This month’s feature highlights five articles, four of which focus on COVID-19, 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/mt3zfdaokyu).

SARS-CoV-2 MUTATION: PATHO BIOLOGY AND IMPLICATIONS
The emergence of distinct SARS-CoV-2 strains in several countries has led to pressing and timely concerns regarding strategies that aim to confer viral immunity and to contain viral spread. In the present issue of Mayo Clinic Proceedings, Badley distills essential concepts regarding the infectivity and pathobiology of SARS-CoV-2 and how viral mutation may influence such processes. Following entry into host cells, the virus commandeers cellular machinery into viral replication, leading ultimately to the extracellular release of offspring virions and viral spread to vicinal cells; viral mutants are inevitably produced because of seemingly inherent error-prone behavior of the replicative processes, thereby failing to faithfully recreate the original invading virus. As emphasized by Badley, mutations may influence at least five major properties/behaviors of SARS-CoV-2 relevant to the severity of COVID-19 and its treatment, and these include: replicative fitness, infectivity, disease-provoking capability, responsivity to antiviral agents, and susceptibility to antibody neutralization. A specific mutation may exert countervailing effects, for example, producing strains that may more likely escape from the effects of antiviral agents or neutralizing antibodies on the one hand, but, on the other, ones concomitantly compromised in their replicative fitness and thus in propagating themselves. It is this integrative effect of a given mutation on these five major processes that ultimately determines whether such a mutation creates a more virulent, fecund strain (thereby promoting the persistence of the pandemic), or a strain with impaired reproductive fitness and thus one that will attrite with time. Badley frames his discussion between two quite sobering concepts: the first is that the potential for the appearance of a vast number of SARS-CoV-2 mutants is great because of the intrinsic propensity for errors in the replicative machinery; and, second, the longer the COVID-19 pandemic persists, the greater the likelihood of the emergence of mutant strains that are robust, replicative, and resistant to available therapeutic strategies. A corollary to this latter concept is that measures that restrain the spread and duration of COVID-19 may decrease the likelihood of the emergence of such mutant strains; and in this regard, Badley underscores public health measures as one of four major ways to restrain the pandemic and appearance of viral variants. Germane to this consideration is the article by Juhn et al in the same issue of Mayo Clinic Proceedings. Juhn et al examined prevalence of SARS-CoV-2 positivity in over 1500 subjects after the Stay-at-Home orders were rescinded. In this cohort, virtually all participants adhered to recommended public health measures (social distancing, wearing a face mask in public, hand hygiene, staying at home), and none were positive for SARS-CoV-2.
interestingly, the prevalence of other seasonal, non-SARS-CoV-2 coronavirus infections was higher than the national average (7% versus 4%). These observations by Juhn et al are important because they speak to personal responsibility and behavior during the current pandemic. While the stochastic and seemingly inevitable cellular errors in replication that cause viral mutation are beyond our control, public health measures that constrain viral spread are entirely within our grasp, and such measures are ones that we must assuredly follow.


RISK FACTORS FOR HOSPITALIZATION AND POOR OUTCOMES IN COVID-19

The need for hospitalization usually indicates an escalation in the severity of medical conditions, and being able to predict who is at such risk and to prognosticate on possible outcomes aids the management of such diseases. Two articles in the present issue of Mayo Clinic Proceedings provide such information regarding COVID-19. Cottini et al report on BMI-associated outcomes in patients with COVID-19 pneumonia (diagnosed by CT-scan) occurring during the months of March and April 2020 in the province of Bergamo, Italy, a province with among the highest rates of COVID-19 and attendant mortality at the time. In this study of 338 patients, 39% and 23% were overweight and obese respectively, and some 31% were hospitalized. The need for hospitalization occurred earlier in obese patients as compared with overweight and normal weight individuals, and obese patients were also at greater risk for hospitalization as compared with those groups. Moreover, obese patients exhibited more progressive disease when hospitalized with higher rates of noninvasive and invasive ventilation and mortality; when managed outside the hospital setting, obese patients more frequently required oxygen therapy. Also in this issue of Mayo Clinic Proceedings is the study by Krishna et al that describes an association of echocardiographic findings with 30-day outcomes in patients hospitalized because of COVID-19. This study involved 179 patients in whom a transthoracic echocardiogram was needed in the course of clinical management; such studies were undertaken at the patient’s bedside and complied with a standardized, abbreviated protocol so as to minimize patient contact. Thirty-day outcomes included prolonged hospitalization (that is, greater than 21 days) and death, with such outcomes occurring in 24% and 15% of patients, respectively; 36% and 26% required mechanical ventilation and circulatory support, respectively. Echocardiographic abnormalities were not infrequently detected, with reduced left ventricular ejection fraction, regional wall motion abnormalities, and increased right ventricular systolic pressure (RVSP) present in 16%, 15%, and 25% of patients, respectively. In a multivariable model, RVSP was one of the main risk factors (others being previous cardiovascular disease, troponin, and D-dimer) that associated with the composite 30-day outcome. A notable finding by Krishna et al is that in those patients in whom a prior echocardiogram was available before these patients developed COVID-19, abnormalities were present in 78% of these patients. This latter finding supports the view that cardiovascular disease may predispose to adverse outcomes in COVID-19, and that the detection of echocardiographic abnormalities in patients with COVID-19 may not necessarily be ascribed to COVID-19 per se. These two studies thus point to obesity and specific echocardiographic findings as possible indicators of a worsening course in COVID-19.


Krishna H, Ryu AJ, Scott CG, Mandale DR, Naqvi TZ, Pellikka PA. Cardiac

SEX DIFFERENCES IN CHRONIC CORONARY SYNDROMES

It is increasingly recognized that the manifestations of disease and response to therapy are significantly influenced by sex and gender. In the present issue of Mayo Clinic Proceedings, Meyer provides a comprehensive and timely review of how these determinants apply to chronic coronary syndromes. Such syndromes arise from obstructive epicardial coronary artery disease (CAD), coronary microvascular disease (CMD), or the coexistence of these two pathologic entities. Because of the vasoprotective effects of estrogens in premenopausal women, obstructive epicardial CAD tends to occur in women in the later menopausal years, and at a considerably older age and with more comorbidities, as compared with the occurrence of this disease in men. However, women are vulnerable to CMD in the early menopausal years, as the vasoprotective effects of estrogen are lost and other risk factors - hypertension, diabetes, dyslipidemia, obesity, and the long-term vasculopathic effects of prior hypertensive disorders of pregnancy - become apparent. Coronary microvascular disease reflects such underlying processes as endothelial dysfunction, an imbalance between microvascular vasodilation/vasoconstriction, and microvascular remodeling. Indeed, CMD underlies the entity termed “ischemia with no obstructive coronary artery disease” which may give rise to debilitating symptoms and impaired functionality, and may predispose to overt cardiovascular events. Meyer sequentially reviews the following topics, especially as they apply to women: the evaluation of the risk for obstructive CAD in symptomatic women and, where indicated, additional diagnostic tests that may be pursued; the relative specificity and value of various tests for epicardial disease and microvascular disease; issues surrounding the diagnosis and management of ischemia with no obstructive coronary artery disease; outcomes following revascularization for obstructive CAD; and sex-based differences in the pharmacokinetics and pharmacodynamics of drugs commonly used in cardiovascular medicine. As emphasized by Meyer, women have been insufficiently represented in clinical trials in cardiovascular disease such that the accrued evidence which informs diagnostic algorithms and management guidelines in women is incomplete. This timely review by Meyer is important because it attunes us to the need to recognize chronic coronary syndromes as they occur in women, and it informs us on relevant aspects of manifestations, consequences, diagnostic evaluation, and management.


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