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REVIEW

Ongoing projects of Turkish Vasculitis Study Group (TRVaS): an update

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ABSTRACT

The Hacettepe University Vasculitis Research Centre (HUVAC) initiated prospective patient registration in 2014 to advance clinical and translational research in vasculitis. The transition to a web-based platform enabled the establishment of the Turkey Vasculitis Study Group (TRVaS), which was formally launched in 2021. By 2025, TRVaS had expanded from its initial six centers to a nationwide network comprising 46 centers—14 pediatric and 32 adult rheumatology clinics. Since its inception, TRVaS has developed structured, disease-specific registries and initiated multiple multicenter projects at both national and international levels. TRVaS continues to strengthen Türkiye's vasculitis research capacity by fostering data collection, promoting large-scale collaboration, and enabling high-quality clinical and translational studies that contribute to global scientific efforts.

Keywords: collaborative networks, national registry, prospective data, vasculitis.

INTRODUCTION

The Hacettepe University Vasculitis Research Centre (HUVAC) was established in May 2014 with the initiation of prospective patient registration to advance clinical and translational research in vasculitis. In 2020, the registry transitioned to a web-based platform, facilitating the development of the Turkey Vasculitis Study Group (TRVaS), which was formally launched in 2021 with an inventory encompassing all vasculitis subtypes and initially involving six centers. By 2025, TRVaS had expanded to include 46 centers — 14 pediatric and 32 adult rheumatology clinics — thereby fostering broader national collaboration (Figure 1). This chapter provides an updated overview of the ongoing projects and key developments within TRVaS.

1. Projects on ANCA-associated vasculitis

1.1. Disease-specific form

A disease-specific form for ANCA-associated vasculitis (AAV) has been developed within the TRVaS database to systematically capture baseline characteristics and clinical information of patients diagnosed with AAV. The form remains active and open for data entry. The data collected will allow a comprehensive evaluation of disease features, treatment protocols, and therapeutic responses in this patient population.

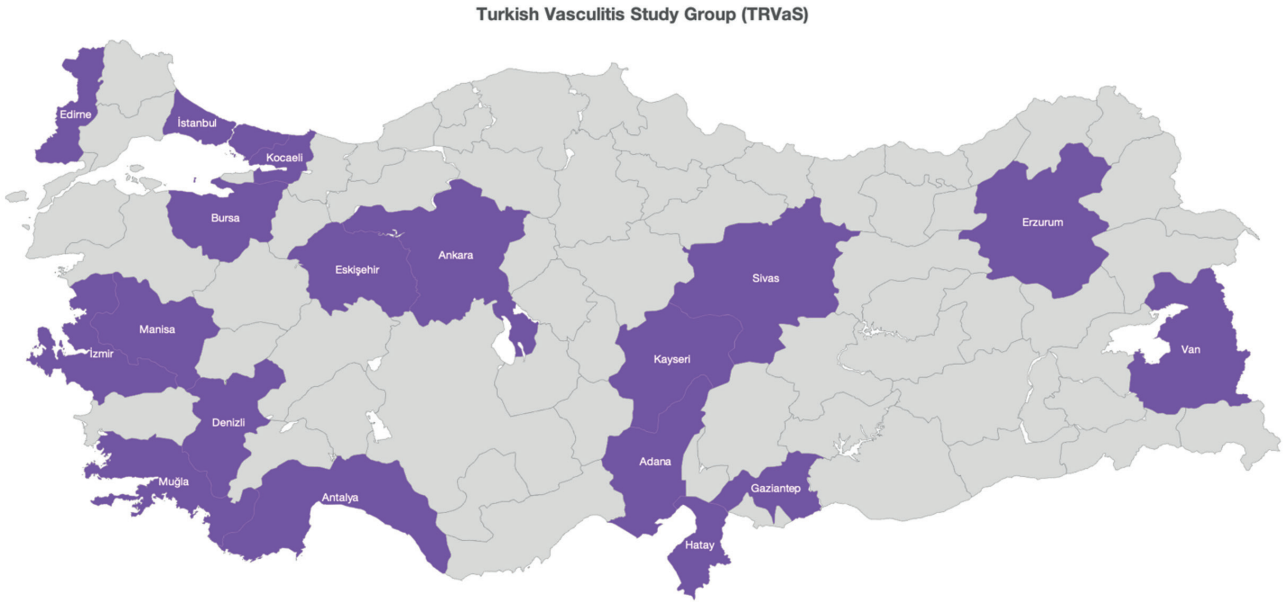

Figure 1. Distribution of TRVaS centers in Turkey. Provinces shown in purple indicate regions with adult and/or pediatric rheumatology centers.

1.2. AAV-Metabolic syndrome

Metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors, including insulin resistance, obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low levels of high-density lipoprotein (HDL) cholesterol. The presence of MetS is associated with an increased risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM).

Recent studies have suggested that the elevated cardiovascular risk observed in patients with AAV may be partly explained by the high prevalence of MetS in this population [1,2]. MetS provides a simple, reliable, and cost-effective indicator of increased risk for both CVD and T2DM. However, data regarding the prevalence of MetS and its associated risk factors in patients with AAV remain limited [3].

To date, a single-center study, which included 37 patients with AAV, has demonstrated an increased frequency of MetS in this patient group [4]. Building on these findings, we have launched the "Multicenter Study on the Prevalence of Metabolic Syndrome in Patients with ANCA-Associated Vasculitis (AAA-METS)" under the umbrella of the Turkey Vasculitis Database (TRVaS), bringing together vasculitis referral centers across Türkiye. This extensive, multicenter study aims to: a. Determine the prevalence of MetS in a broader AAV patient cohort, b. Investigate the association between MetS and clinical/laboratory parameters of AAV, c. Clarify the potential role of MetS in the pathogenesis and cardiovascular comorbidity burden of AAV. The project is still ongoing.

1.3. Understanding Central Nervous System Disease in AAV

Central nervous system (CNS) involvement in AAV is clinically essential but often under-recognized. Reported in about 7–11% of patients overall, CNS disease may manifest as ischemic stroke, intracranial hemorrhage, posterior reversible encephalopathy syndrome (PRES), hypertrophic pachymeningitis, pituitary lesions, spinal cord involvement, seizures, cognitive impairment, and other neuropsychiatric features [5]. Although survival is generally comparable to other AAV phenotypes, persistent neurological sequelae are frequent, especially with pachymeningeal or vasculitic CNS lesions [6]. Evidence to date is mostly from small, single-center series.

To address this gap, the TRVaS has introduced a dedicated CNS involvement form within its national AAV registry. This form collects demographic data, the timing and type of CNS disease (diagnosis vs. relapse), neurological symptoms, modified Rankin Scale (mRS) scores, imaging and CSF findings, histopathology (when available), treatment regimens, and outcomes, including relapse and survival. The AAV-CNS Project aims to: a. Define the prevalence and spectrum of CNS

manifestations in a large multicenter Turkish AAV cohort. b. Characterize clinical, radiological, and immunological patterns, including granulomatous vs vasculitic phenotypes. c. Evaluate treatment strategies, relapse risk, and long-term neurological outcomes.

1.4. Severe infections in patients with AAV and Outcome

Rituximab (RTX) and cyclophosphamide (CYC) are the two most widely used immunosuppressive agents for induction therapy in AAV. While highly effective, both agents are associated with an increased risk of serious infections, which remain a significant cause of morbidity and can significantly affect treatment decisions and long-term outcomes. This project aims to determine the frequency and spectrum of serious infections (grade ≥3 according to Common Terminology Criteria for Adverse Events [CTCAE] v5.0) in patients with organ/life-threatening AAV treated with RTX or CYC. Explore the association between hypogammaglobulinemia and infection risk in these patients. Compare the incidence and characteristics of serious infections in patients with organ-/life-threatening AAV versus those without such severe involvements.

1.5. AAV Projects in Development

Several additional projects are currently underway. The planned introduction of a visit-based follow-up form will enable longitudinal data collection.

The AAV Pulmonary Involvement Project aims to characterize the clinical and radiological features of AAV-associated interstitial lung disease (ILD), evaluate treatment response and disease progression through serial high-resolution chest CT (HRCT) scans, and identify clinical and serological predictors of radiologic progression and outcomes in patients with AAV-ILD.

The AAV Renal Pathology and Prognosis Project seeks to assess the predictive value of renal histopathological scoring systems (applied to kidney biopsy specimens) for determining 6-month renal function and long-term renal survival in AAV. It also aims to correlate histopathological findings with clinical parameters, treatment strategies, and renal outcomes to improve prognostic stratification and guide therapeutic decision-making.

1.6. Submitted TRVaS_AAV Projects

Two recent TRVaS projects have been completed and are currently under peer review in international journals. The first study demonstrated the importance of screening for osteoporosis among patients with AAV. The second study highlighted that the risk of venous thromboembolism is particularly elevated in the early phases of AAV and may be influenced by a high body mass index and disease activity. These results are expected to raise awareness and contribute to the optimization of comorbidity screening in AAV management.

2. Projects on IgG4-Related Disease (IgG4-RD)

In 2022, a baseline registration form for patients with IgG4-RD was established within the TRVaS database to capture disease and treatment-related characteristics systematically. This form records the key variables required for classification according to IgG4-RD criteria, together with detailed clinical, radiological, serological, and histopathological features. The initial data collected through this registry have provided the first multicenter overview of IgG4-RD in Türkiye. They are expected to inform both clinical practice and future research on disease course and treatment outcomes [7].

To facilitate longitudinal follow-up, a yearly visit form was subsequently developed. This form records treatment exposure, disease activity using the IgG4-RD Responder Index, organ involvement over time, damage assessment, physician global disease activity scores, and key laboratory parameters during follow-up. Both forms remain active and open for ongoing data entry, supporting the continuous expansion and refinement of the national IgG4-RD cohort.

3. Projects on IgA vasculitis

A disease-specific form for IgA vasculitis (IgAV) in both children and adults was developed within the TRVaS database to systematically record key disease characteristics, including time of diagnosis, clinical course, laboratory findings, histopathology (when available), presence of comorbidities, and treatment

approaches. This registry was designed to enhance physicians' understanding of the epidemiological and clinical spectrum of IgAV across different age groups, identify prognostic factors, and inform evidence-based follow-up algorithms for patients affected by IgAV. The first analysis of this cohort was published this year, providing new multicenter insights into the presentation and outcomes of IgAV [8]. The form remains active and open for data entry, supporting ongoing and future research projects aimed at improving the management and long-term outcomes of IgAV.

4. Projects on Polyarteritis Nodosa

The rarity of polyarteritis nodosa (PAN) necessitates global collaboration better to define the characteristics and outcomes of this disease spectrum. The GLOBAL-PAN projects represent such an effort, bringing together the TRVaS and European Vasculitis Study Group (EUVAS), the Vasculitis Clinical Research Consortium (VCRC), and several national PAN cohorts. The first investigation from this initiative, GLOBAL PAN-I, published in 2024, reported on the clinical features, laboratory findings, and survival analysis of 358 patients with either cutaneous or systemic PAN [9].

In addition to recent progress, essential aspects of PAN remain unclear, including the geographic influences on clinical presentation, the natural disease course, relapse patterns, and the relationship between monogenic subtypes (FMF-PAN, DADA2-PAN, VEXAS-PAN) and classic PAN. The GLOBAL-PAN II study aims to address these questions by including a larger multinational cohort, which will enable a more precise characterization of disease phenotypes. The initiation of this project is expected in the near future.

As part of long-term objectives, the collaborative group has initiated GLOBAL PAN-III, a new multicenter project designed to investigate genetic susceptibility in PAN, conducted in continued partnership with the University of Pittsburgh, USA. Early results of this project will be presented at the 22nd International Vasculitis Workshop in 2026.

5. Projects on Giant Cell Arteritis

In patients with giant cell arteritis (GCA), both inflammation-induced accelerated atherosclerosis and advanced age contribute to concerns regarding an increased risk of cardiovascular disease. To address this issue, the TRVaS GCA Ankara longitudinal cohort was established this year to investigate the prevalence and characteristics of cardiovascular comorbidities in GCA. This project is currently ongoing, and patients enrolled will be prospectively followed to assess cardiovascular outcomes.

Future Directions

The incorporation of follow-up forms into the TRVaS database is planned. In addition to diagnostic and baseline characteristics, this will facilitate the systematic documentation of disease course, potential complications, relapses, and mortality. This approach will provide a more comprehensive framework for dynamic long-term monitoring of patients.

The FAIRVASC (Findable, Accessible, Interoperable, and Reusable data for Vasculitis) initiative is a Horizon 2020 project that enables rare-disease registries to be queried as a single virtual cohort while data remain at their home institutions. Using anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) as the demonstrator, FAIRVASC resolves three barriers to cross-border research—registry discovery, semantic harmonisation and governance—by combining a shared ontology curated with the Harmonisation Implementation Team (HIT), local "uplift" of relational tables to Resource Description Framework (RDF) via the RDB to RDF Mapping Language (R2RML) by the FAIRVASC Implementation Team (FIT) [10].

TRVaS (Turkey Vasculitis Study Group) has now started to onboarding process for FAIRVASC, and the onboarding process has begun. We are adapting our technical infrastructure to the FAIRVASC stack by mapping the TRVaS baseline and forthcoming visit-based elements to the FAIRVASC ontology, implementing R2RML mappings to generate RDF, setting up a secure local triple store with GDPR-compliant approvals, and integrating HIT/FIT/QIT cycles to validate semantics and federated queries.

This integration will increase statistical power for ultra-rare phenotypes relevant to our programme—such as central nervous system involvement, interstitial lung disease, and renal pathology strata—facilitate international benchmarking of comorbidity screening (e.g., osteoporosis and early venous thromboembolism risk), and accelerate the translation of TRVaS findings into evidence-informed clinical care.

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