Sjögren's Disease: Early Damage Often Present at Diagnosis

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Primary Sjögren's disease (SD) is a chronic autoimmune condition characterized by glandular dysfunction and extraglandular manifestations, significantly impacting patients' quality of life. Understanding the progression of irreversible organ damage and identifying its predictors is crucial for optimizing patient management. This multicentre cohort study provides real-world insights into damage accrual in SD over a five-year period.

KEY TAKEAWAYS

- The Pivot: Irreversible organ damage in Sjögren's disease is often present at diagnosis, not just a late-stage complication.
- The Data: 48% of patients had Sjögren's Syndrome Damage Index (SSDI) e1 at baseline, increasing to 65% after 5 years, with systemic damage becoming most prevalent.
- The Action: Early identification of high-risk patients using clinical, serological, and patient-reported measures may facilitate timely interventions to mitigate long-term damage.

Understanding Damage Accrual in Sjögren's Disease

Primary Sjögren's disease (SD) is a systemic autoimmune disorder primarily known for causing sicca symptoms due to glandular dysfunction, but it also leads to a range of extraglandular manifestations. These manifestations can significantly impair a patient's quality of life. While the impact of SD on daily living is well-recognized, data on the early onset and predictors of irreversible organ damage have been limited. This knowledge gap hinders the development of strategies for early intervention and personalized treatment approaches aimed at preventing long-term complications and improving patient outcomes.

Study Design and Methodology

This multicentre retrospective cohort study included 429 adult patients diagnosed with SD from the Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale (GIRRCS) network. All participants had a minimum of one year of follow-up. Baseline assessments captured several key indicators, including disease activity measured by the European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI), and patient-reported symptoms using the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI)1. Objective measures such as C-reactive protein (CRP) levels, Schirmer's test (ST) results, and autoantibody status (anti-Ro/La) were also recorded. Irreversible damage was systematically evaluated using the Sjögren's Syndrome Damage Index (SSDI), which assesses damage across ocular, oral, and systemic domains. The study employed Cox proportional hazards models and Kaplan-Meier curves to analyze predictors of damage accrual over the five-year follow-up period. Additionally,

exploratory Least Absolute Shrinkage and Selection Operator (LASSO) and principal component analysis (PCA) were utilized to investigate domain-specific contributions to damage and to understand the relationships between subjective and objective disease measures1.

Key Findings: Early and Progressive Damage

The study revealed that irreversible damage in SD is often present early in the disease course. At baseline, nearly half (48%) of the patients had an SSDI score of 1 or greater, indicating existing damage. Specifically, ocular damage was observed in 25.4% of patients, systemic damage in 22.5%, and oral damage in 14.3%1.

Over the five-year follow-up period, the cumulative prevalence of damage increased significantly, affecting 65% of the cohort. The distribution of damage also shifted, with systemic damage becoming the most prevalent (40.8%), followed by ocular damage (34.2%) and oral damage (21.7%)1.

Predictors of Damage Accrual

Several factors were identified as significant predictors of damage accrual. A higher baseline ESSDAI score was found to predict damage across all domains (ocular, oral, and systemic), highlighting the importance of systemic disease activity in driving irreversible changes. Elevated ESSPRI scores, reflecting patient-reported symptoms, were specifically associated with an increased risk of oral damage. An abnormal Schirmer's test, an objective measure of tear production, strongly predicted ocular damage1.

Furthermore, specific serological markers and clinical manifestations were linked to domain-specific damage. The presence of anti-Ro/La antibodies, elevated CRP levels, and a history of recurrent oral infections were associated with higher rates of damage in relevant domains. LASSO analyses provided further granularity, indicating that glandular, peripheral nervous system, and pulmonary ESSDAI domains independently contributed to systemic damage. PCA confirmed that patient-reported symptoms and objective systemic disease activity represent distinct yet complementary dimensions of the disease, suggesting that both should be considered in comprehensive patient assessment1.

Clinical Implications and Future Directions

The findings from this study underscore that irreversible organ damage in primary Sjögren's disease is not solely a late-stage complication but can be present at diagnosis and progresses over time, affecting multiple organ systems. The identification of specific clinical, serological, and patient-reported measures as predictors of damage accrual offers valuable insights for clinical practice.

Why this matters for clinical practice today: These data suggest that clinicians should proactively screen for organ damage at the time of Sjögren's disease diagnosis and continue vigilant monitoring. Integrating baseline ESSDAI, ESSPRI, Schirmer's test results, and serological markers like anti-Ro/La antibodies and CRP into routine assessments could help identify patients at higher risk for damage progression. Early identification may allow for more timely and targeted therapeutic interventions, potentially altering the disease trajectory and improving long-term outcomes for patients. Recognizing that patient-reported symptoms (ESSPRI) and objective disease activity (ESSDAI) provide independent information emphasizes the need for a holistic assessment approach.

The study's conclusions suggest that early identification of high-risk patients, based on a combination of clinical, serological, and patient-reported measures, could enable timely interventions to prevent further damage, guide treatment decisions, and ultimately improve long-term outcomes for individuals living with Sjögren's disease.

Limitations and Next Steps

As a retrospective cohort study, this research is subject to certain limitations, including potential biases inherent in retrospective data collection and the possibility of unmeasured confounders. The study population was drawn from a specific network in Italy, which may limit the generalizability of the findings to other populations. Future prospective studies with larger and more diverse cohorts are needed to validate these findings and further explore the complex interplay of factors contributing to damage accrual in SD. Longitudinal studies could also investigate the impact of specific therapeutic interventions on preventing or mitigating damage progression, building upon the insights gained from this real-world analysis.

REFERENCES

1. 1. Berardicurti O, Marino A, Navarini L, et al. Real-world damage accrual in Sjögren's disease: a 5-year multicentre GIRRCS cohort analysis. RMD Open. 2026;12(2):e006772. doi:10.1136/rmdopen-2026-006772