



IMMUNOMODULATORY THERAPIES FOR PREVENTING THROMBOSIS IN IMMUNE-MEDIATED MICROVASCULAR THROMBOTIC DISEASES

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Abstract

Immune-mediated microvascular thrombotic diseases (IMTD), such as systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), increase the risk of microvascular thrombosis due to chronic inflammation and autoimmune activity. While anticoagulant therapy is crucial for managing thrombotic events, immunomodulatory therapies may provide additional benefits by targeting underlying immune dysfunction. This study evaluated the efficacy of biologic agents (IL-6 antagonists, TNF inhibitors, rituximab) and complement inhibitors in reducing thrombotic risk over 12 months in 50 patients with IMTD (aged 18–65). Inflammatory markers (CRP, IL-6) and thrombotic indicators (D-dimer, fibrinogen) were elevated at baseline and significantly decreased post-therapy ($p < 0.01$). Rituximab reduced antibody levels by 30% in SLE patients ($p < 0.05$), with a 15% reduction in thrombotic events. IL-6 antagonists decreased inflammation and thrombotic risk by 20% ($p = 0.03$). However, bleeding risk was observed in 8% of patients. These findings highlight the potential of immunomodulatory therapies as adjuncts to anticoagulants, though larger trials are needed.

Keywords: Immunomodulatory therapy, microvascular thrombosis, autoimmune diseases, IL-6 antagonists, TNF inhibitors, rituximab, anticoagulants

Introduction



Immune-mediated microvascular thrombotic diseases (IMTD) are characterized by thrombus formation in small blood vessels due to aberrant immune activation, leading to organ ischemia and other serious complications [1]. Systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), and other vasculitides belong to this group, with chronic inflammation and increased thrombotic risk as common features [2]. Anticoagulants, such as warfarin and direct oral anticoagulants (DOACs), are critical for preventing thrombosis but do not address the underlying inflammatory causes [3]. Immunomodulatory therapies, including IL-6 antagonists, TNF inhibitors, and B-cell depletion agents, have the potential to reduce thrombotic risk by mitigating inflammation [4]. This study investigates the efficacy of these therapies in preventing thrombosis in IMTD patients, contributing to the development of personalized treatment strategies.

Relevance

Balancing thrombotic and bleeding risks in IMTD treatment is a complex challenge, as anticoagulant therapy does not fully address the root causes of inflammation [5]. Immunomodulatory therapies may reduce thrombotic risk by targeting inflammation, but their efficacy and safety remain underexplored. This study provides critical data to advance personalized treatment approaches in clinical practice.

Objective

To evaluate the efficacy of immunomodulatory therapies in reducing microvascular thrombotic risk in IMTD patients and determine their potential as adjuncts to anticoagulant therapy.

Materials and Methods

A prospective cohort study was conducted from March 2023 to March 2025 at a quaternary medical center. Fifty IMTD patients (aged 18–65), diagnosed based on clinical and immunological criteria, were enrolled [6]. Patients received DOACs (apixaban 5 mg twice daily or rivaroxaban 20 mg once daily) and immunomodulatory therapy (IL-6 antagonists, TNF inhibitors, or rituximab). Blood samples were collected at baseline, 3, 6, and 12 months, measuring D-dimer (immunoassay), fibrinogen (Clauss method), CRP, and IL-6 (ELISA) [7]. Clinical outcomes (thrombotic events, bleeding) were recorded. Data were analyzed using R v4.3 with mixed-effects models and Cox regression ($p < 0.05$).

Results and Discussion

At baseline, D-dimer levels were 1.6 $\mu\text{g/mL}$ (IQR 1.1–2.2), decreasing to 0.5 $\mu\text{g/mL}$ (IQR 0.3–0.7) at 12 months ($p < 0.001$), with greater reductions in patients



receiving IL-6 antagonists alongside DOACs ($p=0.01$) [8]. Fibrinogen levels remained elevated in 60% of patients (mean 4.0 ± 0.8 g/L), correlating with CRP ($r=0.65$, $p<0.01$) [9]. Rituximab reduced antibody levels by 30% in SLE patients ($p<0.05$), with a 15% decrease in thrombotic events. IL-6 antagonists reduced inflammation and thrombotic risk by 20% ($p=0.03$). Bleeding risk was observed in 8% of patients, highlighting safety concerns [10]. These results confirm the potential of IL-6 antagonists and B-cell depletion agents in preventing thrombosis, though bleeding risks warrant consideration. Study limitations include a small sample size and lack of a control group.

Conclusion

Immunomodulatory therapies, particularly IL-6 antagonists and rituximab, show promise as adjuncts to anticoagulants in reducing microvascular thrombotic risk in IMTD patients. They mitigate inflammation and thrombotic events, but bleeding risks require monitoring. Future multicenter studies will aid in standardizing these therapies.

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