

MAYO CLINIC
PROCEEDINGS

In the Limelight: July 2022



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/hBsvMXbo1Q>).

ADHERENCE TO A MEDITERRANEAN DIET AND LIFESTYLE REDUCES PAIN

The Mediterranean diet with its constituents of fruits, vegetables, whole grains, nuts, olive oil, and seafood, among others, seems to possess an innate wholesomeness lacked by a calorie-enriched diet largely based on synthetic foodstuffs, saturated fat, simple sugars, and red meat. Indeed, there is considerable evidence that consumption of a Mediterranean diet is associated with a reduced risk for cardiovascular disease, type 2 diabetes, dementia, and other diseases. Remarkably, based on the current study by Delgado-Velandia et al, the beneficial effects of a Mediterranean diet may also extend to the mitigation of pain. As pointed out by these investigators, overarching a Mediterranean diet is a Mediterranean lifestyle which can be broadly subdivided into three components (in this study designated as "blocks"): 1) type of food consumption (some foods itemized above); 2) eating habits (water, salt, and wine intake; snacks; and frequency of nibbling between meals); and 3) a component that relates to physical activity, rest, social habits, and conviviality. In their study, adherence to a Mediterranean lifestyle was quantitated by assigning, as appropriate, points to 27 items encompassed by the three blocks, with non-adherence to an item scored as zero and adherence scored

as 1 point; the aggregate score constituted the MEDLIFE index. Delgado-Velandia et al utilized data from The Study on Cardiovascular Health, Nutrition and Frailty in Older Adults in Spain (Seniors -ENRICA) in its two prospective cohorts, the earlier cohort with individuals aged 60 years or older, and the latter one with individuals 65 years or older. Assessment of pain was based on a questionnaire used in the Survey of Chronic Pain in Europe. Individuals in the highest category of MEDLIFE adherence, compared with those in the lowest category, were more likely to experience reduced rather than exacerbated overall pain after a median follow-up of 2.6 years. Such adherence was also associated with a reduction in the frequency and severity of pain, and in the number of locations of pain. Additionally, when analyses were undertaken for each of the three blocks, individuals in the highest quartile of MEDLIFE adherence, compared with those in the lowest quartile, improvement of pain was observed for the Mediterranean food consumption block and for the block that comprised physical activity, rest, social habits, and conviviality. This important study by Delgado-Velandia et al shows that adherence to a Mediterranean diet and lifestyle may mitigate chronic pain syndromes, ones that, not infrequently, are physically incapacitating, emotionally distressing, and refractory to pharmacologic approaches. Moreover, the salutary effects of the Mediterranean lifestyle seem to go beyond those of the diet itself, with its additional attentiveness to regular physical activity and individual serenity, and its emphasis on, its reaching out to, and its connectedness with community.



See also pages
1282, 1294, 1305



Scan to View Video

Delgado-Velandia M, Ortolá R, García-Esquinas E, et al. Adherence to a Mediterranean lifestyle and changes in frequency, severity, and localization of pain in older adults. *Mayo Clin Proc.* 2022;97(7):1282-1293. doi 10.1016/j.mayocp.2022.01.009.

CAR-T THERAPY AND AKI

Among the salient complications of cancer and its treatment is kidney disease, the latter now entailing such specialized knowledge and occurring with such frequency and significance so as to engender a new subspecialty: onco-nephrology. The causes for cancer-related kidney disease are many, as they may arise from — either singly or in combination — the cancer itself, cancer therapies, attendant volume depletion, sepsis, or exposure to other nephrotoxic drugs/agents. Specific therapies directed against cancer, such as long-established chemotherapeutic agents, more recently developed targeted therapies, and novel immunotherapies, are all recognized as causes of acute kidney injury (AKI, *NEJM* 376, 1770, 2017). The present study by Farooqui et al is the largest retrospective analysis to-date of the occurrence of AKI in patients with non-Hodgkin lymphoma (NHL) treated with chimeric antigen receptor-T (CAR-T) therapy. In this study of 83 patients, 14 patients developed AKI in the month after such therapy. Ten patients were diagnosed as having renal intrinsic AKI, 2 with pre-renal AKI, and 2 considered to have obstructive AKI; renal replacement therapy was required in 2 patients. By 1 month after CAR-T therapy, AKI resolved in 10 patients. In most patients with AKI, inflammatory capillary leak and/or a net fluid deficit were predisposing conditions; tumor lysis syndrome occurred in a single patient. The incidence of AKI during the month of follow-up was associated with impaired renal function at baseline, exposure to intravenous contrast dye, prophylaxis for tumor lysis syndrome, and the dosages of corticosteroids and tocilizumab used in managing the cytokine release syndrome (CRS). Such prophylaxis for tumor lysis syndrome may reflect the clinical estimation of the tumor

burden, and in this regard, higher peak uric acid and creatine kinase and the change in lactate dehydrogenase from baseline all correlated with the incidence of AKI; uric acid is a marker of cell turnover while creatine kinase and lactate dehydrogenase are markers of cell injury. The administration of higher dosages of corticosteroids and tocilizumab may reflect more severe CRS, and, accordingly, more vigorous therapy in attempting to quell CRS-associated inflammation; however, incident AKI did not significantly increase as the grading of CRS increased. The study by Farooqui et al thus delineates factors that incur the risk of AKI in patients with NHL treated with CAR-T therapy. The presence of such factors in patients treated with CAR-T should underscore vigilance regarding renal function, adequacy of the extracellular fluid volume, and renal perfusion; the avoidance of nephrotoxins; and the need for strategies that reduce the risk of tumor lysis syndrome and mitigate the severity of an inflammatory milieu.

Farooqui N, Sy-Go JPT, Miao J, et al. Incidence and risk factors for acute kidney injury following chimeric antigen receptor T-cell (CAR-T) therapy. *Mayo Clin Proc.* 2022;97(7):1294-1304. doi 10.1016/j.mayocp.2022.05.018.

TREATING CYST INFECTIONS IN POLYCYSTIC KIDNEY DISEASE

Urinary tract infection may occur in up to 50% of patients with autosomal dominant polycystic kidney disease (ADPKD), the most common inherited disease afflicting the kidney. Treatment of such infections may be especially challenging when the infectious process involves kidney cysts as such cysts are frequently not in communication with the urinary space. Such sequestration of cysts, the lack of cyst irrigation by urine, and impaired diffusion of antibiotics into cysts may all predispose to failure of antibiotic treatment of infected cysts as well as recurrent infection after a course of antibiotics is completed. Dang et al addressed these issues in a retrospective study of outcomes following antibiotic treatment of 139 cyst

infections (CIs) in 90 patients cared for at their ADPKD Center over an 18-year time-frame. Cyst infection was defined as definite (based on cyst puncture, which is uncommonly done), probable (based on clinical assessment and imaging procedures), and possible (based on clinical and biochemical findings). Definite and probable cyst infections exhibited a relatively high rate of treatment failure and recurrence (34% and 18%, respectively), both of which were markedly lower in possible CIs (4% and 7%, respectively). Treatment failure was associated with male sex, peak C-reactive protein level, and thickening of the cyst wall, but not with the type of antibiotics initially used or with cyst size. Recurrent infections progressively diminished with increased duration of antibiotic therapy; antibiotic treatment that was equal to or greater than 28 days in duration was associated with quite low recurrences (2%). Recurrences were higher in kidney transplant recipients, and this likely

reflected concomitant immunosuppression. Interestingly, lipid soluble antibiotics (fluoroquinolones, bactrim) are often recommended in treatment of infected cysts because they may be more likely to diffuse into cysts. However, Dang et al observed that such antibiotics were associated with less recurrences on univariate but not on multivariate analyses. While the therapeutic benefit of lipid soluble antibiotics for infected cysts merits further study, what is a clear and critical message of this paper is the need for antibiotic therapy to be maintained for a minimum of 28 days.

Dang J, Scemla A, Loheac C, et al. Efficacy of prolonged antibiotic therapy for renal cyst infections in polycystic kidney disease. *Mayo Clin Proc.* 2022;97(7):1305-1317. doi 10.1016/j.mayocp.2022.01.027.

Karl A. Nath, MBChB
Editor-in-Chief