

Aortitis – An Interdisciplinary Challenge

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Abstract. *The term ‘aortitis’ comprises a heterogeneous spectrum of diseases, with varied etiology and clinical presentations, whose common characteristic is the inflammation of the aortic wall. Since aortitis can mimic almost all common cardiovascular disorders, its clinical recognition remains a challenge. Some cases of aortitis remain undetected for a long time and may be diagnosed after severe life-threatening complications have already arisen. The diagnosis of aortitis is based on the presence of homogeneous circumferential thickening of the aortic wall detected on aortic imaging, or typical histological features in combination with clinical findings and laboratory parameters. Management of aortitis is usually conservative (immunosuppressive drugs in noninfectious aortitis; antimicrobial drugs in infectious). However, if vascular complications such as aortic aneurysm, rupture, or steno-occlusive events appear, aortic surgery or endovascular therapy may be required. This review article summarizes the current knowledge regarding the etiology, clinical presentation, diagnosis, and treatment of inflammatory diseases of the aorta to promote better clinical management of these entities.*

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Like no other form of aortopathy, inflammatory diseases of the aorta comprise a broad spectrum of vascular disorders with a wide range of clinical manifestations and heterogeneous etiologies, including infectious aortitis (IA), noninfectious aortitis (NIA), or chronic inflammatory diseases with an aortic involvement (1-3). The broad clinical spectrum of aortitis ranges from asymptomatic incidental findings to acute aortic syndrome. The lack of widespread expertise often makes the diagnosis of aortitis an interdisciplinary challenge and may contribute to diagnostic error or delayed diagnosis (4, 5), associated with a high complication rate and poor prognosis. On appearance of severe life-threatening complications, individualized endovascular or open surgical treatment is required. The aim of this review was to address the current knowledge on the etiology, clinical presentation, diagnosis, and treatment of inflammatory diseases of the aorta to promote timely diagnosis, effective treatment, and close monitoring of these entities.

Epidemiology

The prevalence of aortitis among the population has been insufficiently investigated. The available data are mostly limited to retrospective evaluation of surgical aortic specimens from symptomatic or critically ill patients in whom aortitis has caused potentially life-threatening complications, such as aortic aneurysm and dissection. Therefore, no conclusions can be drawn on the epidemiology of aortitis in the general population.

A 12-year nationwide population-based study from Denmark of 1,210 surgical patients reported on the prevalence and predictors of aortitis (6). Aortic aneurysms and dissections were the most common (76.2%) indications for surgery.

Table I. Differential diagnostic spectrum of infectious and non-infectious aortitis.

Infectious aortitis (Selection of pathogens and associated diseases)	Non-infectious aortitis Modified classification based on the Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (CHCC) (26)
<p>Bacterial</p> <p><i>Staphylococcus</i> spp. (endocarditis)</p> <p><i>Streptococcus</i> spp. (endocarditis, pneumonia)</p> <p>Non-typhoid <i>Salmonella</i> spp. (enteritis)</p> <p><i>Escherichia</i> spp. (multiple infections)</p> <p><i>Treponema pallidum</i> (syphilis)</p> <p><i>Mycobacterium</i> ssp. (tuberculosis)</p> <p>Virus-associated aortitis</p> <p>HIV (AIDS)</p> <p>Hepatitis B</p> <p>Hepatitis C</p> <p><i>Herpes</i> spp. (Herpes zoster)</p> <p>Fungal* aortitis</p> <p><i>Candida</i> species</p> <p><i>Aspergillus</i></p> <p><i>Cryptococcus</i></p>	<p>Large-vessel vasculitis</p> <p>Takayasu arteritis (TA)</p> <p>Giant-cell arteritis (GCA)</p> <p>Small-vessel vasculitis</p> <p>Microscopic polyangiitis (MPA)</p> <p>Granulomatosis with polyangiitis (GPA)</p> <p>Variable vessel vasculitis</p> <p>Behcet's disease</p> <p>Cogan syndrome</p> <p>Single-organ vasculitis</p> <p>Isolated aortitis</p> <p>Vasculitis in systemic diseases</p> <p>Rheumatoid vasculitis</p> <p>Systemic vasculitis in sarcoidosis</p> <p>HLA-B27-positive seronegative spondyloarthropathies (ankylosing spondylitis, Reiter syndrome, etc.)</p> <p>Relapsing polychondritis</p> <p>Lupus vasculitis</p> <p>Vasculitis with probable etiology</p> <p>Hepatitis C virus-associated cryoglobulinemic vasculitis</p> <p>Hepatitis B virus-associated vasculitis</p> <p>Drug-associated immune complex vasculitis</p> <p>Vasculitis associated with tumors or radiation</p>

*Should not be confused with the historical description of the 'fungal-like' macroscopic aspect of a (mostly bacterial) mycotic aneurysm with subsequent aneurysm formation, first described in 1885 by William Osler in patients with infectious endocarditis (56).

Aortitis was found in 37 (6.1%) patients, with nearly three-quarters of cases being idiopathic and the rest being associated with diseases known to cause aortitis [giant-cell arteritis (GCA), Crohn's disease, rheumatoid arthritis, systemic lupus erythematosus, infections, and Marfan's disease]. Predictors of aortitis included a history of connective tissue disorders, diabetes, and aortic valve pathology.

Rojo-Leyva *et al.* assessed the prevalence of 'idiopathic' aortitis in a surgical cohort of patients, where 168 (14%) showed inflammation. The cause of the inflammation was as follows: 75 cases (6.2% of the cohort) were from a previous intervention or infection, 41 (3.4%) were due to arteriosclerosis, and the remaining 52 (4.3%) were described as 'idiopathic' (7).

Even though sufficient epidemiological data on the incidence of NIA are lacking, in some case series of patients undergoing aortic surgery, the frequency of autoimmune aortitis varied between 1.8% and 8.8% (7-9). Moreover, systematic screening examinations with various imaging

modalities in patients with GCA revealed an involvement of the aorta in 40-80% at the time of diagnosis (10-12). The number of unreported cases is likely to be high.

Classification

There is no universally accepted classification of this group of disorders. Regarding the major pathogenic mechanism, inflammatory diseases of the aorta are divided into two major groups (Table I), those caused by a direct inflammatory response to a pathogen ('infectious') and those caused by immunologically mediated inflammation of the vessel wall ('non-infectious'). However, over the past decade, it has been increasingly recognized that the relationship between infection and autoimmunity is complex and multifactorial and cannot be readily classified within these two categories. In vasculitis, for example, an infection can induce an NIA by generating immune complexes or cross-reactivity (13, 14). Moreover, primary infectious

Table II. *Rheumatic diseases with high prevalence ($\geq 10\%$) of aortic involvement [modified according to (57)].*

Giant cell arteritis (primary large-vessel vasculitis)	Common disease (incidence 3.5/100,000/year), Women > men, age >50 years General symptoms: Fatigue, fever, weight loss Cranial (temporal arteritis): New headache Hypersensitivity of the scalp, chewing and tongue pain, abnormalities of the temporal artery (pain, lumps, lack of pulse), visual disturbances Extracranial: Claudication of the upper and lower extremities
Takayasu arteritis (primary large-vessel vasculitis)	Rare disease (prevalence in Europe up to 30/million) Women > men, age <40-50 years 'Early, inflammatory-phase': General symptoms (fatigue, weight loss) 'Pulseless phase': syncope, ischemic stroke, claudication of the upper and lower extremities, arterial hypertension (renal arteries), angina pectoris (coronaries)
Cogan I – syndrome (variable vessel vasculitis)	A rare disease, women=men, mostly between the ages of 20-40 years. A characteristic common occurrence of eye inflammation (interstitial keratitis, uveitis, photophobia, visual disturbance) and an audio-vestibular disorder similar to Meniere's disease (internal deafness, dizziness)
Ankylosing spondylitis	Common disease (0.1 to 1.4% of the adult population, depending on the frequency of HLA-B27), men > women, mostly aged 20-40 years, deep-seated inflammatory back pain (sacroiliitis, spondylitis, creeping onset, improvement through movement)
Relapsing polychondritis	A rare disease, women < men, mostly aged 40-60 years. Chondrites of the auricle, nasal septum, respiratory tract, polyarthritis, eye inflammation, acoustic or vestibular dysfunction.

genesis is also discussed in many immunological diseases, in addition to the disposition to autoimmunity (13, 15). On the other hand, the use of corticosteroids and immunosuppressive drugs in patients with NIA may increase their susceptibility to secondary infections.

Therefore, it is not always certain whether it is processes directly caused by infectious pathogens, immunologically mediated inflammation (idiopathic or triggered by an infection), side-effects of treatment, or secondary bacterial infection as a result of immune suppression which play a key role in the pathogenesis of aortitis (16). In the future, new diagnostic methods may help to better elucidate the relationships between earlier infections and diseases (17).

Infectious Aortitis

IA is a rare but potentially life-threatening disorder, which, in contrast to NIA, is associated with a high rate of rupture and therefore requires prompt evaluation and treatment (1, 18, 19). Usually, IA results from hematogenous dissemination, septic embolization of the aortic vasa vasorum (*e.g.* infective endocarditis), contiguous spread from adjacent structures (*e.g.* from adjacent infected lymph nodes or lung foci), endovascular or open surgical intervention, or penetrating trauma. The abdominal aorta is affected in two-

thirds of cases. Positive blood cultures are found in 50-85% of patients with acute bacterial aortitis (20). Various microorganisms have been associated with IA, with the most common being *Staphylococcus* (30%), *Streptococcus* (20%), *Salmonella* (20%), *Escherichia coli* (15%), and others (15%) (21). While aortitis due to *Mycobacterium tuberculosis*, *Treponema pallidum*, β -hemolytic group A streptococci, *Pneumococcus* and *Hemophilus influenzae* have become very rare since targeted antibiotic regimens have been introduced, the prevalence of aortic infections associated with intravenous drug abuse (mainly caused by Gram-positive bacteria such as *Staphylococcus*, *Streptococcus*, and *Enterococcus*) and intravascular interventions have increased (22). Aortic graft infections are serious complications of open and endovascular surgery, with an incidence rate of 0.6-3% that are associated with 30-60% perioperative mortality and severe complications such as limb amputation rates between 10% and 40% (23-25).

Among the Gram-negative bacteria, in addition to *Escherichia* spp., *Salmonella* is particularly noteworthy. Nontyphoid *Salmonella* gastroenteritis is observed worldwide, with 100 million cases annually, and bacteremia is observed in about 10% of these patients. Given that endothelial involvement occurs in 10% of cases, the risk of *Salmonella*-associated aortitis is not insignificant (21).

Table III. *Spectrum of clinical presentation of aortitis.*

Clinical manifestations	Symptoms	Diagnosis
Incidental finding	Asymptomatic	Laboratory, ultrasound, other non-invasive vascular imaging modalities
Local and systemic inflammation	Fever (of unknown origin), fatigue, weight loss, chest, abdominal and back pain associated with general symptoms	Increased inflammatory laboratory tests (blood sedimentation rate, C-reactive protein, serum protein electrophoresis), targeted non-invasive vascular imaging modalities
Acute aortic syndrome	Intramural hematoma Aortic dissection Aortic rupture	D-Dimers Computed tomography
Heart	Acute or chronic aortic valve insufficiency. Stable angina pectoris or acute coronary syndrome	Echocardiography, cardiac biomarkers, non-invasive cardiovascular imaging modalities, coronary angiography
Other internal organs	Acute: Embolic complications (<i>e.g.</i> acute mesenteric or renal ischemia) Chronic: Steno-occlusive disease with chronic organic ischemia (<i>e.g.</i> renovascular hypertension, renal failure)	Non-invasive vascular imaging modalities (computed tomography, magnetic resonance, ultrasound)
Limb ischemia	Acute: Acute occlusion of the extremity arteries or acral embolization Chronic: Claudication	First choice of imaging modality - ultrasound, other non-invasive vascular imaging modalities (computed tomography, magnetic resonance)

Non-infectious Aortitis

According to the Chapel Hill Consensus classification of vasculitides (26), noninfectious vasculitides are classified according to the vessels affected into large, medium, small, and variable vessel vasculitis, single-organ vasculitis, vasculitis associated with systemic autoimmune disease, and vasculitis related to probable etiology. Aortic involvement is a common finding in patients with GCA and Takayasu arteritis (TA). Still, aortitis may occur in association with chronic inflammatory or systemic rheumatic diseases (*e.g.* rheumatoid arthritis, systemic lupus erythematosus rheumatoid arthritis, HLA-B27- associated spondyloarthropathy, Behcet's disease, sarcoidosis, Cogan syndrome, Crohn's disease, IgG4-related disease, and relapsing polychondritis), or idiopathic aortitis. Rheumatic diseases with a high prevalence of aortic involvement are summarized in Table II.

Regarding the etiology of isolated (idiopathic) aortitis, it is unclear whether this represents a distinct disease entity or a manifestation of primary vasculitis that is subclinical in other locations at the time of presentation. Other investigators found that isolated aortitis and primary vasculitis have different epidemiological and clinical profiles, and therefore postulated that they do not necessarily

represent the same disease (27). Furthermore, isolated aortitis does not fit the diagnostic criteria of GCA or TA (28, 29). However, it was recognized that some patients initially felt to have idiopathic aortitis actually had a systemic form of vasculitis, which fully manifested later (30).

Finally, other rare cases of aortitis associated with use of drugs, such as granulocyte colony-stimulating factor (31), as well as tumor chemotherapy and radiation therapy, have been reported (32, 33).

Clinical Presentation

The clinical presentation of aortitis is highly variable and often has nonspecific features. The clinical symptoms of aortitis include constitutional symptoms, such as fever, fatigue, or malaise caused by systemic inflammation and signs of ischemia due to regional involvement and ostial stenosis of the aortic branches or peripheral embolization. Depending on the location of the aortic involvement, the clinical spectrum of aortitis may include transient ischemic attack; stroke; angina pectoris; myocardial infarction; occlusive disease of the renal, splenic, or mesenteric arteries; and peripheral arterial occlusive disease (Table III). The symptoms of ischemia may develop over time or abruptly in cases of acute peripheral

Table IV. *Imaging modalities of aortitis.*

Imaging modalities	Properties	Findings
Ultrasound	High-resolution morphological and hemodynamic assessment of the aorta, outgoing vessels, and the aortic valve	Assessment of wall thickness and structure ('halo sign', degenerative changes), presentation of stenosis and occlusions, assessment of heart valves including differential diagnosis of valve endocarditis
Computed tomography	Excellent spatial resolution Overview display including 3D reconstruction and late venous phase Radiation and contrast medium exposure	Assessment of structural aortic changes (wall thickness and structure, such as ectasia, aneurysm, stenosis, calcification, occlusion, and thrombus) Limited use in the assessment of vascular wall inflammation
Magnetic resonance imaging	Good spatial resolution Better soft tissue assessment compared to computed tomography, no corresponding assessment of the calcification of the vascular wall	Assessment of early inflammatory vascular changes, as well as late structural changes, such as stenosis and aneurysms
Positron-emission tomography	Low spatial resolution but significantly increased in combination with computed tomography or magnetic resonance imaging	A very sensitive method for the detection of inflammation of the vascular wall

embolization. When the proximal aorta is involved, aortic valve regurgitation with symptoms of acute congestive heart failure can be present. The most common late manifestation of TA is occlusive disease of the aorta and great vessels from the arch of the aorta. In a recent meta-analysis by Kim *et al.*, the prevalence of ischemic complications such as stroke and myocardial infarction was 8.9% and 3.4%, respectively, during the disease course (34). In contrast to TA, GCA is more commonly associated with medial necrosis and aneurysm development. In a retrospective study, patients with GCA were 17 times more likely to develop thoracic aortic aneurysms and 2.4 times more likely to develop abdominal aortic aneurysms during follow-up than individuals of the same age from the general population (2). The incidence of aortic aneurysm and dissection is increased 5 years after GCA diagnosis. Moreover, aortic manifestations in GCA were associated with a 3.4-fold increase in mortality (35). Finally, aortic involvement in patients with primary large-vessel vasculitis is associated with higher cardiovascular and all-cause mortality as compared to patients without aortic manifestation (9).

The clinical presentation of IA is nonspecific. Generally, this diagnosis should be considered in elderly or immunocompromised patients with a previously degenerative damaged aortic wall presenting with back or abdominal pain, fever, and positive blood cultures.

Aortic Imaging

Non-invasive aortic imaging is an essential tool for diagnosing large-vessel vasculitis, and comprehensive reviews for its use

in clinical practice have been published (36, 37). Therefore, we only provide an overview of the different imaging modalities (Table IV) to shed light on some important aspects related to aortitis. Ultrasound (US), computed tomography (CT), magnetic resonance (MRI) imaging, and positron-emission tomography in combination with CT provide distinct and complementary information concerning the vascular involvement of large-vessel vasculitis. In addition to the method-related peculiarities, the choice of modality should be based on the availability and expertise in their use and interpretation.

Ultrasound. In 2018, the European League Against Rheumatism recommended that in patients with suspected large-vessel vasculitis, US and MRI should be the first choices (11). Based on the definitions of normal and abnormal arteries provided by the Outcome Measures in Rheumatology US Large Vessel Vasculitis Group (38), US can provide important initial information on the structure and thickness of the vascular wall (Figure 1). Furthermore, US can serve as a fast-track tool for visualizing some complications of aortitis, such as dissection or aneurysm. However, the European League Against Rheumatism points out the limited value of US in the assessment of aortitis, mainly due to limited access to the thoracic aorta (11).

Magnetic resonance. The increased vessel wall thickness of the aorta or its branches with linear mural contrast enhancement on T1-weighted sequences and vessel wall edema on T2-weighted sequences are key signs of vessel inflammation/hypervascularity (Figure 2) and are highly indicative of large-

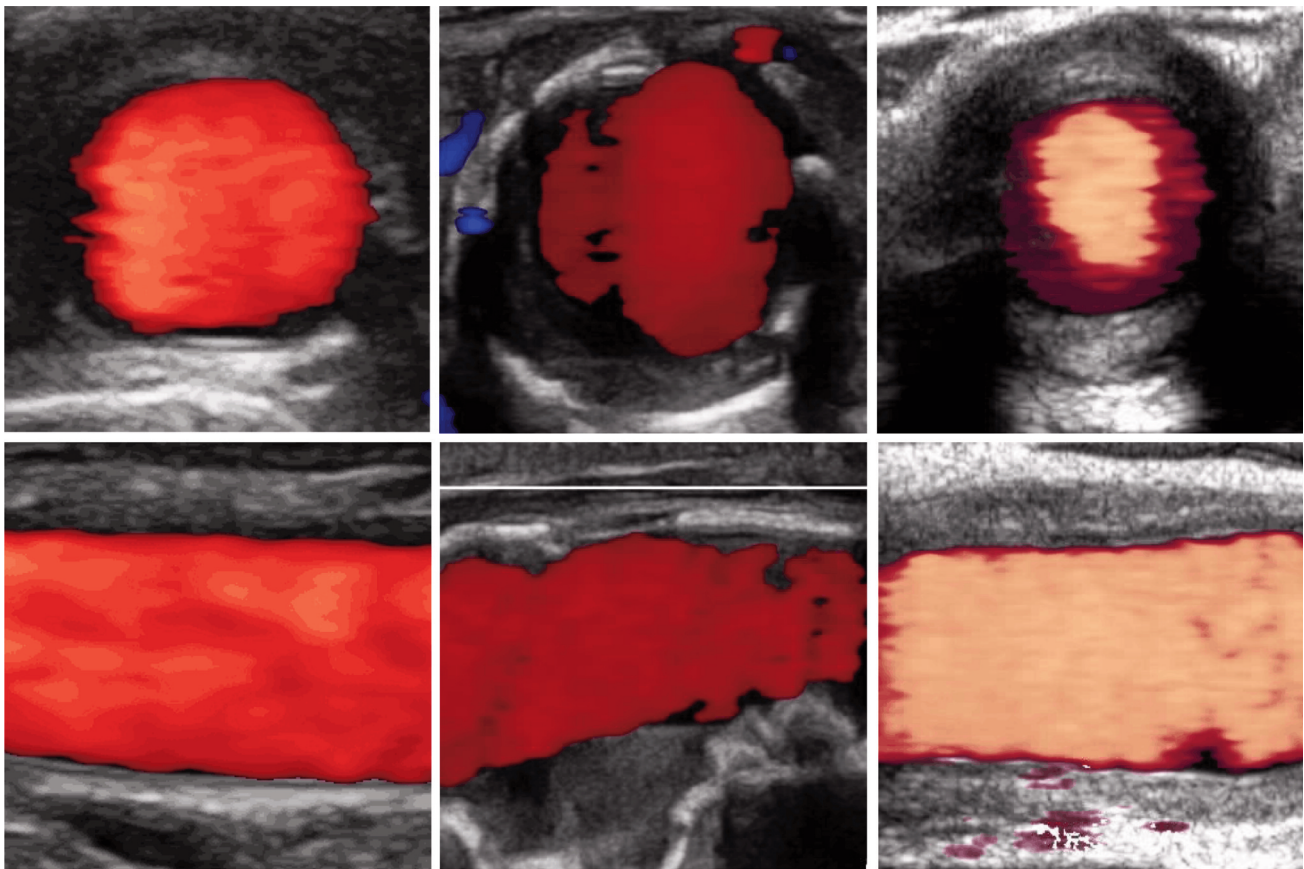


Figure 1. Typical ultrasound images of the abdominal aorta in transverse (upper panel) and longitudinal (lower panel) planes and their descriptions according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) definitions in giant-cell arteritis (38). Ultrasound images of a normal aorta (A), aorto-sclerosis (B) and aortitis (C). A: The intima-media complex of a normal abdominal aorta is narrow and presents as a homogenous, hypoechoic structure, delineated by two parallel hyperechoic margins ('double line pattern'), which is surrounded by mid-echoic to hyperechoic soft tissue. B: In contrast, the ultrasound image of the abdominal aorta of a 66-year-old man with generalized atherosclerosis shows heterogeneous and, in part, hyperechoic, irregularly delineated, and eccentric vessel wall alteration and wall-adherent thrombus formation. C: In the ultrasound image of the aorta of a 55-year-old woman with giant-cell vasculitis, the 'halo sign' is visible both in longitudinal and transverse planes: A homogenous, hypoechoic wall thickening, well-delineated towards the luminal side, most commonly concentric in transverse scans.

vessel vasculitis (39). When it comes to distinguishing the arterial wall from the neighboring soft tissues, the MRI technique is clearly superior to the CT technique. It is noteworthy that gadolinium enhancement is not specific for inflammation of the arterial wall and has also been shown in atherosclerotic plaques (40).

Computed tomography. Calcifying plaques are best visualized by CT, which can distinguish between atherosclerotic and inflammatory lesions. CT angiography may show arterial wall thickening with a double-ring pattern (mural enhancement and low-attenuation ring) (41) on delayed images (Figure 3).

PET in combination with CT. In the case of vessel wall inflammation in large-vessel vasculitis, the accumulation of

radiolabeled ^{18}F -fluorodeoxyglucose can provide a semiquantitative assessment of inflammation activity (Figure 4) (42), particularly in combination with CT, *e.g.* signs of diseases associated with vasculitis such as polymyalgia rheumatica (43). However, the specificity value of vessel ^{18}F -fluorodeoxyglucose uptake might be limited in the elderly, in whom age-associated vessel changes, including atherosclerosis, influence uptake. Therefore, discriminating between atherosclerotic and vasculitic lesions may be a challenge (44).

Histopathology

Histological analysis remains the gold standard for the diagnosis of large-vessel vasculitis (45). However, aortic biopsy is not performed routinely in suspected cases. The

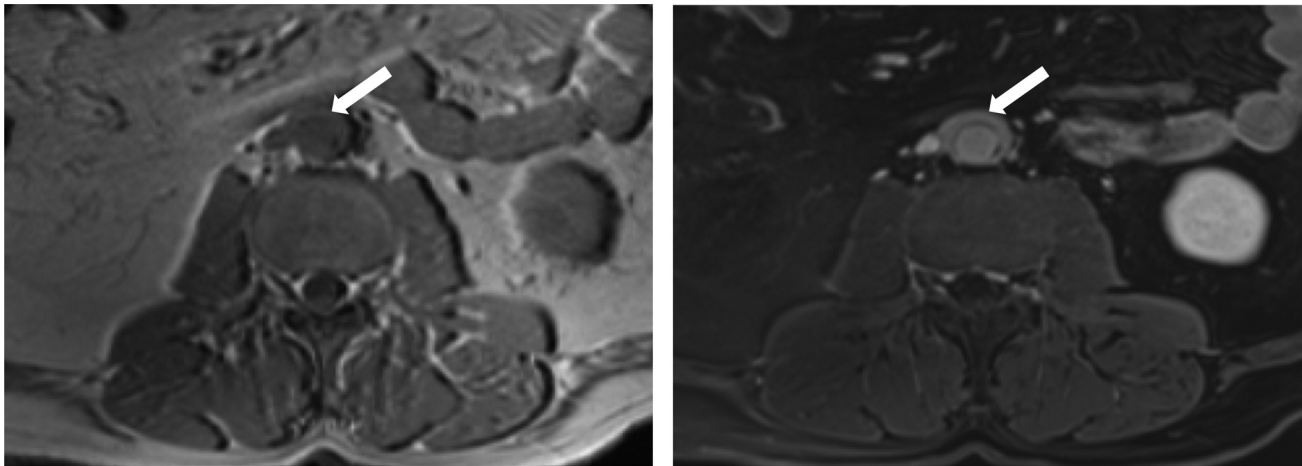


Figure 2. Magnetic resonance (MR) images of aortitis. A: Axial T1-weighted MR image prior to contrast material application shows a hyperintense circular cuff around the lumen of the abdominal aorta. B: Corresponding axial T1-weighted fat-suppressed post-contrast MR image demonstrates intense uptake by the thick cuff around the lumen of the abdominal aorta.

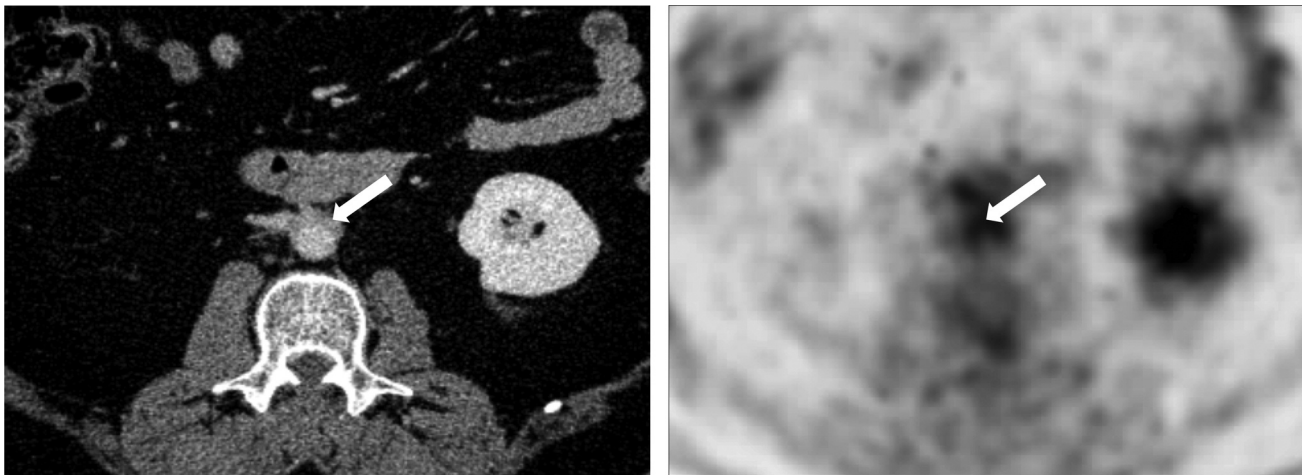


Figure 3. Computed tomographic angiography image of aortitis, correlating tracer uptake in positron-emission tomography imaging in combination with computed tomography and fused images. A: Axial post-contrast computed tomography in portal-venous phase shows semicircular thickening around the intraabdominal aortic wall in aortitis. B: Positron-emission tomography imaging in combination with computed tomography shows the corresponding semicircular tracer uptake around the aortic wall.

available data are limited to the results of histological assessment of surgical samples after operative therapy of large aortic aneurysms and dissections as well as postmortem samples. Therefore, more data are available from these critically ill patients than from those who underwent conservative non-surgical treatment. Aortitis may exhibit various histological patterns, which can also provide some information on the causes underlying these diseases. The Standards and Definitions Committee of the Society for

Cardiovascular Pathology and the Association for European Cardiovascular Pathology have issued guidelines for diagnosing aortic diseases in surgical pathology specimens (46). Histological assessment of surgical specimens of the aorta typically reveals four main patterns: Granulomatous/giant cell pattern (TA, GCA), lymphoplasmacytic pattern (IgG-aortitis, syphilitic aortitis, systemic lupus erythematosus-aortitis), neutrophilic pattern (IA), and mixed inflammatory pattern (Behcet's disease, Cogan syndrome, relapsing polychondritis).

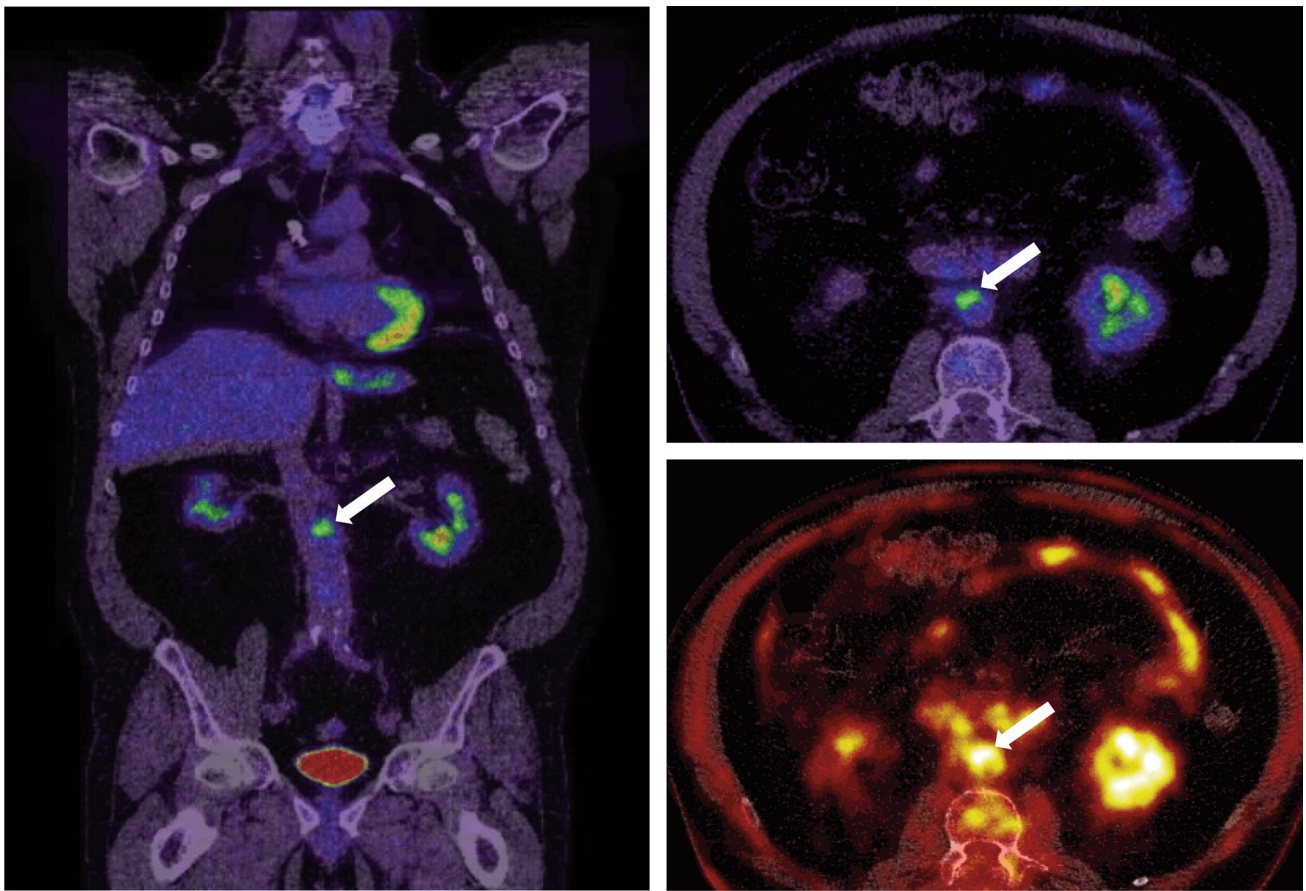


Figure 4. Positron-emission tomography imaging of aortitis in combination with computed tomography. A: Coronal view shows significant fluorodeoxyglucose uptake of the infra-abdominal aortic wall, suggesting inflammation in aortitis. B: Corresponding images in axial view (upper) and fused image (lower).

Most often, inflammation involves T-cells and macrophages and is transmural; however, it may also be more localized. For example, in the *vasa vasorum*, infiltration by eosinophils or neutrophils is rare. In addition to classic stains (hematoxylin-eosin, elastic fibers), tissue examination should also include immunohistochemical and molecular analyses (*e.g.* detection of pathogenic organisms based on polymerase chain reaction).

Biomarkers

Several inflammation-related biomarkers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), have emerged as part of the multimodal approach for the diagnosis of aortitis (47). The guidelines established by The American College of Rheumatology recommend ESR for the diagnostic assessment of GCA (48). However, these biomarkers are not specific and do not necessarily correlate with disease activity, and the correlation between serological levels of inflammatory markers and tracer uptake in PET findings

remain unclear (49). Furthermore, normal ESR or CRP levels do not rule out histologically active aortitis.

Several other parameters, such as heavy chain myosin of smooth vascular muscles, calponin, soluble elastin fragments, tenascin C, and various matrix metalloproteinases have been investigated. However, these parameters are not yet established in clinical practice. Pentraxin-3, a biomarker produced by vascular endothelial cells, smooth muscle cells, macrophages and neutrophils, has been proposed as a useful parameter for the assessment of disease activity. However, it is not specific for vascular wall inflammation. Nevertheless, its less dependence on cortisone therapy makes its use advantageous. Therefore, it can be useful for assessing the activity of large-vessel vasculitis under treatment in patients with normal CRP (50). Depending on the clinical manifestation, basic serological diagnostics should include the determination of antinuclear and anti-neutrophil cytoplasmic antibodies, rheumatoid factor, and anti-IgG4 antibodies. Notably, all these blood tests have limited sensitivity and specificity.

In summary, the assessment of the activity of aortitis can only be assessed in combination with clinical findings together with suitable laboratory parameters and sometimes additional imaging modalities.

Management

The specific treatment depends on whether the aortitis is caused by an infection or an autoimmune disorder and aims to stop disease progression and prevent and treat complications. Importantly, an essential part of aortitis treatment is the management of relevant cardiopulmonary comorbidities as well as the modification of cardiovascular risk factors, since these often determine the overall morbidity and mortality. Moreover, chronic inflammation along with long-term corticosteroid therapy may promote atherosclerosis and worsen some traditional risk factors associated with cardiovascular morbidity. Therefore, close monitoring of vascular complications is required.

Infectious aortitis. As a severe and potentially fatal disorder, IA requires rapid interdisciplinary assessment and treatment. As soon as the diagnosis of IA is suspected, broad-spectrum antibiotic therapy should be established. If the infectious agent is unknown, antibiotic therapy should target both Gram-positive and Gram-negative bacteria. The optimal duration of antibiotic treatment depends on several factors, such as the immune status. Overall, a treatment course of at least six to 12 weeks is generally recommended, and antibiotics are often given for 6 or 12 months, or even lifelong on an individual case basis (51). A fulminant clinical course of IA and complications such as aortic rupture, especially in cases of IA caused by Gram-negative bacteria, is not unusual (20, 52). Therefore, early open aortic surgery or catheter-based intervention (possibly as a ‘bridging’ procedure) must be evaluated. However, given that aortic surgery performed in the setting of acute infection is associated with a very high complication rate, as compared to those performed at the stage of controlled inflammation, the timing for intervention should be considered carefully. Ideally, the operation is performed after the acute infection and inflammation have resolved. Although open surgery is currently regarded as the gold-standard treatment for IA complicated with aortic aneurysm (51, 53), endovascular aortic repair is associated with superior short-term survival and may be considered particularly for critically ill high-risk patients. Infection-related complications and long-term survival were studied in a large European multicenter study of 123 patients treated for mycotic aortic aneurysms with endovascular aortic repair (54). The authors demonstrated the feasibility of this approach and reported a survival rate of 91% at 30 days and 75% at 1 year. Considering the significant number of infection-related deaths (19%) within a mean follow-up time of 35 months, nearly half of the deaths occurred after the discontinuation of antibiotic treatment. Advanced age, rupture,

suprarenal abdominal aneurysm location, and non-*Salmonella*-positive culture were associated with the adverse outcomes.

Non-infectious aortitis. In cases of suspected or proven aortitis treatment, the aim is to control inflammation, typically with corticosteroids and immunosuppressive drugs. Therapy for NIA can be based on the recommended therapy for primary vasculitis. High-dose glucocorticoid therapy (40-60 mg/day prednisone-equivalent) should be initiated immediately for induction of remission in NIA, associated with large-vessel vasculitis. Once a disease is controlled, the glucocorticoid dose should be reduced to a target dose of ≤ 5 -10 mg/day after 1 year. In addition to conventional immunosuppressants, adjunctive therapy may be required in selected patients with NIA due to GCA (with refractory or relapsing disease) using biologicals such as the interleukin-6 receptor antagonist tocilizumab (55). Methotrexate may be used as an alternative. Latent chronic infections (such as tuberculosis or chronic hepatitis) must be excluded prior to long-term immunosuppressive therapy. Regular follow-up and monitoring of disease activity are indispensable in all patients with aortitis and are primarily based on symptoms, clinical findings, and levels of inflammatory biomarkers. In the case of discrepancies, adequate imaging modalities may be helpful. Finally, long-term follow-up should be scheduled on an individual patient basis.

Conclusion

Inflammatory diseases of the aorta are severe vascular disorders with highly variable clinical presentation and etiology that require a multimodal, interdisciplinary approach, including good knowledge of rheumatic diseases, infectiology and histopathology, and multimodal imaging, as well as expertise in open aortic surgery and catheter-based interventions.

However, limited emphasis has been given to inflammatory diseases of the aorta, which are often associated with delayed diagnosis and a high complication rate. Due to the overall increasing size of the aging population, associated with the overall burden of cardiovascular disease, multimorbidity, the use of immunosuppressive agents as well as the expanded use of modern vascular and endovascular surgical techniques, the diagnosis of aortitis should be increasingly suspected.

Conflicts of Interest

All the Authors declare that there are no conflicts of interest regarding this review article.

Authors' Contributions

TS and MSi designed the article. TS, KA and MSi carried out a comprehensive literature search. MSi and MSa prepared the images and legends. KA and MK offered scientific advice. All Authors revised the article. MSi was the supervisor.

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