Review

Behçet's syndrome: one year in review 2026

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ABSTRACT

This critical review aims to highlight the publications on Behçet's syndrome (BS) during 2025. Recent studies have further elucidated the immunopathogenesis of BS, highlighting the interplay between innate and adaptive immune responses. Neutrophil hyperactivation, macrophage heterogeneity, and T cell imbalance emerge as central mechanisms, with growing evidence supporting the role of intercellular crosstalk and epigenetic regulation. Monocytes and non-coding RNAs emerge as areas of interest, while confirming the already established role of Th1/Th17 immune activation. These findings contribute to a more integrated understanding of disease mechanisms and may inform future targeted therapeutic strategies. While most studies are limited by small patient numbers and lack of validation in independent cohorts, the overall direction of research is encouraging. BS remains a diagnostically challenging systemic vasculitis. A meaningful proportion of patients develop significant organ damage without satisfying formal classification criteria. There is growing interest in the diagnostic utility of multimodal imaging for Behçet's uveitis. Phenotypic clustering offers a promising modality for understanding disease mechanisms, but there are substantial methodological inconsistencies across cohorts. Roflumilast and dusquetide might be promising agents for severe oral ulcers. Vascular involvement appears to be the most frequent de novo manifestation during treatment with monoclonal TNF inhibitors. High CRP level and large aneurysm diameter are associated with the need of surgery in patients with arterial involvement.

Introduction

Behçet's syndrome (BS) is a multisystem variable vessel vasculitis with a heterogeneous disease course affecting the skin, mucosa, musculoskeletal system, eyes, nervous system, gastrointestinal system and vessels of all size and type. The aim of this review is to provide a critical digest of the studies published during 2025, reporting on the epidemiology, immunopathogenesis, genetics, clinical manifestations, and management of BS.

Epidemiology

There are conflicting data on trends in the prevalence and incidence of BS in different countries. Some previous studies have suggested a decrease, which was attributed to improvements in environmental factors and hygiene (1). Others have shown an increase, attributed to improved recognition and diagnosis of this relatively rare condition (2, 3). A retrospective claims-based study showed an increasing trend in Germany (4). In this database of approximately 4 million people, the prevalence was 3.9, 4.1, and 4.7, and the incidence was 0.5, 0.5, and 0.6 per 100,000 in the years 2016, 2017 and 2018, respectively. Previous studies from Germany had reported prevalence estimates per 100,000 of 0.65 in 1984, 1.68 in 1989, 2.26 in 1994, 0.72 in 2005 and 0.9 in 2012 (5-7). Some of the earlier studies provided ethnicity-based analyses, showing higher rates among people of Turkish descent compared with ethnic Germans. However, this information was not available in the current claims-based study. Surprisingly, less than half of the patients received BS-related treatment, with glucocorticoids, colchicine and azathioprine being the most frequently prescribed drugs. The authors attributed this to the presence of mild forms of BS and a lack of disease awareness leading to undertreatment of BS in Germany. A similar increase in BS prevalence was reported from Norway over a 23-year period from 1999 to 2021 (8). BS prevalence increased

from 2.36 per 100,000 in 1999 to 7.14 per 100,000 in 2021. However, immigration from endemic countries and increasing use of the less specific ICBD criteria may be responsible for at least some of this increase. Overall incidence was 0.29 per 100,000 person-years and was higher among individuals of non-Norwegian ancestry. A claims-based study from Japan covering 2017-2021, showed that prevalence increased by 3% annually, whereas incidence decreased by 5% (9). Regarding clinical phenotypes, the frequency of gastrointestinal involvement decreased by 2% annually. The study also examined changing trends in management and observed a 5.6% increase in TNF inhibitor use. It may be speculated that the decrease in gastrointestinal involvement, which is a relatively late manifestation in the disease course, may be associated with increased use of TNF inhibitors for other manifestations. However, the data were not analysed to further explore this possibility.

There have been only a few previous reports of BS from sub-Saharan Africa. A systematic review of these reports until 2023 identified 2 children and 230 adults (69% men) (10). Interestingly, only 10% were HLA-B51/B5 positive, although it should be noted that HLA-B testing was available in only one third of the patients. Another interesting finding was the high neuro-Behçet's rate (39%), with parenchymal CNS involvement in 72% of them. Neuro-Behçet's was frequent among both patients living in sub-Saharan countries and those of sub-Saharan ancestry living in Europe or the Caribbean, suggesting a possible role for genetic rather than environmental factors. Almost half of the patients reported here were from Senegal, but there are no formal prevalence studies to assess differences in BS prevalence across sub-Saharan countries.

Take home messages

- Recent data suggest that the prevalence of BS is increasing in several countries, although changes in immigration patterns and disease recognition may contribute to the observed trends (4, 8, 9).
- BS is rare among individuals with sub-Saharan ancestry, with a high frequency of neurological involvement (10).

Immunology

Recent studies have further highlighted that BS arises from a complex interplay between innate and adaptive immune dysregulation, in which environmental triggers act on a genetically predisposed background, leading to a sustained inflammatory response with both autoinflammatory and autoimmune features (11). Over the past year, emerging evidence has refined this model, particularly by elucidating cellular crosstalk mechanisms and identifying novel molecular pathways potentially involved in disease expression and organ-specific damage.

A central role for innate immunity continues to be supported, with neutrophils and monocytes/macrophages emerging as key contributors to inflammation. Emerging data also suggest that monocytes may act as key initiating cells in the inflammatory cascade. Using freely available gene expression databases, a group applied a computational approach to identify five genes that could potentially serve as diagnostic markers for BS and also found that monocytes appear to be among the first immune cells activated in the disease (12). The study is entirely computer-based, with no new patient samples collected, which limits its immediate clinical relevance. However, the nomination of monocytes as a trigger cell population is consistent with findings from other recent studies, strengthening the overall case for their importance in BS.

Recent studies have highlighted that neutrophil hyperactivation remains a hallmark of BS, not only through increased reactive oxygen species production but also via enhanced formation of neutrophil extracellular traps (NETosis), which appear to correlate with disease activity and vary according to clinical status (13). These findings support a role for NETosis as a contributor to tissue and vascular damage rather than a simple epiphenomenon. In addition, recent experimental data suggest that modulation of metabolic and inflammasome pathways may attenuate neutrophil hyperactivation and NETosis (14). Beyond quantitative activation, emerging evidence suggests qualitative alterations in neutrophil function. In a recent study, defective neutrophil-derived exosomes were shown to impair their regulatory interaction with macrophages, leading to enhanced macrophage activation through dysregulated microRNA signalling (15). These observations further expand the concept that neutrophils may contribute to disease not only through direct effector functions but also via altered intercellular communication. Consistently, transcriptomic analyses have identified signatures of altered oxidative stress responses, interferon signalling, and pro-inflammatory cytokine production in neutrophils from BS patients, supporting their central involvement in disease pathogenesis.

In a recent study, a distinct subset of THBS1-high macrophages was identified in vascular BS and was associated with vascular inflammation and aneurysm-related remodelling through interaction with smooth muscle cells (16). These findings support a role for macrophage heterogeneity in vascular damage and further reinforce the importance of TNF-driven pathways in BS.

Adaptive immune dysregulation remains a key component of BS immunopathology. Recent studies have further highlighted T cell imbalance, characterised by expansion of Th1 and Th17 subsets and impaired regulatory T cell (Treg) function. In a recent single-cell analysis, naive CD4+ T cells were found to be reduced and to preferentially differentiate towards effector phenotypes, with enrichment of inflammatory pathways such as NF-κB and JAK-STAT signalling (17). This study identified IL-32 as a potential upstream regulator promoting Th1/Th17 polarisation, thereby linking systemic immune activation to local tissue inflammation. The role of the Th17 axis appears to be context-dependent. Emerging evidence suggests that increased IL-17 levels correlate with disease activity, particularly in mucocutaneous manifestations (18), although its contribution may vary across different organ involvements. These findings support a role for Th17 responses in selected dis-

ease phenotypes rather than a uniform pathogenic mechanism across all manifestations. In addition, reduced levels of regulatory cytokines such as IL-35 have been reported in neuro-Behçet's, supporting impaired immunoregulatory pathways (19).

Epigenetic regulation represents an additional layer of complexity in BS immunopathogenesis. In a recent integrated analysis of DNA hydroxymethylation and transcriptomic profiles, widespread alterations in immune-related pathways were observed, particularly those associated with pathogen response and cytokine signalling (20). These findings support a role for epigenetic mechanisms in modulating immune responses, potentially influencing the balance between effector and regulatory T cell subsets.

In addition to classical inflammatory pathways, recent studies have highlighted the potential contribution of cellular stress responses. Dysregulation of the integrated stress response, involving the eIF2α/ATF4 axis, has been reported in monocytes from BS patients, suggesting that intracellular stress signalling may contribute to immune activation independently of genetic susceptibility (21). These observations further expand current models of disease pathogenesis beyond traditional immune pathways.

Finally, recent studies have explored novel biomarkers to improve disease characterisation. Immune-related molecules, including cytokines, microRNAs, and specific immunoreactivities, such as those directed against neurofilament proteins, have shown potential diagnostic or disease-specific associations (22). However, these findings should be interpreted cautiously and require validation in larger and more diverse cohorts before clinical application.

In summary, recent evidence further supports a model of BS as a multi-layered immune disorder characterised by the convergence of innate and adaptive immune dysregulation. Neutrophil and macrophage dysfunction, T cell imbalance, and altered intercellular communication emerge as recurring themes. The integration of high-dimensional approaches, including single-cell and multi- omics analyses, is providing new insights into disease mechanisms and may contribute to the development of more targeted therapeutic strategies.

Take home messages

- Neutrophil and macrophage dysregulation, including NETosis and altered cell-cell interactions, remain central in BS pathogenesis (13, 14).
- T cell imbalance, particularly involving Th1/Th17 pathways and impaired regulation, continues to emerge as a key mechanism (17-19).
- Recent studies highlight additional layers, including epigenetic and stress-response pathways, contributing to disease complexity (20, 21).

Genetics

A study from China (23) asked a simple question: if we pool all the published genetic, protein, and metabolic data on BS, what picture emerges? The authors gathered data from multiple previous studies and identified 82 molecules that were consistently altered in BS patients. The main message is that BS is fundamentally driven by overactivation of two types of immune cells, Th1 and Th17, which then set off a chain of events including blood vessel damage and increased clotting tendency. This is not entirely new, but the study's value lies in bringing together three different types of biological data at once, giving a more complete picture than any single study could. The weakness is that it reanalyses old data rather than generating new experiments, so the findings are associative and not yet proven to be causal.

An Iranian group (24) measured the levels of two long non-coding RNAs (molecules called NEAT1 and HOTAIR) in BS patients and found them significantly altered compared to healthy controls, with changes correlating with inflammatory markers. Long non-coding RNAs are stretches of genetic material that do not code for proteins but regulate how other genes are switched on or off. This is the first study to place these specific molecules in the context of BS, and it opens a potentially important new avenue for biomarker research. The main limitation is the small number of patients studied, and the correlational design means we cannot yet say whether these molecules are causing inflammation or are simply a consequence of it. Independent replication is needed.

A group from Italy tested whether a previously described signature of three circulating microRNAs, small regulatory RNA molecules, that distinguish BS patients with vascular complications, is present in patients with antiphospholipid syndrome (APS) (25). They found that while the two diseases share some epigenetic features, the three-miRNA profile can discriminate between BS and APS in patients with vascular involvement, which could eventually have diagnostic value. The study is limited by small patient subgroups and the absence of follow-up data to track whether miRNA levels change with treatment.

Take home messages

- Non-coding RNAs, both lncRNAs and circulating miRNAs, are credible epigenetic contributors to BS and show early promise as disease biomarkers (24).
- Small sample sizes, ethnic homogeneity and lack of longitudinal validation are limitations that multicentre studies must address (24, 25).

Clinical manifestations

Diagnosis

A large tertiary-centre study showed that 15-40% of patients diagnosed with BS do not fulfil ISG or ICBD criteria, at presentation or during follow-up (26). Despite this, 31-48% develop major organ involvement and require immunosuppressive therapy. Similarly, a multicentre study identified that 41% of clinically diagnosed patients did not meet formal classification criteria at presentation (27). An inception cohort study of 55 patients with "probable" BS found that 81% presented with major organ involvement at baseline (28). It should be noted that patients with major organ involvement who do not fulfil criteria may be more prone to be labelled as BS, despite diagnostic uncertainty, in order to avoid treatment delay that can result in damage. On the other hand, physicians may be more likely to follow milder patients who

have only mucocutaneous involvement and do not fulfil criteria, with symptomatic topical measures and without a diagnostic label.

Eye involvement

Data from the international AIDA Network registry indicate that Arab ethnicity (OR 3.6), a positive family history (OR 4.32), and major oral aphthous ulcers (OR 3.26) significantly increase the risk of ocular involvement in patients initially presenting with only mucocutaneous symptoms (29).

Additionally, COVID-19 infection has been reported to be associated with an increased risk of uveitis flares in patients with BS (30).

Optical coherence tomography angiography (OCTA) has emerged as a valuable tool for detecting both subclinical and active retinal inflammation. Ghanbarnia *et al*. demonstrated an inverse relationship between retinal inflammation and vessel density (VSD), with the deep vascular complex showing greater susceptibility to inflammatory changes, suggesting that OCTA biomarkers hold promise for monitoring retinal inflammation (31). In parenchymal neuro-Behçet's patients without ocular involvement, significantly reduced VSD, particularly in the inferior peripapillary quadrant, along with a wider foveal avascular zone and decreased choriocapillaris flow were reported (32).

A study comparing ocular outcomes of Behçet's uveitis between the years 2009-2015 and 2016-2021 showed that sight-threatening complications such as macular oedema, cataracts and optic atrophy were less in the latter group and attributed this to early initiation of biological therapy (median 3.3 months) (33).

Musculoskeletal manifestations

Arthritis and arthralgia occur frequently as peripheral oligoarthritis, clustering with skin lesions (34). It is also noted that arthritis prevalence decreases over time. Enthesitis most often affects the Achilles tendon and co-occurs with arthritis, pustular skin lesions, and epididymitis (35). Musculoskeletal symptoms are associated with significantly worse quality of life (36).

Cardio-vascular involvement

Several imaging studies point toward better non-invasive detection of vascular inflammation. Superb microvascular imaging detected venous vessel-wall inflammatory signals in Behçet-related superficial thrombophlebitis more reliably than in non-Behçet lesions (37). Lower-extremity vein wall thickness was significantly increased in BS when compared to antiphospholipid syndrome, inflammatory bowel disease and healthy controls (38, 39). Pulmonary artery wall thickness on echocardiography was significantly elevated in BS, especially in those with major organ involvement (40). Shear wave elastography demonstrated that common carotid artery wall stiffness is increased in BS, especially during active disease (41).

DVT was the presenting manifestation in 16.7% of vascular BS patients, particularly young men, suggesting the need for early suspicion (42). Cardiovascular involvement affected 12.8% of patients in a large cross-sectional study from Shanghai, China, with lower-extremity DVT and aortic regurgitation as the most common manifestations (43). Pulmonary vascular involvement in BS occurs mainly in younger men and is frequently accompanied by parenchymal abnormalities such as ground-glass opacities and atelectasis as revealed in thoracic CT studies (44). A 5-year follow-up study showed that pulmonary hypertension in BS generally remained stable except in patients with Group 4 pulmonary hypertension related to pulmonary artery involvement (45).

Intracardiac thrombus is a severe, relapse-prone vascular complication of BS which is associated with venous involvement, pulmonary artery thrombosis and elevated inflammatory markers (46). Thrombus pathology is rich in neutrophils and macrophages. Arterial complications can be extreme, such as giant pseudoaneurysm in the subclavian artery (47). Aortic regurgitation driven by inflammatory aortic wall infiltration supports achieving remission with biologics before surgery (48). The histopathology of post-thrombotic venous leg ulcers in BS is more consistent with stasis dermatitis rather than frank vasculitis [49]. These ulcers often remain difficult to heal for many years despite intensive immunosuppressive and local wound care.

Neurological involvement

Neuro-Behçet's affected 10–15% of patients across cohorts, was predominantly parenchymal in form, and carried significantly higher mortality (50-52). A 30-year tertiary-centre study found no clear male predominance and identified an association with HLA-B51 (52). Cyclophosphamide and infliximab were associated with better neurological outcomes. Genital ulcers at disease onset and subsequent ocular involvement independently predicted CNS disease (51).

Phenotypic clustering

A systematic review reported that phenotype clusters across BS cohorts vary substantially, with much of the inconsistency stemming from methodological differences, rather than genuine biological variation (53). Clustering is a promising framework for dissecting disease pathogenesis; however, cross-cohort conclusions should be drawn carefully.

Within individual cohorts, four to five major phenotypic patterns emerge consistently, including mucocutaneous-articular, neuro-ocular, vascular-systemic with marked sex differences and distinct treatment needs across groups (54, 55). Large cohort surveys from Japan, Korea and multinational Europe, confirm that BS follows a more severe course in men, with more frequent ocular and vascular involvement (56-58). In line with these, HLA-B51 positivity is associated with male sex, ocular, CNS, and vascular involvement (57). Familial BS may present earlier, with more genital ulcers and papulo-pustular lesions (59). In children, seven overlapping clusters have been identified with meaningful regional variation across Turkey, Iran and Europe (60). The study suggests that BS heterogeneity begins well before adulthood.

Paediatric cohort

Many patients with paediatric-onset Behçet's developed new major organ involvement or relapsed after transition to adulthood, emphasising the need for

long-term follow-up during adulthood (61). In children, cardiac involvement was not rare: valvulitis and intracardiac thrombus were the main manifestations, and younger age, elevated ESR, higher platelet counts and erythema nodosum may help identify those at greatest risk (62). Early but clinically silent cardiovascular abnormalities can be seen in paediatric BS, including impaired ventricular performance, elevated pulmonary arterial pressure, and increased aortic stiffness (63).

Pregnancy

Pregnancy outcomes were generally reassuring, with flares mainly mucocutaneous or articular (64). There were no neonatal deaths reported among 153 pregnancies.

Disease activity and damage

Higher disease activity correlates with worse dermatologic quality of life, greater anxiety and depressive symptoms (65). Sleep and circadian disturbances are mainly linked to active disease and fibromyalgia (66). On the other hand, elevated obstructive sleep apnoea risk is seen across the broader BS population. BS overall damage index (BODI) was validated as a reliable damage assessment tool for retrospective BS studies. However, several clinically relevant damage items, including hypertension, glaucoma, liver failure, lung parenchymal involvement, and lymphedema are missing (67).

Miscellaneous

Trisomy 8-associated autoinflammatory disease differs from BS by featuring older age at onset, prominent fever and gastrointestinal involvement, fewer classic mucocutaneous and ocular features, and substantially higher mortality (68). BS could be associated with impaired mucociliary clearance and reduced olfactory function (69).

Take home messages

- Classification criteria are insufficient in real-word practice and many patients who do not fulfil criteria have major organ involvement requiring immunosuppressive treatment (26-28).
- Phenotypic clustering offers promise in understanding disease mechanisms, yet cross-cohort comparisons remain unreliable without methodological standardisation (53).
- Male sex and HLA-B51 positivity define a more severe disease subgroup with more frequent ocular, vascular, and CNS involvement (42, 44, 54-58).

Management

Emerging drugs

Roflumilast, a PDE4 inhibitor that is approved for chronic obstructive lung disease, has higher binding affinity and longer plasma half-life than apremilast. A single centre, 12-week study from Korea showed beneficial effect of roflumilast on 46 patients (37 BS, 9 recurrent aphthous stomatitis) having active oral ulcers despite conventional treatment (70). The response rate at week 12 was 92% with per protocol analysis and 72% with intention to treat analysis. Ten patients discontinued the trial mostly due to gastrointestinal (GI) adverse events. Similarly, a longer multicentre study from Spain also reported beneficial results on 33 patients (22 recurrent aphthous stomatitis, 11 BS patients) during treatment with roflumilast for 52 weeks (71).

Dusquetide is a novel innate defence regulator showing promise in suppressing severe oral mucositis induced by chemotherapy and radiotherapy for head and neck cancer. A pilot, open-label trial tested the efficacy of dusquetide on 8 BS patients with active oral ulcers (72). Given as twice weekly infusions for 4 weeks, dusquetide was effective in reducing the number, duration and pain of ulcers in 7 patients. Its effect persisted for 4 weeks follow-up after stopping treatment. The area under the curve for ulcer days was similar to that seen with the active arm of the placebo controlled apremilast trial. These encouraging results await confirmation with further studies.

A retrospective, multicentre study compared apremilast 30 mg twice daily with TNF inhibitors in the treatment of refractory oral ulcers of BS (73). There were 39 patients in each study arm, two-thirds receiving apremilast (64%) or TNF inhibitors (67%) for the first time. Patients allocated to TNF inhibitors had more frequent major organ involvement. Compared to baseline, both treatment arms significantly suppressed oral and genital ulcers at 3 and 6 months with no difference between groups. The steroid sparing effect was more prominent with apremilast, possibly reflecting physician reluctance in decreasing steroids in the TNF inhibitors group because of more frequent major organ involvement.

TNF inhibitors

TNF inhibitors, especially infliximab (IFX) and adalimumab (ADA) are now being increasingly used even as first line agents for severe manifestations of BS. A previous observation with IFX had shown de novo emergence of new manifestations in 7% of the patients (74). This time, a retrospective study evaluated 335 BS patients (63% men) for the development new manifestations after the initiation of ADA (75). Uveitis was the most frequent (39%) indication for ADA followed by vascular involvement (24%) and arthritis (18%). During a median follow-up of 23 months, 14 patients (4%) developed a new manifestation. Vascular involvement was again the most frequently occurring new manifestation (5 patients) followed by arthritis (3 patients) and parenchymal CNS involvement (2 patients). These manifestations were mainly managed by switching to another biologic or intensifying the dose of adalimumab.

A single-centre, retrospective study from Italy looked at drug retention rates in 60 BS patients (57% women) treated with IFX for various indications over a period of 20 years (76). The median duration of treatment was 37 months and the retention rates at 1, 2 and 5 years were 78%, 63% and 35%, respectively. The most common reasons for discontinuation were loss of efficacy (25%), emergence of *de novo* manifestations (21%) and allergy (18%). The higher frequency of de novo manifestations compared to those reported in the above-mentioned studies might be explained with longer duration of follow-up. The type of organ involvement had no impact on the discontinua-

tion of IFX. There was a trend for more frequent use of IFX for mucocutaneous manifestations over time.

A retrospective study from Japan looked at risk factors that predict switching from conventional agents to TNF inhibitors in 63 BS patients with GI involvement (77). During a median follow-up of 36 months (range 1 to 231 months) 35 patients (56%) continued on conventional agents, with 89% of them achieving endoscopic remission and 28 patients (44%) required switch to TNF inhibitors. High CRP, large ulcer size, proton pump inhibitors use and haematochezia were independent risk factors for switching to TNF inhibitors. Of 28 patients switching to TNF inhibitors, 22 (79%) continued this treatment for at least 1 year with the majority of them achieving clinical and endoscopic remission.

A systematic review and meta-analysis from China assessed the efficacy and safety of monoclonal TNF inhibitors in the treatment of vascular involvement (78). Included were 12 studies involving 297 BS patients. Not surprisingly, venous involvement was more frequent than arterial involvement. IFX was the most frequently used TNF inhibitor (81%), followed by ADA (16%) and golimumab (3%). Except for 2 patients receiving TNF inhibitors as first line treatment, all patients were refractory to conventional agents. The clinical response was 95% at 12 months and the radiological response was 93% at 6 months. The reported frequency of severe adverse events was 11% with infections being the most common cause (45%).

Surgery

A retrospective study from Korea looked at the long-term outcome of 30 BS patients who underwent a total of 54 operations for arterial involvement during a period of 30 years (79). The majority of the patients had thoracic (5 patients) or abdominal (10 patients) aorta aneurysms, 14 had peripheral artery involvement and 1 had visceral artery involvement. The initial operations were open surgery in 21 patients and endovascular intervention in 9 patients. Endovascular intervention was mainly selected for abdominal aorta aneurysms and open surgery was preferred for peripheral artery involvement. Twelve patients needed 24 re-operations with 1 patient experiencing 5 re-operations. The overall survival rates at 1, 5 and 15 years were 97%, 93% and 87%, respectively. Post-operative medication use was similar among patients needing re-operation and those not needing re-operation.

A retrospective study from China compared surgical and medical treatment among 96 BS patients with 151 arterial aneurysms (80). Fifty-nine patients (46%) were treated surgically and 37 patients received medical treatment only. CRP was significantly higher and pseudoaneurysms were larger in the surgery group. During a median follow-up of 53 months 10 patients in the medical treatment group and 2 in the surgery group died. The risk of rupture was higher when the diameter exceeded 4.0 cm for abdominal aneurysms and 2.5 cm for peripheral aneurysms.

Finally, EULAR has issued the 2025 update of the EULAR Recommendations for the management of BS. However, these recommendations are beyond the scope of the review, as they were published in 2026 (81).

Take-home messages

- Apremilast might be an alternative to TNF inhibitors for refractory oral and genital ulcers in patients with no major organ involvement (73).
- High CRP, large ulcer size, PPI use and haematochezia appear to be independent risk factors predicting switch to TNF inhibitors in patients with gastrointestinal involvement (77).
- Pulmonary artery involvement responds more favourably to monoclonal TNF inhibitors compared to other forms of vascular involvement (78).

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