In the Limelight: November 2019

This monthly feature highlights three articles in the current print and online issue of Mayo Clinic Proceedings. These articles are also featured on the Mayo Clinic Proceedings’ YouTube Channel (https://youtu.be/ILSh5n5Gg00).

PATIENT REPORTED OUTCOMES: GENERAL AND ONCOLOGIC CONSIDERATIONS

Patient reported outcomes (PROs) are health-related assessment and feedback that are provided directly by the patient, optimally via standardized and validated tools, and are done so without the aid of an intermediary. As such, PROs may reflect the “voice of the patient” that may be truer as it is not susceptible to what can be “lost in translation.” Patient reported outcomes are increasingly and appropriately emphasized in current paradigms governing the practice of medicine that are founded on patient-centric care and shared decision making. Patient reported outcomes are relevant to and may benefit not only patient care, but also health care policy, medical research, and the search for more effective therapies. In the current issue of Mayo Clinic Proceedings, Warsame and D’Souza provide a scholarly and comprehensive overview of PROs that both outlines the key broad concepts in the field and delineates the specifics and granularity of PROs as they pertain to the subspecialty of oncology. These authors begin with a perspective regarding the development, raison d’être, and current definition of PROs, and how PROs increasingly ramify into diverse fields and disciplines, the latter consideration underscored throughout throughout the review. Warsame and D’Souza discuss how PROs aid in processes that secure approval by the Food and Drug Administration (FDA) of new drugs and labeling claims in the course of which they provide a compelling example of labeling claims in which PROs provided the basis for oncologic therapy (ruxolitinib for constitutional symptoms in myelofibrosis); they also enumerate specific circumstances wherein PROs may be especially helpful. The authors discuss how PROs complement traditional endpoints in clinical trials in oncology by assessing functional status and quality of life, among other patient-relevant considerations; how PROs aid in patient stratification in clinical trials as, in several types of cancers, PROs can prognosticate on patient survival; and how PROs contribute to the assessment of drug toxicity. These discussions then lead into contributions of PROs in comparative effectiveness research and databases in oncology. This informative and timely review culminates in illustrating the contribution of PROs to patient-provider communication and other aspects of clinical oncologic care and in delineating the existing challenges in realizing the full potential of PROs in oncologic practice.


CARDIORESPIRATORY FITNESS, GRIP STRENGTH, AND THE RISK OF HEART FAILURE

Cardiorespiratory fitness (CRF) is both a biomarker of and a determinant of health. Enhanced CRF predicts less all-cause mortality and mortality caused by...
cardiovascular disease, and a diminished risk for hypertension, diabetes, and stroke. Indeed, the benefits of CRF may go beyond conditions linked to cardiovascular disease, and may extend to disparate diseases such as cancer, chronic kidney disease, depression, and dementia. In the present issue of Mayo Clinic Proceedings, Sillars et al examine the association of CRF and heart failure (HF) using the UK Biobank. The UK Biobank is a vast repository of epidemiologic, clinical, and laboratory data collected on approximately half million subjects in the United Kingdom between the years 2006 to 2010, with the aim of ascertaining the risks for and the course and consequence of assorted diseases. Sillars et al selected in their analysis patients who were without comorbidities at baseline and were event-free after 2 years, and in more than 57,000 such subjects with CRF data, they demonstrated that increased CRF was associated with a decreased risk for HF: an increase of 1 metabolic equivalent (MET) in CRF was accompanied by 18% decrease in the risk for HF. Since CRF, as measured in the UK Biobank, required graded exercise testing and the calculation of oxygen consumption, Sillars et al questioned whether a simpler, easier-to-assess index of muscular integrity and functionality would also associate with HF. The authors utilized grip strength (GS) as such an index; GS when increased, like CRF, predicts reduced all-cause mortality. Grip strength data were available in approximately 375,000 subjects without comorbidities at baseline and who remained event-free after 2 years. In these subjects, GS was associated with a lower risk for HF, with each 5 kg increase in GS accompanied by 19% reduction in risk for HF. In discussing their findings Sillars et al make a number of important points. First, as compared with data in the literature, the present findings of Sillars et al would suggest that risk factors such as diminished CRF and GS may have a greater effect on the propensity for HF as compared with genetic determinants; the former two indices may be improved by behavioral and lifestyle changes, whereas genetic determinants are fixed. Second, their study involved a general population without comorbidities at baseline and thus their findings indicate the potential of CRF and GS in forecasting the risk of HF developing de novo. Third, because of the simplicity and ease of measurement of GS, the latter may be considered as an office-based screening tool for patients in assessing their risk of developing HF.


SERONEGATIVE RHEUMATOID ARTHRITIS NEEDS A BIOMARKER

The search for novel biomarkers that can disclose diseases before conventional biomarkers can is ongoing in virtually all disciplines of medicine. Such biomarkers offer improved specificity and sensitivity in diagnosing disease and may point to specific therapeutic strategies and/or the timing for the initiation of such strategies, all of which may improve patient outcomes. For example, this search in patients with acute myocardial injury led to troponins, while in acute kidney injury a number of biomarkers are now recognized as more sensitive than serum creatinine (for example, urinary [IGFBP7].[TIMP2]) and are under consideration for their prognostic and therapeutic significance. This need for biomarkers may be especially relevant for diseases that are facsimiles of others, but lack serologic biomarkers possessed by these other diseases. Germane to this consideration is the study by Coffey et al in the current issue of Mayo Clinic Proceedings that examined outcomes in two forms of rheumatoid arthritis (RA), the more common type that is seropositive (for rheumatoid factor and/or anti-citrullinated peptide antibody) and the less common type that is seronegative for these two biomarkers. Diagnostic criteria for RA in this study by Coffey et al involved the 1987 American Rheumatism Association criteria and the 2010 American College of Rheumatology/European League Against Rheumatism...
criteria, the 2010 scoring system more broadly emphasizing earlier, more acute manifestations of RA and the presence of serologic factors. In this study involving 214 patients who fulfilled both the 1987 and 2010 criteria, 145 were seropositive and 69 were seronegative. In patients with seronegative RA, as compared with seropositive RA, the time periods were all markedly longer from first joint swelling to achievement of 1987 and 2010 classification criteria and to a clinical diagnosis of RA, and from first joint swelling to commencing disease-modifying antirheumatic drug (DMARD) therapy. Remission rates in patients with seronegative RA were substantially less than those in patients with seropositive RA when the complete Boolean definition of remission was utilized. It is perhaps not surprising that this delay in initiating treatment in seronegative RA was attended by diminished rates of remission as the evidence is clear that the efficacy of DMARD therapy necessitates expeditious initiation within a certain timeframe in the course of the disease. While this study did not address the basis for the delay in initiating therapy in the seronegative RA, Coffey et al suggest that this may originate from the greater diagnostic challenges in this seronegative subset of patients. Interestingly, a certain percentage of seronegative RA patients may seroconvert, but at a later time point in the course of the disease and one at which DMARD may not be effective. These novel findings by Coffey et al should stimulate the search for a serum biomarker for RA detectable in patients presenting with features of RA but lacking the presence in serum of rheumatoid factor and/or anti-citrullinated peptide antibody.


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