In the Limelight: November 2022

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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/UElWmE3Nf90).

ALL PLANT-BASED DIETS ARE NOT CREATED EQUAL IN CONFERRING HEALTH BENEFITS

Dietary constituents are broadly classified into animal-derived and plant-based foods, and substantial and mounting epidemiologic evidence indicates that consumption of the latter compared with the former are associated with health benefits and lower mortality. But do all plant-derived dietary constituents uniformly and unerringly confer such health benefits? In the present issue of *Mayo Clinic Proceedings,* Delgado-Velandia et al addressed this question in a study involving almost 12,000 individuals broadly representative of the adult Spanish population, and who were followed for approximately 10 years after their recruitment between 2008 to 2010. These individuals were participants in the prospective cohort "Study on Nutrition and Cardiovascular Risk in Spain (ENRICA)." To assess the effects of the composition of plant-based diets, the authors used the previously introduced distinction between healthy plant-based diets (vegetables, fruits, whole grains, legumes, olive oil) and unhealthy plant-based diets (refined grains, potatoes, fruit juices, sugar-enriched beverages, and desserts). Dietary intake was assessed by a validated diet history and, based on 18 major food groups, scores were obtained for a healthy plant-based diet (hPDI) or an unhealthy plant-based diet (uPDI). The data demonstrate that all-cause mortality and cardiovascular (CV)-related mortality were decreased by 14% and 37%, respectively, for each 10-point increase in hPDI. Notably, no significant associations were discerned for uPDI either with all-cause mortality or CV-related mortality. Other relevant findings in this study are that consumption of animal-derived foods and fruit juices were associated with higher risk of CV-related mortality, consumption of vegetable oils was attended by lower risk of all-cause mortality, and the Mediterranean diet score, like hPDI, was generally associated with lower all-cause and CV-related mortality. To explain the health benefits of healthy plant-based diets, the authors suggest that the antioxidant and anti-inflammatory effects of many components of these diets underlie the accompanying reduced risk of all-cause mortality and CV-related mortality. This important study of Delgado-Velandia et al indicates that the health benefits of plant-based diets are not invariantly derived from such food groupings, but rather from specific plant-based dietary components. The well-accepted adage "we are what we eat," would thus underscore the wisdom and importance of diets rich in vegetables, legumes, whole grains, fruits, nuts, and vegetable oil.

Delgado-Velandia M, Maroto J, Ortolá R, García-Esquinas E, Rodríguez-Artalejo F, Sotos-Prieto. Plant-based diets and all-cause and cardiovascular mortality in a nationwide cohort in Spain: the ENRICA Study. *Mayo Clin Proc.* 2022;97(11):2005-2015. doi.org/10.1016/j.mayocp.22.06.008

RETARDING CKD PROGRESSION BY OPTIMIZING THE DOSING OF ACEi/ARBs

Salient considerations in the management of patients with proteinuric chronic kidney disease (CKD) include blood pressure (BP) control; optimizing salt and water balance; correcting metabolic complications; and retarding the rate of decline of kidney function such that arrival of endstage kidney disease (ESKD) is delayed or, optimally, averted. As regards the latter, there is compelling evidence that angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs) effectively delay the progression of CKD by actions that

lower BP, proteinuria, and renal inflammation and fibrosis. However, as emphasized by the KDIGO 2021 Clinical Practice Guidelines for the Management of BP in CKD (https://www.kidney-international.org/article/S0085-2538(20)31270-9/fulltext), the efficacy of these agents in retarding the progression of proteinuric CKD requires that their doses be escalated to ones maximally approved and to the extent that such doses are tolerated; the rationale for this guideline is that such doses of these agents were generally employed in clinical trials that established their efficacy. The current study by Chu et al shows that in proteinuric CKD, ACEi/ARBs are often submaximally dosed. These authors used the database of the OptumLabs Data Warehouse to examine how ACEi/ARBs were dosed in over 100,000 adult patients in whom these medications were prescribed between January 1, 2017, and December 31, 2018. In these patients, overall, less than one third (29.8%) were administered maximal doses of ACEi/ARBs. The authors also defined criteria that may proscribe increasing the dose of ACEi/ARBs; these criteria included systolic BP less than 120 mmHg, serum potassium (K^+) greater than 5.0 mEq/L, an eGFR lower than 15 ml/min per 1.73 m^2, and the occurrence of acute kidney injury (AKI) within the preceding year. In patients without these criteria (approximately 75,000), the percentage of patients who received maximal doses of ACEi/ARBs marginally increased to 32.3%. Submaximal ACEi/ARB dosing was more likely to occur in patients who were less than 40 years old, female, Hispanic, or those patients exhibiting a lower BP, a higher serum K^+, a prior episode of AKI, less albuminuria, concomitant heart failure, or absence of diabetes. It should be noted that while some of these proscriptions against dose escalation may be absolute (for example, low BP), others are relative and can be safely managed (for example, marginally elevated serum K^+ which can be controlled by increased doses of loop diuretics and/or by newer K^+-binding agents). The progression of CKD to ESKD markedly increases morbidity and mortality, necessitates new therapies, and significantly alters the life of a patient with CKD. Delaying this outcome can be achieved by ACEi/ARBs, but the full efficacy of these agents is dose-dependent.

Chu CD, Powe NR, Estrella MM, et al. Submaximal angiotensin-converting enzyme inhibitor and angiotensin receptor blocker dosing among persons with proteinuria. *Mayo Clin Proc*. 2022;97(11):2099-2106. doi.org/10.1016/j.mayocp.22.07.010

IS THE RISK FOR HYPERTENSION INCREASED IN NIGHT SHIFT WORKERS?

Human biologic processes are commonly characterized by a daily rhythmicity governed by central and peripheral circadian clocks. For example, in normotensive individuals, the blood pressure profile is characterized by a 10-20% drop during nighttime and a rise in BP in the early hours of the morning, with BP peaking in the afternoon (*Free Rad Biol Med*. 2018;119:108-114). Abnormalities in this physiologic profile in BP may associate with and/or predispose to hypertension and other cardiovascular diseases. The intrinsic functioning of circadian clocks is influenced by cues derived from such sources as the light-dark cycle, mealtime, and social interaction. Such clues may be attenuated or lost in certain circumstances, a salient one being night shift work. Indeed, night shift work has been linked to a variety of diseases, in part because of attendant stress imposed on the circadian rhythmicity of biologic processes. Xiao et al provide new insights regarding night shift work and the occurrence of hypertension. These investigators employed the large prospective observational study of the UK Biobank and classified some 230,000 of the participants in this study as day workers, shift workers but never or rarely night shift, irregular shift workers including night shift, and permanent night shift workers. The data demonstrate that night shift work associated with hypertension, and in the three types of night shift work, a higher risk of hypertension was observed compared with the day shift work, with the risk increasing as the frequency of night shift work increased. In modeling that

adjusted for other factors relevant to hypertension, the risk for hypertension with night shift work was still significant. Furthermore, these investigators capitalized on the availability in the UK Biobank of genotyping data, from which they derived a polygenic risk score (PRS) for hypertension; notably, the risk of hypertension was increased in permanent night shift workers with a high PRS compared with day workers with a low PRS. This important study demonstrates that there is an increased risk for hypertension in night shift workers, a risk that itself may be conditioned by genetic factors.

Xiao Z, Xu C, Liu Q, et al. Night shift work, genetic risk, and hypertension. *Mayo Clin Proc*. 2022;97(11):2016-2027. doi.org/10.1016/j.mayocp.22.04.007

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