

WHAT THE NEIGHBORS SAY

1 | POSTDISCHARGE THROMBOSIS IN COVID-19—PREVENTABLE?

Giannis et al. Postdischarge thromboembolic outcomes and mortality of hospitalized patients with COVID-19: the CORE-19 registry. *Blood* 2021; 137(20): 2838–2847. 10.1182/blood.2020010529

Hospitalized COVID-19 patients are at risk of both venous thromboembolism (VTE) and arterial thromboembolism (ATE), and it appears that mortality in these patients may be due to thrombotic events even more commonly than has previously been appreciated. In this study, Giannis and colleagues conducted a large, prospective study of consecutive hospitalized COVID-19 patients, both to quantify the risk of postdischarge VTE, ATE and all-cause mortality (ACM), and also to determine how effective postdischarge thromboprophylaxis was. Among 4906 patients, many of which had a variety of comorbidities, postdischarge thromboprophylaxis was prescribed in 13.2%. Thrombosis rates during 90 days postdischarge were 1.55% for VTE and 1.71% for ATE, with an ACM of 4.83%. The composite primary outcome rate was 7.13% in these patients and was significantly associated with advanced age, prior VTE, ICU stay, chronic kidney disease, peripheral arterial disease, carotid occlusive disease, coronary artery disease, or an IMPROVE-DD VTE score ≥ 4 . Interestingly, postdischarge anticoagulation (mostly at prophylactic doses) was associated with a reduction of the risk of major thromboembolic events and death by 46%. One limitation of this study is the relatively small subgroup receiving postdischarge thromboprophylaxis, but the striking findings argue strongly for randomized trials of safety and efficacy of extended postdischarge thromboprophylaxis in severely ill COVID-19 patients.

2 | INITIAL SIGNS OF VWD IN INFANTS

Dupervil et al. Characteristics, complications, and sites of bleeding among infants and toddlers less than 2 years of age with VWD. *Blood Adv* 2021; 5(8): 2079–2086. <https://doi.org/10.1182/bloodadvances.2020004141>

While the clinical presentation of von Willebrand disease (VWD) in adolescents and adults is very well documented, the signs and symptoms related to this bleeding disorder are not well known for very young children. In the study of Dupervil and colleagues, data has been extracted from the US Hemophilia Treatment Center

Network to document bleeding presentations in 105 infants and toddlers with VWD. As might be anticipated, a significant number (68%) of children were tested for VWD based upon a family history of the disorder. The mean age at diagnosis was 7 months, and infants with type 2 VWD were diagnosed earlier than those with type 1 or 3 disease. 70% of patients experienced bleeding (68% of bleeds occurring before 1 year) with oral mucosa (32%), circumcision-related (12%) and intra/extracranial bleeds (10%) representing the most common types of events. Of the intracranial bleeds documented, none were associated with delivery. 47% of patients required treatment with a VWF/FVIII concentrate. In summary, a significant number of infants and toddlers were diagnosed and treated for VWD in the first year of life, most often with a prior family history of the disorder.

3 | REGULATION OF THE FVIII INHIBITOR RESPONSE

Doshi et al. B cell-activating factor modulates the factor VIII immune response in hemophilia A. *J Clin Invest*. 2021;131(8):e142906. <https://doi.org/10.1172/JCI142906>

Neutralizing anti-factor VIII (FVIII) antibodies develop in ~30% of severe hemophilia A patients, most often within the first 50 exposures to their replacement therapy. Despite several decades of investigation, the pathogenic mechanisms responsible for this serious treatment complication remain poorly understood. In a recent report, Bhavya Doshi and colleagues have focused on events underlying FVIII-specific B cell development to advance mechanistic knowledge of FVIII inhibitor development, and to identify potential targets for mitigation of the problem. The B cell-activating factor (BAFF) cytokine family plays a critical role in B cell differentiation and in this investigation, patient samples and mouse models were used to investigate the potential role of BAFF in modulating FVIII immunogenicity. BAFF levels were elevated in pediatric and adult inhibitor patients and decreased to control non-inhibitor levels following successful immune tolerance induction. In naive HA mice, anti-BAFF antibody therapy prior to FVIII immunization prevented inhibitor formation and resulted in long-term tolerance to FVIII. This study suggests that BAFF plays an important role in FVIII inhibitor development and has also demonstrated that anti-CD20/anti-BAFF combination therapy may be clinically useful for ITI.