This month’s feature highlights three articles that appear in the current issue of Mayo Clinic Proceedings. These articles are also featured on the Mayo Clinic Proceedings’ YouTube Channel (https://youtu.be/4urC1tIh2Oc).

INTERRUPTING THE PROGRESSION OF COVID-19 BY ANTI-SPike MONOCLONAL ANTIBODIES: OUTCOMES IN TWO ERAS

In patients at a high risk for progressive disease, anti-spike monoclonal antibodies interrupt the progression of COVID-19 from its mild to moderate stage to severe disease, the latter usually attended by an increased need for hospitalization and increased morbidity and mortality. In a prior issue of Mayo Clinic Proceedings, Razonable et al discussed the framework - and its modus operandi - that exists at Mayo Clinic for the administration of anti-spike monoclonal antibodies to patients with mild to moderate COVID-19 (Mayo Clin Proc 2021; 96(5):1250-1261). In the present issue of Mayo Clinic Proceedings, and drawing upon data obtained from this program at Mayo Clinic sites in 4 states, O’Horo et al assessed the efficacy of anti-spike monoclonal antibodies against SARS-CoV-2 during time periods in which specific SARS-CoV-2 variants were predominant. In late 2020, the SARS-CoV-2 alpha variant appeared, became dominant in early 2021, and was accompanied by the beta variant, which was detected in a smaller number of COVID-19 cases. In the summer of 2021, the delta variant emerged, quickly achieved dominance among viral variants, and seemed to evince a greater proclivity to elude neutralizing antibodies and to inflict more severe disease. In this study by O’Horo et al, patients with infection before April 30, 2021, at any of the Mayo Clinic sites, were considered as having the alpha/beta variants, whereas patients who were infected after July 1, 2021, were regarded as having the delta variant. Eligibility for anti-spike monoclonal antibody therapy required that patients were within 10 days of the onset of symptoms of COVID-19; COVID-19 was mild to moderate; and that patients fulfilled the criteria for the Food and Drug Administration (FDA) emergency use authorization (EUA) which predicted a high risk for severe COVID-19 based on patient characteristics and medical conditions. The Charlson Comorbidity Index (CCI), which encompasses 19 comorbid conditions, was determined for each patient. The data demonstrate that the odds of severe infection were 3.0% and 4.9% in the alpha/beta-predominant and delta-predominant time periods respectively; and that the delta-predominant time period exhibited higher odds for more severe disease, especially so when such odds were adjusted for the CCI. These findings are especially notable in that on May 14, 2021, the FDA EUA criteria expanded such that during the delta-predominant era, infusions were administered to patients with less comorbidities. An added consideration is that during the alpha/beta-predominant era, the anti-spike monoclonal antibody administered was bamlanivimab whereas in the delta-predominant period, patients were treated with the casirivimab-imdevimab combination. However, prior studies by this group based on real-world clinical outcomes demonstrated that rates of

See also pages 225, 238, 327
hospitalizations were not different between these two regimens (J of Infect Disease, 2021). Based on the present data, O’Horo et al conclude that the delta variant may be more virulent than the alpha/beta variants, but the authors leave open the much less likely possibility that the casirivimab-imdevimab combination may be less effective than bamlanivimab. This study by O’Horo et al is important and timely because it evaluates therapeutic strategies for COVID-19 within the context of evolving therapies and emerging viral variants, the latter consideration especially germane given the current threat imposed by the now present omicron viral variant and the specter of a resurging pandemic.


ABDOMINAL OBESITY AND CARDIOMETABOLIC HEALTH OUTCOMES

Obesity is a major cause for morbidity and mortality in the United States where the age-adjusted prevalence of obesity is approaching 50%. Worldwide, the prevalence of obesity has increased several fold in recent decades. Abdominal obesity, in particular visceral adipose tissue (VAT), is of special concern as a predictor of disease. In the present issue of Mayo Clinic Proceedings, Tejani et al examined the association between cardiometabolic health outcomes and types of abdominal fat deposition. Their study focused on VAT and fat that is deposited in organs that are generally non-adipose tissue-containing such as the liver (abbreviated liver fat or LF). These authors utilized the Dallas Heart Study, the central aim of which is the prevention and management of heart disease. The Dallas Heart Study incorporated, among other assessments, baseline imaging of participants who were then followed for more than 10 years for incident cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Based on assessment of VAT and LF, participants were classified as having either high or low VAT and high or low LF. Their findings demonstrate that participants with high VAT, irrespective of whether they had high or low LF, were at an increased risk of CVD and T2DM, while participants with high LF and low VAT were at an increased risk for T2DM. Tejani et al also examined such associations in another data base, namely, the UK Biobank. Using these data, Tejani et al found that significant associations with CVD only held true for individuals with high VAT and low LF, after adjusting for age and BMI. Tejani et al discuss the implications of their findings, including among others, the following considerations. First, obesity, as defined by anthropometry, does not fully convey the risk for disease as the type of abdominal fat deposition may be associated with an increased risk for specific types of cardiometabolic disease (CVD or T2DM). Second, investigation of therapeutic approaches for weight loss may consider including an assessment of the site and type of adiposity of participants in such studies and how the specific types of fat deposits are altered in response to these strategies. Third, the intriguing and perhaps unexpected finding that low LF when present with high VAT robustly associates with CVD is germane to strategies that seek to lower LF in nonalcoholic fatty liver disease; specifically, the present findings would suggest that lowering LF without concomitantly lowering VAT may increase the risk for CVD. This study provides new data demonstrating that the prognostic significance of fat deposition depends upon the site, amount, and nature of the accumulated adipose tissue, and interacting effects of such deposits.

STROKE RISK IN THE NON-ELDERLY STRONGLY ASSOCIATES WITH SOCIAL DETERMINANTS OF HEALTH

Mortality from stroke in the elderly is decreasing whereas the prevalence of stroke and its attendant mortality have increased in non-elderly individuals in recent years. In the current issue of Mayo Clinic Proceedings, and based on data obtained from the National Health Interview Survey, Khan et al examined the association between social determinants of health (SDOH) and the prevalence of stroke in young (18 to 45 years old) and middle aged (45 to 64 years old) individuals. SDOH was scored based on a model developed by the Kaiser Family Foundation that involved a cumulative assessment of responses to 39 sub-components that encompassed 5 domains, the latter involving economic stability, access to health care, community and social contexts, neighborhood, food, and education. More than 50% of the study group were in the young age range, in whom 20% of strokes occurred. Individuals with a stroke reported unfavorable responses to the vast majority of the 39 SDOH sub-components. Approximately 50% of strokes were reported in individuals with the fourth quartile of the SDOH score. Notably, there was a progressive increase in prevalence of stroke adjusted for age as the score for SDOH increased from the first to the fourth quartile. Stroke was almost 3 times more likely to occur in individuals with SDOH scores in the fourth quartile as compared with those in the first quartile, after adjustments for assorted demographic characteristics and risk factors for cardiovascular disease. This important study underscores the importance of SDOH in the prevalence of stroke in young and middle age individuals and why addressing SDOH is such a vital component of major health care initiatives.


Karl A. Nath, MBChB
Editor-in-Chief