man immunodeficiency virus testing and management. These services can help intensivists make clinically appropriate decisions while understanding how these decisions conform to state laws.

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Rheumatoid Arthritis Interstitial Lung Disease: Mycophenolate Mofetil as an Antifibrotic and Disease-Modifying Antirheumatic Drug

We applaud the National Institutes of Health for funding this important study by Gochuico et al.1 Continued research is crucial for gaining insight into the natural history of interstitial lung disease (ILD) related to connective tissue diseases (CTDs). Assessment and response criteria are profoundly lacking, making it very challenging to develop and gauge effective targeted therapy. In addition, only investigative attention to screening will be able to reveal whether drug-associated CTD-ILD (eg, biological agents, methotrexate) are the primary culprits or triggers exacerbating pre-existing subclinical ILD. Among CTDs, the prevalence of occult ILD may be greater than 30%.2,3 Early detection and treatment is imperative.

We report our experience with 4 patients with systemic sclerosis ILD, 2 with polymyositis ILD, 1 with Sjogren ILD, and 3 with rheumatoid arthritis (RA)-ILD,4 all of whom were treated with mycophenolate mofetil, with 9 patients receiving mycophenolate for longer than 1 year. Notable improvement was demonstrated in symptoms, alveolitis, performance status, and quality of life, with stabilization or improvement on physiological and imaging studies. Importantly, prednisone therapy was discontinued or drastically reduced without worsening.

Of interest, 2 patients with RA initially presented with ILD and later developed synovitis, with results from physiological and imaging studies showing stabilization or improvement with mycophenolate therapy. The first patient experienced quiescence of both ILD and RA with mycophenolate and hydroxychloroquine therapies. The second patient, initially wheelchair and not using supplemental oxygen, improved or drastically reduced without worsening.

Mycophenolate is a specific immunosuppressant targeting lymphocytes and is known to inhibit proliferation and activity of “nonimmune” cells implicated in fibrosis, especially fibroblasts, smooth muscle cells, and endothelial cells.3,7 Relevant to the findings in the article by Gochuico et al,1 mycophenolate inhibits the expression of fibrosing cytokines such as transforming growth factor β, interferon γ, platelet-derived growth factor, connective tissue growth factor, fibroblast growth factor, tumor necrosis factor, and interleukin 6, preventing deposition and contraction of collagen, extracellular matrix proteins, and smooth muscle actin.5-9

The efficacy of mycophenolate observed in our series of patients with CTD-ILD is similar to that described elsewhere for scleroderma, undifferentiated and mixed CTD, Sjogren ILD, polymyositis, and dermatomyositis.10 In scleroderma specifically, increased vital capacity11 as well as improvement or stabilization of lung function in forced vital capacity and diffusion capacity for carbon monoxide have been documented for up to 24 months.12,13 This is indeed hopeful for scleroderma ILD, since the 24-month data for cyclophosphamide therapy is disappointing.14

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From the periodontal surgery subgroup, in which the surgical procedure involved at least one-third of the gingival soft tissue of the jaw, unusual bleeding complications occurred in only 2 patients, with an international normalized ratio greater than 3.5, and in 2 patients in whom warfarin sodium was substituted by LMWH. In these 4 cases, bleeding was controlled by local measures. Thus, bridging therapy with LMWH was unnecessary in most cases and, when applied, resulted in complications.

Second, regarding the inclusion of oral procedures in the study by Garcia et al., the authors do not mention the extent of abnormal postoperative, clinically significant bleeding in the dental surgery group. Oral surgical treatments cause a relatively large release of tissue factor, which in turn facilitates the formation of the thrombus even in patients receiving anticoagulant therapy. Furthermore, the treatment of excessive bleeding is simple, and bleeding is usually arrested with local hemostatic measures. Therefore, the continuation of anticoagulant therapy before dental and oral procedures is advocated. Hence, the evidence-based recommendations in the clinical guidelines suggest the continuation of warfarin treatment with no preoperative modification, provided that the international normalized ratio is below 3.5. In accordance with the report by Garcia et al., our findings, and the dental literature, bridging treatment should be avoided in dental clinics.

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The Hurdles of Translating a Single-Center Observation Into Practice

W e have carefully read the article by Peterson et al focusing on the prognostic value of the exercise treadmill test with regard to future major adverse events. They concluded that an exercise capacity less than predicted has an independent impact on the future risk of cardiac events and overall mortality. Some points with regard to the baseline characteristics of the population and the reliability of the predictive model deserve further elucidation.

First, the clinical indications for an exercise treadmill test included preoperative screening, risk stratification, and “other reasons.” Together, these accounted for more than 25% of the study population (ie, approximately 2430 patients). The remaining population was referred with the diagnosis of chest pain. This heterogeneity profoundly alters the risk of future car-

In the study reported by Garcia et al, we found 2 points of interest from the oral medicine perspective. First, Garcia et al reported that the use of low-molecular-weight heparin (LMWH) as bridging treatment in surgical procedures caused excessive postoperative bleeding.

In a pilot study performed by us during the years 1995 to 2000 (unpublished data) at the Oral Medicine Department, Assuta Hospital, Tel-Aviv, Israel, bleeding tendency was investigated in 500 patients treated with anticoagulants after various dental and oral surgical procedures. Of 43 procedures performed in 30 patients...