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This month's feature highlights six 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/QnoCy2AhMoI).

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THE JOURNEY FROM PHYSICIAN BURNOUT TO PHYSICIAN WELL-BEING

Physician burnout is a tragic and costly phenomenon that profoundly impairs patient care, the delivery of patient care by health care centers, and the professional and personal lives of physicians so afflicted. In addition to the personal pain it imposes, the inherent tragedy of this condition is that it leaves afflicted physicians bereft of that laudable altruistic motivation of promoting healing and health in others, and which, in the first place, led them to undertake the long and challenging training required for a medical career. A pioneering group that has led the way in defining, elucidating, and discerning solutions for physician burnout is that of Shanafelt, West, Dyrbye, and colleagues. *Mayo Clinic Proceedings* is privileged to publish in its current issue a Special Article by Shanafelt that comprehensively charts this field, beginning with the initial recognition of this condition, delineating its current state and salient issues, and looking ahead to the continued implementation of strategies and processes that will mitigate burnout and promote physician well-being. Shanafelt identifies three phases, designating each with a title that encapsulates the key issue. The first phase is that of the "Era of Distress" that reflects the field as it existed up to some 15 years ago. This phase is characterized by a lack of recognition or the deliberate sidestepping of the issue of physician distress, with little scholarship and research addressing this issue; during this phase there was the pervasive view that if such a condition existed, it was a reflection of the "personal weakness" of the physician, the latter generally expected to be invulnerable to such stress, the challenges of a burgeoning professional workload, and an increasingly complex health care environment. Shanafelt categorizes the second phase as "Physician Well-being 1.0", one that continues to the present day. This phase is characterized by awareness and attention to the problem, scholarship and research to define the drivers and consequences, and early intervention efforts. During this phase, substantive changes in the demographic profile of physicians, the training of physicians, and the practice environment occurred; health care systems and their leadership recognized the adverse effects of physician distress on patient care and on their return on investment in delivering patient care. Key insights during this phase were that a "culture of wellness" should be created and fostered for physicians, and that the primary underpinnings of physician distress reside in the medical practice environment, with all its complexity and change, emphasis on relative value units (RVUs), quality assessment, regulatory and administrative oversight and restrictions, reimbursement issues, and reliance on the electronic health record. Despite this recognition, the solutions devised largely focused on cultivating personal resilience so as to endure a broken system. Over the last 3-4 years, leading institutions began to usher in a new phase labeled by Shanafelt "Physician Well-being 2.0." Broadly considered, this is an effector phase which seeks to introduce system-based and organization-based

processes and initiatives which, in aggregate, would enable the practice environment to mitigate distress, promote well-being, and cultivate a professional culture of vulnerability and self-compassion. Key characteristics of this phase include initiatives that focus on people, teams, and community; regulatory and administrative decisions that heed the voice and needs of clinicians; emphasis on value on investment, rather than return on investment; and research focused on systems-based interventions to ameliorate the problem. As regards the latter issue, *Mayo Clinic Proceedings* is also privileged to publish in this issue original articles by West et al, Dyrbye et al, and Vilendrer et al that exemplify the transition to Well-being 2.0 proposed by Shanafelt. Such contributions, in aggregate, reflect the journey of and progress made in this field, and which have taken it from its somber provenance of "physician burnout" to its current, more sanguine stage of "physician well-being." This outstanding Special Article by Shanafelt is a landmark perspective regarding this field and a compelling clarion call for needed system-level strategies and action.

Shanafelt TD. Physician well-being 2.0: Where are we and where are we going? *Mayo Clin Proc*. 2021;96(10):2682-2693.

West CP, Dyrbye LN, Satele DV, Shanafelt TD. Colleagues Meeting to Promote and Sustain Satisfaction (COMPASS) groups for physician well-being: a randomized clinical trial. *Mayo Clin Proc*. 2021;96(10):2606-2614.

Dyrbye LN, Major-Elechi B, Hays JT, Fraser CH, Buskirk SJ, West CP. Physicians' ratings of their supervisor's leadership behaviors and their subsequent burnout and satisfaction: a longitudinal study. *Mayo Clin Proc*. 2021;96(10):2598-2605.

Vilendrer SM, Kling SMR, Wang H, et al. How feedback is given matters: a cross sectional survey of patient satisfaction feedback delivery and physician well-being. *Mayo Clin Proc*. 2021;96(10):2615-2627.

UNCOVERING THE PATHOGENESIS OF ACUTE KIDNEY INJURY IN COVID-19

Among the major complications of COVID-19 is acute kidney injury (AKI), the latter occurring in more than 50% of COVID-19 patients in the intensive care unit (ICU), many of whom may require renal replacement therapy. AKI is also a major determinant of outcomes in COVID-19 as it increases the duration of hospitalization, morbidity, mortality, and health care costs. The mechanisms implicated in AKI include the following: hemodynamic/vasomotor instability, volume depletion, systemic inflammatory responses, myocardial dysfunction and its adverse renal effects, endothelial activation, thrombotic microangiopathy, and rhabdomyolysis. Additionally, the causative virus, SARS-CoV-2, can infect the kidney as the kidney richly expresses the receptor (ACE2) that mediates the cellular entry of SARS-CoV-2; such cell entry enables viral-induced cell injury/death in the kidney and the instigation of local inflammatory cascades. In the present issue of *Mayo Clinic Proceedings*, the seminal study by Alexander et al examined the nature of AKI in COVID-19, specifically questioning the extent to which such AKI resembles sepsis-associated AKI (S-AKI). This renal autopsy study included histopathologic studies, and genomic and proteomic analyses. Based on the presence of apoptosis, microvascular changes, macrophage-enriched inflammatory infiltrates, and interstitial $CD3^{+}CD4^{+}$ T cell congregating around antigen-presenting cells, the authors conclude that AKI in COVID-19 is similar to S-AKI, a conclusion supported by "omic" data. Specifically, in AKI occurring in COVID-19 and in S-AKI, transcriptomic analyses showed an enrichment of genes involved in apoptosis, autophagy, major histocompatibility complex class I and II, and type 1 T helper cell differentiation; proteomic analyses showed an enrichment of proteins involved in necroptosis and sirtuin pathways. Ultrastructural mitochondrial damage is known to occur in S-AKI, a finding the present study also demonstrates along with downregulation of proteins related to oxidative phosphorylation. This study by Alexander el al is significant and timely from several perspectives that include the following: 1) it shows how autopsy studies may be undertaken so as to capitalize on innovative techniques, and accordingly derive novel insights, as afforded by a multi-omics approach; 2) it attests to the fundamental role of inflammation as a major pathway by which

organ injury occurs in COVID-19, in general, and in the kidney in particular; 3) as the kidneys analysed in the present study were negative for the presence of SARS-CoV-2, the current observations underscore the fact that viral tropism of the kidney is not essential for the occurrence of AKI in COVID-19; 4) this study uncovers the occurrence of prominent mitochondrial damage and functional impairment in oxidative phosphorylation, thereby highlighting mitochondrial impairment in the pathogenesis of AKI in COVID-19; indeed, this concept now broadly permeates current perspectives regarding the pathogenesis of AKI in general; and 5) this article adumbrates new diagnostic and therapeutic strategies for AKI occurring in COVID-19. The COVID-19 pandemic brought a new disease with many distinct and unexpected pathogenetic pathways in the causation of organ and tissue injury. However, at least for the kidney, as clearly shown by Alexander et al, the pathogenesis of AKI in COVID-19 bears remarkable resemblance to the pathogenesis of a disease recognized for so long in nephrology and the ICU, namely, sepsis-associated AKI.

Alexander MP, Mangalaparthi KK, Madugundu AK, et al. Acute kidney injury in severe COVID-19 has similarities to sepsis-associated kidney injury: A multi-omics study. *Mayo Clin Proc.* 2021;96(10):2561-2575.

INNOVATING THE ECG TO IDENTIFY LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

Asymptomatic left ventricular systolic dysfunction (LVSD) predisposes to overt heart failure and attendant morbidity and mortality, complications that may be mitigated by the institution of appropriate therapy. In the present issue of *Mayo Clinic Proceedings*, the study of Kashou et al assessed whether an artificial intelligence (AI)-augmented ECG algorithm may predict current and future LVSD. The basis for their community-based study is two-fold. First, the authors point out that a relatively simple noninvasive method for the detection of asymptomatic LVSD would add significantly in detecting patients in the community at risk for ensuing cardiovascular morbidity and mortality. Second, prior seminal retrospective studies by Attia et al from Mayo Clinic published in 2019 (*Nature Medicine* 2019;25(1):70-74) developed and validated an AI-enabled ECG to identify asymptomatic LVSD. Kashou et al studied a randomly selected sample of individuals participating in the Rochester Epidemiology Project. ECGs and echocardiograms were performed as a study protocol, and not because of any clinical indication. LVSD surveillance was undertaken for 10 years after enrollment, the latter conducted between 1997 and 2000. Preclinical LVSD was defined by an ejection fraction less than 40% and without a diagnosis of heart failure. The findings of Kashou et al demonstrate that AI-ECG detected LVSD both in the total population and in the a high-risk subgroup with high sensitivity and specificity; and that over the 10-year period, incidence rates of LVSD were approximately 10% for those with a positive AI-ECG compared with 5% for those with a negative AI-ECG. These findings, as the authors discuss, provide a basis for multi-center prospective studies on community-based populations that assess the rigor, reproducibility, and cost effectiveness of this noninvasive screening approach in detecting asymptomatic LVSD. The fundamental AI approach applied to the ECG in both the study by Kashou et al and the earlier study of Attia et al is that of convolutional neural network (CNN). CNN was introduced in the 1980s, some 100 years after that of the ECG. These two papers on AI-enabled ECG provide a remarkable example of how more recent innovation in medicine may reach back and be applied to the 100-year older ECG, thereby enabling this time honored, noninvasive, and relatively inexpensive tool to predict a disease in ways never previously imagined.

Kashou AH, Medina-Inojosa JR, Noseworthy PA, et al. Artificial intelligence-augmented electrocardiogram detection of left ventricular systolic dysfunction in the general population. *Mayo Clin Proc.* 2021;96(10):2576-2586.

Attia ZI, Kapa S, Lopez-Jimenez F, et al. Screening for cardiac contractile dysfunction using an artificial intelligence-enabled electrocardiogram. *Nat Med.* 2019;25(1):70-74. DOI: 10.1038/s41591-018-0240-2.

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