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IN THE LIMELIGHT

In the Limelight: January 2023

This month's feature highlights four 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/1P_TRcsCHSM).

IMPROVING CLINICIAN WELL-BEING

The prior issue of *Mayo Clinic Proceedings* highlighted an article by Shanafelt et al that called attention to significantly worsened clinician burnout and declining satisfaction with work life balance during the first two years of the pandemic (*Mayo Clin Proc.* 2022;97(12):2248-2258). This issue of *Mayo Clinic Proceedings* contains two articles that propose and explore strategies that seek to improve clinician well-being and to mitigate clinician burnout. The Special Article by Shanafelt et al emphasizes the following considerations: the pivotal role of health care organizations in this objective; the need for a common organizational framework and culture and system level strategies that promote clinician well-being; the critical importance of directing such strategies to the level of the work unit (for example, department, division, clinic, others); and the central role of a unit well-being leader. Strategies at the level of the work unit should identify the specific experience and needs of a given work unit, create consistent structure and processes for interventions targeting work unit well-being, integrate such initiatives with organizational improvement framework, and employ relevant metrics to assess progress of the work unit. These and other recommendations are incorporated by Shanafelt et al into a series of steps that may be considered by organizations as they create a framework and milieu geared to the improvement of clinician well-being. The accompanying Original Article by Trockel el al assesses the efficacy of a popular opinion leader (POL) in enabling organizational intervention intended to promote professional well-being. In this study involving Stanford University HealthCare Alliance clinics, clinics meeting enrollment criteria were matched by size and baseline scores for gratitude and assigned to either delayed (control) or immediate intervention. Findings from surveys in 2019 after the introduction of the intervention were compared with average baseline scores in surveys before the intervention. Trained POLs facilitated the engagement of clinicians in interactive wellness workshops that focused on gratitude, mindfulness, cognitive reframing, and behavioral strategies. The data demonstrate that this intervention employing a POL-based approach led to 75% of clinicians at intervention attending at least one workshop, and that a beneficial impact was observed in professional fulfillment and gratitude. Moreover, this intervention was associated with fewer clinicians expressing the intent to leave the organization. As is generally agreed, occupational distress in clinicians largely evolved because of challenges, constraints, and adverse conditions in the work environment. In this regard, Shanafelt et al underscore the need for strategies within a cohesive interacting organizational infrastructure and milieu that are directed, in particular, to the work unit, while Trockel et al point out the influential role of respected clinicians in effectively engaging colleagues in wellness interventions that foster professional fulfillment.

Shanafelt TD, Larson D, Bohman B, et al. Organization-wide approaches to foster effective unit-level efforts to improve clinician well-being. *Mayo Clin Proc.* 2023;98(1):162-179. https://doi.org/10.1016/j.mayocp.2022.09.002

Trockel MT, Menon NK, Makowski MS, et al. IMPACT: evaluation of a controlled organizational intervention utilizing influential peers to promote professional fulfillment. *Mayo Clin Proc.* 2023;98(1):75-87. https://doi.org/10.1016/j.mayocp.2022.06.035

See also pages 75, 88, 100 and 162

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HFrEF PATIENTS WITH STAGE 4/5 CKD BENEFIT FROM ARNIs

The demonstration that the treatment of patients with heart failure with reduced ejection fraction (HFrEF) with an angiotensin receptor-neprilysin inhibitor (ARNI) led to less cardiovascular mortality and rates of hospitalization compared with treatment with enalapril was a major therapeutic advance in heart failure (PARADIGM-HF Study, McMurray et al, *N Engl J Med* 2014; 371(11):993-1004). Such studies, however, generally excluded patients with advanced kidney disease (GFR $<$ 30 ml/min per 1.73 m^2, Stage 4/5 CKD), the latter not uncommonly occurring in patients with HFrEF. The occurrence of kidney disease of such severity in HFrEF raises the question whether ARNIs are effective and safe in such settings. This issue is addressed by Chang et al using data from patients in two Taiwanese multicenter heart failure cohorts with similar protocols and managed by guideline-directed medical therapy; enrollment criteria included patients with symptomatic HFrEF who were 20 years or older and with baseline eGFR $<$ 30 ml/min per 1.73 m^2. Propensity score matching was employed to adjust for confounders. After such matching, the final analysis involved 278 patients on ARNIs and 232 patients not on ARNIs. At one year, the ARNI group compared with the non-ARNI group exhibited significantly higher left ventricular ejection fraction and eGFR and significantly lower all-cause mortality and rates of hospitalization. An additional finding was that the majority of patients with stage 4/5 CKD tolerated ARNIs as permanent discontinuation of ARNIs occurred in 13.7% of treated patients, the major reasons being worsening renal impairment/hyperkalemia or hypotension. In discussing their findings, Chang et al underscore the following points. First, these data are derived from real-world observations and provide relevant information regarding the use of ARNIs in HFrEF with concomitant stage 4/5 CKD. Second, ARNIs are generally well tolerated. Third, the use of ARNIs was associated with improved renal function, the latter likely reflecting any one or combination of the following effects: improved LVEF; the beneficial renal hemodynamic effects of higher systemic levels of atrial natriuretic peptides that attend the use of ARNIs; and the recognized antioxidant and anti-inflammatory effects of these agents. Such improvement in renal function has salutary implications for heart failure itself: dysfunction of the kidney in heart failure may vitiate protective renal responses in heart failure, thereby exacerbating heart failure and potentially driving cycles of ever worsening heart and kidney failure.

Chang H-Y, Lin C-C, Chao C-J, et al. Real-world experience of angiotensin receptor—neprilysin inhibition in reduced ejection fraction heart failure patients with advanced kidney disease. *Mayo Clin Proc.* 2023;98(1):88-99. https://doi.org/10.1016/j.mayocp.2022.06.007

ANKYLOSING SPONDYLITIS, AGE, AND HEMATOLOGIC MALIGNANCY

Diseases attended by chronic inflammation may predispose to hematologic malignancies. Alehashemi and Ward examined whether such predisposition occurs in ankylosing spondylitis (AS). Using US Medicare data from 1999 to 2015, these investigators identified three cohorts of beneficiaries: one with AS, another with inflammatory bowel disease (IBD, a disease with immunopathogenetic features similar to AS and a control for chronic inflammation), and a third which comprised an unaffected control with neither AS nor IBD (unaffected control). Beneficiaries in these cohorts were 65 years of age at the time of enrollment in 1999, and those treated with TNF inhibitors during this period were excluded so as to avoid the confounding effects of such therapy; mean duration of follow-up in years was 9.9 (AS), 9.3 (IBD), and 8.0 (unaffected control). The findings of Alehashemi and Ward demonstrate that the standardized incidence ratio was increased for non-Hodgkin lymphoma, chronic lymphocytic leukemia, and multiple myeloma in AS compared with unaffected controls, whereas the risks for such diseases were comparable in the AS and IBD groups.

Mayo Clin Proc. ■ January 2023;98(1):1-3 ■ https://doi.org/10.1016/j.mayocp.2022.11.013
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As their study did not include analyses on younger patients, Alehashemi and Ward undertook a systematic review of published studies that explore the association between AS and hematologic malignancies because such published studies largely involved young and middle-aged patients. Such a review of 21 studies revealed little or no association of AS with hematologic malignancies; 2 cohort studies reported an increased occurrence of multiple myeloma with AS, with the mean age reported for one of these studies being 53.5 years. Among the conclusions of this study by Alehashemi and Ward are that such hematologic malignancies tend to occur in elderly patients with AS, but generally do not occur in young and middle-aged patients; clinicians caring for elderly patients with AS thus need to be cognizant of this risk for these hematologic malignancies and that such risks do not necessarily reflect the use of TNF inhibitors *per se*. Finally, such risks for hematologic malignancies in elderly patients with AS are reminiscent of what occurs in IBD - such congruence of findings in AS and IBD exemplifies the promalignant effects of immunosenescence in synergy with chronic proinflammatory conditions.

Alehashemi S, Ward MM. Risk of hematological malignancies in elderly patients with ankylosing spondylitis: a cohort study and systematic review. *Mayo Clin Proc.* 2023;98(1):100-110. https://doi.org/10.1016/j.mayocp.2022.06.030

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