 months. Tapering should be slower in patients presented with organ/system threatening manifestations and patients with frequent relapses.

# Approach to comorbid diseases and pregnancies

Recommendation 22: There is insufficient evidence in the literature to support giving low-dose aspirin and statin treatments to all TAK for primary protection against cardiovascular risks. However, these treatments can be given to patients with conventional cardiovascular risk factors or to patients with high-risk arterial involvement (such as coronary, cerebral, pulmonary artery), with expert opinion. The risk of bleeding due to low-dose aspirin therapy is very low. (LoE: 4, SoR: D)

In a retrospective study, ischaemic strokes and transient ischaemic attacks were observed in 8.3% and 6.3% of TAK patients, respectively (77). Acute myocardial infarction occurred 12.5% and unstable angina in 4.2% cases. No TAK patient presented acute limb ischaemia or acute intestinal ischaemia. Other intermittent ischaemic manifestations attributed to arterial stenosis but not to arterial thrombosis were abdominal angina found in 4.2% and stable angina pectoris in 4.2% of TAK patients. Ischaemic events observed in TAK patients were mainly cardiovascular and cerebrovascular events and, similarly to GCA, those events have been shown to be preventable through aspirin use. The frequency of bleeding complications was very low in patients on antiplatelet therapy. Only one patient out of 30 who were on low dose aspirin treatment experienced significant vaginal bleeding, possibly due to uterine myoma, rather than low dose aspirin (77).

Recommendation 23: There is accelerated atherosclerosis in TAK which is considered to be secondary to inflammation. Cardiovascular risk is found to be higher in TAK cases than in control groups. Uncontrolled diabetes mellitus

and hyperlipidaemia can worsen the prognosis by accelerating atherosclerosis and causing aneurysm development. In addition to monitoring of blood pressure from appropriate extremities, signs of end-organ damage associated with HT such as hypertensive retinopathy, left ventricular hypertrophy and microalbuminuria should also be monitored. In the presence of diabetes mellitus, HT, and hyperlipidaemia, it is recommended to keep the GC dose lower. (LoE: 4, SoR: D)

Most of the studies in the literature that investigated the association of TAK and HT concentrate on the renovascular HT and HT due to the stenosis of aortic branches. There are no studies showing the negative impact of essential HT on TAK, but theoretically, all kinds of HT are expected to worsen the prognosis of TAK regardless of its aetiology.

History of HT increases the risk of developing atherosclerosis (OR=4.088). More importantly, if the LDL-C/HDL-C ratio was above the predicted cut-off value 3.038, the incidence of As increased by 8.5 times (p=0.023) and with TG/HDL-C ratio above predicted 0.909 cut-off value, by 3.725 times (105). The risk of aneurysms in patients with TAK with elevated serum LDL-C levels was 5.8-fold higher than that of patients with normal LDL-C levels (OR=5.767). The cut-off values of serum TG and LDL-C levels for increased aneurysm risk were 4.60 mmol/l and 3.08 mmol/l, respectively (106).

Recommendation 24: The most common inflammatory diseases that may accompany TAK are inflammatory bowel diseases (IBD) and axial spondyloarthritis (AxSpA). Closer monitoring is required in these patients and generally no difference in prognosis was observed. (LoE: 3, SoR: B)

TAK does co-occur with other inflammatory diseases such as IBD, AxSpA and less frequently with Behçet's syndrome in about 1/5 of the patients (107, 108). There is an increase in the use of biological treatments in AxSpA cases accompanied by TAK, compared to isolated AxSpA cases. TAK.SpA classified patients also required more biologic therapies than non-SpA patients (64.3%

vs. 29.1%, p=0.014) due to refractory TAK (109). In combined diseases, the management is determined by the treatment of the more severe and dominant disease. Usually, the other disease also benefits from this treatment.

Recommendation 25: The presence of TAK is not a contraindication to pregnancy. However, there are fetomaternal risks. All female patients of reproductive age diagnosed with TAK should be informed about pregnancy planning from the first visit. (LoE: 3, SoR: C) Previous studies have shown an increased risk of unfavourable fetomaternal outcomes among patients with TAK compared to the general population (110, 111). Preeclampsia (3–83%), prematurity (5-46%) and intrauterine growth retardation (4-52%) are the most important fetomaternal complications in TAK pregnancies. TAK has no effect on conception, but there is an increase in abortion rates (3–26%) (112). An increased risk of fetal malformations has not been reported.

Recommendation 26: In the preconception period, pregnancy risk status should be determined taking into account disease activity, extent of disease, course of arterial hypertension and cardiac functions. (LoE: 3, SoR: C)

The presence of high disease activity, extensive arterial involvement (especially abdominal aorta and renal arteries), uncontrolled arterial HT, and cardiac involvement have been reported to be associated with unfavourable fetomaternal outcomes (113-115). In the preconception period, evaluation of these risk factors and determining appropriate preventive strategies that may be needed are crucial for better fetomaternal outcomes.

Recommendation 27: Pregnancy planning should be postponed in the presence of active disease, uncontrolled arterial HT, PH, severe cardiac valve disease, and heart failure. (LoE: 3, SoR: C) The presence of active disease, uncontrolled arterial HT, PH, severe cardiac valve disease, and heart failure have been associated with unfavourable pregnancy outcomes including fetal

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Table III. Recommendations for co-morbid diseases and pregnancy.

n.	Recommendation	Level of evidence	External voting	Strength of recommendation
22	There is insufficient evidence in the literature to support giving low-dose aspirin and statin treatments to all TAK patients for primary protection against cardiovascular risks. However, these treatments can be given to patients with conventional cardiovascular risk factors or to patients with high-risk arterial involvement (such as coronary, cerebral, pulmonary artery), with expert opinion. The risk of bleeding due to low-dose aspirin therapy is very low.	4	8.41	D
23	There is accelerated atherosclerosis in TAK which is considered to be secondary to inflammation. Cardiovascular risk is found to be higher in TAK cases than in control groups. Uncontrolled diabetes mellitus and hyperlipidaemia can worsen the prognosis by accelerating atherosclerosis and causing aneurysm development. In addition to monitoring of blood pressure from appropriate extremities, signs of end organ damage associated with HT such as hypertensive retinopathy, left ventricular hypertrophy, and microalbuminuria should also be monitored. In the presence of diabetes mellitus, HT, and hyperlipidaemia, it is recommended to keep the glucocorticoid dose lower.	4	9.04	D
24	The most common inflammatory diseases that may accompany TAK are inflammatory bowel diseases, axial spondyloarthritis (AxSpA), and granulomatous diseases. Closer monitoring is required in these patients and generally no difference in prognosis was observed.	3	8.75	В
25	The presence of TAK is not a contraindication to pregnancy. However, there are fetomaternal risks. All female patients of reproductive age diagnosed with TAK should be informed about pregnancy planning from the first visit.	3	9.67	С
26	In the preconception period, pregnancy risk status should be determined taking into account disease activity, extent of disease, course of arterial HT and cardiac functions.	3	9.67	С
27	Pregnancy planning should be postponed in the presence of active disease, uncontrolled arterial HT, PH, severe cardiac valve disease, and heart failure.	3	9.71	С
28	In patients who need to continue medical treatment throughout pregnancy, immunosuppressive and antihypertensive medications that are currently being used should be modified to be suitable for pregnancy in the preconception period, and the efficacy of current medications should be monitored in sufficient time.	3	9.54	С
29	Patients who are considered to carry a high risk because of renal artery involvement, arterial HT, and heart involvement should be monitored more closely during pregnancy.	3	9.75	С
30	Low-dose aspirin therapy may be considered throughout pregnancy in cases of HT and increased disease activity due to the increased risk of preeclampsia and eclampsia.	3	8.33	С
31	TAK does not directly influence the preference of delivery method. In patients with impaired cardiac function, uncontrolled HT and risk of cerebral hypoperfusion, the mode of delivery should be decided on a multidisciplinary basis.	4	9.38	D
32	There are no data on unfavourable consequences of using oral contraceptives (OC) in TAK but considering the effects of OCs on thrombosis, barrier methods should be prioritised for contraception.	4	8.91	D

and maternal death (116-118).

Pregnancy can be considered when active disease and arterial HT are under control. There is a risk of maternal death in pregnant patients with TAK who have severe PH and heart failure, and it is recommended that those patients should not be encouraged to become pregnant (21, 119, 120).

Recommendation 28: In patients who need to continue medical treatment throughout pregnancy, ISs and antihypertensive medications that are cur-

rently being used should be modified to be suitable for pregnancy in the preconception period, and the efficacy of current medications should be monitored in sufficient time. (LoE: 3, SoR: C)

Data on the use of medications in pregnant women with TAK are very limited. There is no clinical study highlighting one of the immunosuppressive drugs more favourably in the pregnant patient with TAK. It is appropriate to avoid high doses of GCs as much as possible, especially in cases of hypertension or heart failure. Considering that serum

acute phase reactants physiologically increase during pregnancy, overdiagnosis of disease activity may be possible with these biomarkers alone, therefore they should be interpreted together with clinical findings. Low-dose GCs as well as azathioprine and TNF-inhibitors are compatible with pregnancy (116, 121). Current HT guidelines recommend labetalol, nifedipine, and methyldopa as acceptable first-line agents in pregnant women (122). Medical treatment of pregnant patients with TAK should be decided on an individual basis and the

Table IV. Recommendations on interventional approaches.

n.	Recommendation	Level of evidence	External voting	Strength of recommendation
33	In patients with TAK, medical therapy should be the first consideration. However, the need for vascular intervention should be evaluated in cases of haemodynamically significant vascular stenosis or occlusion despite effective immunosuppressive treatment.	3	9.39	С
34	The decision to pursue surgical intervention should be made by a multidisciplinary team, including a rheumatologist, cardiologist, neurologist, cardiovascular surgeon, and interventional radiologist, with consideration of the specific vascular region involved.	4	9.86	D
35	In cases where surgical intervention is necessary, it is crucial that patients receive adequate immunosuppressive therapy prior to the procedure to suppress disease activity. In emergency situations, vascular intervention should be carefully planned and performed under the protection of perioperative glucocorticoid therapy.	3	9.82	С
36	In patients with TAK, the indication for interventional procedures and the type of intervention (open surgery or endovascular procedure) can vary depending on the affected vascular region. Interventions involving vascular areas other than the lower extremities and renal arteries have been reported to carry significant risks. Therefore, caution is advised when considering vascular interventions in these regions.	3	8.86	С
37	In life-threatening situations, such as critical stenosis of the coronary and visceral arteries, emergency vascular intervention should be considered despite the associated risks.	4	9.43	С
38	In cases of renal artery involvement, endovascular intervention should be prioritised over open surgery. Balloon angioplasty is preferred due to its lower restenosis rate.	4	9.17	В
39	Given the risk of complications such as stroke and death, endovascular interventions should be the primary option in cases involving supra-aortic artery involvement.	4	8.43	В
40	In cases of coronary artery involvement, open surgery is generally more successful than percutaneous coronary interventions and may be the preferred option.	4	8.09	С

suitability of the planned medications for pregnancy should also be considered.

Recommendation 29: Patients who are considered to carry a high risk because of renal artery involvement, arterial HT, and heart involvement should be monitored more closely during pregnancy. (LoE: 3, SoR: C)

Pregnant women with TAK have an increased risk of developing or worsening HT and preeclampsia. Baseline HT and renal artery stenosis are risk factors for preeclampsia and prematurity (123). Similarly, different studies published in the past have emphasised that HT is one of the most important risk factors for unfavourable fetomaternal outcomes (124, 125). Patients with HT, renal artery involvement, and valvular heart involvement should be more closely monitored throughout pregnancy. HT should be treated optimally, to reduce the risk of preeclampsia/eclampsia. There is currently no data indicating that pregnancy is a factor that activates the disease or negatively affects disease long term outcome (126, 127).

Recommendation 30: Low-dose aspirin therapy may be considered throughout pregnancy in cases of HT and increased disease activity due to the increased risk of preeclampsia and eclampsia. (LoE: 3, SoR: C)

There is insufficient evidence to support the routine use of aspirin throughout pregnancy in pregnant women with TAK. However, the presence of HT and increased disease activity are risk factors for preeclampsia in pregnant women with TAK. Aspirin is known to reduce the risk of preeclampsia, and current gynaecological and obstetric guidelines recommend routine use of low-dose aspirin if there is an increased risk of preeclampsia (128-130).

Recommendation 31: TAK does not directly influence the preference of delivery method. In patients with impaired cardiac function, uncontrolled HT and risk of cerebral hypoperfusion, the mode of delivery should be decided on a multidisciplinary basis. (LoE: 4, SoR: D) While general anesthesia may affect

cerebral perfusion in patients with carotid artery involvement, uncontrolled HT endangers vaginal birth. The gynecologist, anesthesiologist, rheumatologist and, if necessary, a cardiologist should decide together on a case-bycase basis whether the method of delivery will be vaginal or by cesarean section (117, 121, 131).

Recommendation 32: There are no data on unfavourable consequences of using oral contraceptives (OC) in TAK but considering the effects of OCs on thrombosis, barrier methods should be prioritised for contraception. (LoE: 4, SoR: D) OCs affect haemostasis by a variety of mechanisms. They have procoagulant effects, increase coagulation factors and lead to increased activated protein C resistance by altering the balance of natural anticoagulants. The use of OC is known to increase the risk of thrombosis in the general population (132, 133). Although no data is available for OC use in TAK, the expert panel suggests the use of barrier methods preferably.

# Recommendations regarding vascular interventions

Recommendations 33: In patients with TAK, medical therapy should be the first consideration. However, the need for vascular intervention should be evaluated in cases of hemodynamically significant vascular stenosis or occlusion despite effective ISs. (LoE: 3, SoR: C) Research indicates that vascular intervention should not be prioritised due to its associated mortality risks in TAK patients. However, there have been documented reports where such interventions were necessary despite the efficacy of ISs (134-141). In a large cohort of 251 patients with TAK, 42 required surgical intervention for the aortic arch and its branches (52%), large vessels (24%), abdominal aorta (21%), and coronary arteries (4%) (141). In another cohort of 146 patients diagnosed with TAK, 61 required surgical intervention despite medical treatment (136).

Recommendation 34: The decision to pursue vascular intervention should be made by a multidisciplinary team, including a rheumatologist, cardiologist, neurologist, cardiovascular surgeon, and interventional radiologist, with consideration of the specific vascular region involved. (LoE: 4, SoR: D) An analysis of the results from two retrospective studies, which evaluated the long-term outcomes of open surgery and endovascular procedures highlighted the importance of a multidisciplinary approach and the optimisation of patient management to minimise postoperative complications (135, 136).

Recommendation 35: In cases where vascular intervention is necessary, it is crucial that patients receive adequate ISs prior to the procedure to suppress disease activity. In emergency situations, vascular intervention should be carefully planned and performed under the protection of a perioperative GCs. (LoE: 3, SoR: C)

Research has shown that patients who underwent vascular intervention during the active phase of TAK or who did not receive GCs or ISs prior to surgery experienced a higher rate of post-procedural failure and complications

(134-144). Patients with asymptomatic disease who did not require GCs may not undergo any revisions during follow-up, whereas patients with active disease who were not on long-term GCs had reported high revision rates (up to 67%) at both the 5-year and 10-year follow-up periods (141).

Recommendation 36: In patients with TAK, the indication for interventional procedures and the type of intervention (open surgery or endovascular procedure) can vary depending on the affected vascular region. Interventions involving vascular areas other than the lower extremities and renal arteries have been reported to carry significant risks. Therefore, caution is advised when considering vascular interventions in these regions. (LoE: 3, SoR: C) The assessment of multicentre retrospective outcomes for endovascular and open surgical interventions in patients with TAK revealed that complication and mortality rates varied depending on the specific organ and vessel affected, as well as the chosen intervention method (135-137). In one study involving 61 TAK patients who required surgical intervention, surgery-related mortality was reported in 6 patients (10%): one with an abdominal aortic aneurysm, two with aortic valve disease, two with superior mesenteric artery occlusion, and one with carotid artery disease (135). However, studies focusing on patients with renal artery involvement (145-147) and those with iliac artery involvement reported a lower incidence of significant complications (148).

Recommendation 37: In life-threatening situations, such as critical stenosis of the coronary and visceral arteries, emergency vascular intervention should be considered despite the associated risks. (LoE: 4, SoR: C)

In published retrospective studies, the primary indications for both endovascular and surgical interventions were vascular stenosis or occlusion, with smaller number of cases involving aneurysms and pseudoaneurysms. Additionally, there were reported instances of severe complications such as restenosis, bleeding, aortic dissection, and rupture

following the procedures (134-141). In long-term follow-up, 30 patients with TAK were scheduled for surgical procedures after achieving disease control. However, it was found that 5 patients required immediate intervention during the active disease phase due to critical end-organ involvement, such as coronary artery involvement (138). Fields et al. reported that among the 42 patients who required surgery, 6 underwent the procedure despite having active disease due to severe symptoms associated with the affected organs. Specifically, three patients experienced cerebrovascular events, two endured cardiac failure, and one suffered from both heart failure and acute renal failure (141).

Recommendation 38: In cases of renal artery involvement, endovascular intervention should be prioritised over open surgery. Balloon angioplasty is preferred due to its lower restenosis rate. (LoE: 3, SoR: B)

Research on patients with renal artery involvement has shown that endovascular intervention achieves better renal artery patency compared to surgical intervention with fewer complications due to its less invasive nature (145). Among endovascular procedures, balloon angioplasty has demonstrated superior outcomes in terms of procedural success (146, 147). In a study assessing the long-term endovascular results of 152 patients with renal artery involvement, encompassing a total of 188 renal arteries, 63 arteries were treated with stent placement, and 93 underwent balloon angioplasty. The restenosis rate for stent placement was 15 out of 63 arteries (23.8%), which was higher than the restenosis rate of 12 out of 125 (9.6%) observed with balloon angioplasty (147).

Recommendation 39: Given the risk of complications such as stroke and death, endovascular interventions should be preferred in cases involving supra-aortic artery involvement. (LoE: 3, SoR: B) Studies have shown that postoperative complications occur at higher rates following open surgery compared to endovascular procedures. In two studies that compared endovascular and surgical

interventions in patients with isolated supra-aortic involvement, stroke, and cerebral haemorrhage were reported after open surgery in 1/17 (6%) and 2/15 (13%) patients, respectively (149-150).

Recommendation 40: In cases of coronary artery involvement, open surgery is generally more successful than percutaneous coronary interventions and may be the preferred option. (LoE: 3, SoR: C)

Regarding success rates for coronary artery involvement, open surgery is superior to percutaneous coronary interventions. Published studies have reported higher rates of coronary artery restenosis in percutaneous coronary interventions, with rates of 39.3%, 63.2% and 56%, compared to significantly lower restenosis rates in coronary artery bypass grafting, reported as 8.7%, 25% and 20%, respectively (151-153).

### Discussion

The management and the follow-up of TAK patients are challenging for physicians during daily practice due to lack of validated biomarkers for clinical activity and insufficient randomised controlled trials for treatment. The low prevalence of TAK in most parts of the world also contributes to this challenge limiting clinical experience. The first TTASG recommendations deriving from a current literature review and large clinical experience, aim to guide clinicians not only in Turkey, but also in other countries who are providing health care to patients with TAK.

Among the various issues of disease management in TAK, probably the most controversial area is the use of imaging in disease follow-up. Although, new or increasing vascular lesions are found more frequently in patients with symptomatic clinical findings or increased acute-phase response, we recommend routine non-invasive imaging, as progression of vascular inflammation may occur even in patients with clinically-quiescent disease.

GCs is still the mainstay of treatment of TAK for remission-induction in both newly diagnosed and relapsing patients. We recommend high dose GCs (0.5–1 mg/kg/day prednisolone equivalent).

Although there is no data reporting the superiority of pulse GCs over high dose GCs, we recommend pulse GCs in the presence of severe organ involvement. Relapse rates range from 44-80% in patients with TAK under GC monotherapy (9, 73, 154). Despite a lack of solid data comparing conventional ISs and biologics as the first steroid-sparing agent, we recommend MTX, AZA, LEF or MMF as the first choice during remissioninduction in TAK. Due to its toxicity profile, CyP should only be considered in the presence of system/organ- threatening or refractory disease as the first choice. TNFi or TCZ can be considered in patients with relapsing or refractory disease despite conventional ISs.

We do not routinely suggest the use of anti-aggregant or cholesterol-lowering therapies due to a lack of data for their beneficial effects. However, close monitoring for accelerated atherosclerosis is mandatory in TAK, as a higher risk of cardiovascular events is observed. Among various co-morbid conditions, diseases in the spondyloarthropathy spectrum is the most prominent in TAK (inflammatory bowel disease, ankylosing spondylitis and psoriasis). Presence of a co-morbid inflammatory disorder complicates the management and therapeutic decisions should be made according to more severe disease spectrum.

order in reproductive ages, planning of pregnancy should be prioritised from the disease onset. Pregnancies during active disease increase feto-maternal complications and should be avoided. Despite new efficacious treatments such as biological agents, a significant portion of TAK patients require vascular interventions to prevent critical ischaemia. Endovascular interventions are preferably chosen for most arteries. Effective IS use is necessary to prevent re-occlusions.

As TAK is mainly a young female dis-

Long-term prognosis of TAK is currently better with therapeutic advances of ISs and endovascular interventions. However, as RCTs are very limited in number without conclusive results, most data come from case series with low-level evidence. Further multicentre, collaborative controlled trials are required to guide management decisions.

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