EDITORIAL

Epidemiology and Population Health

Physical activity and fitness vs adiposity and weight loss for the prevention of cardiovascular disease and cancer mortality

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Considerable and unequivocal evidence demonstrates the importance of obesity as a risk factor for numerous chronic diseases, especially cardiovascular disease (CVD), disabilities, and reduced quality and duration of life [1, 2]. Despite this recognition, the rate of obesity continues to rise in the United States and worldwide. The importance of physical activity (PA), exercise, and cardiorespiratory fitness (CRF) has also been recognized, yet physical inactivity and sedentary behavior remain highly prevalent worldwide [1–3]. The relative importance of obesity, PA, and CRF, both individually and jointly, and changes in these parameters, continues to be debated.

In the current issue of the International Journal of Obesity, Ahmadi and colleagues [4] assessed longitudinal data from Taiwan's MJ cohort on 116, 228 adults with repeated measures of PA, body mass index (BMI), waist circumference (WC), and body fat percentage (BF %) 4.6 years apart with assessment of mortality from CVD and cancer over 12 years. Increasing PA over time was associated with lower all-cause mortality (ACM) and CVD-mortality, by 15 and 28%, respectively. On the other hand, reducing adiposity attenuated but did not offset mortality risk for ACM, CVD-mortality, and cancer-mortality, whereas only maintaining a healthy adiposity over time offset mortality risk. Lower mortality risk was associated with increases in PA across adiposity change groups. Decreased adiposity somewhat attenuated the negative association of decreased PA. The authors concluded that the beneficial association of joint changes in PA and adiposity was primarily driven by PA.

A primary finding of the Ahmadi et al. paper is that PA drives the interaction between PA, WC and ACM/CVD-mortality, although the authors may have somewhat understated the relative contribution of PA. Of interest from a public health perspective is the observation that increasing PA essentially eliminates most of the risk for ACM and CVD-mortality associated with a stable or increased WC. This is a finding that is entirely consistent with numerous observations demonstrating that exercise is associated with benefits across a wide range of health outcomes in association with no or minimal weight loss – certainly weight loss below the suggested threshold of 5%, which has recently been reviewed [1]. However, considerable evidence suggests that a monolithic focus on weight loss as the only determinant of success for strategies that aim to reduce obesity is not justified and, more importantly, eliminates opportunities to focus on other potentially important lifestyle behaviors that are associated with substantial health benefits. The finding that obesity and related health risks can be considerably reduced by adoption of a physically active lifestyle and a healthy diet, even in the presence of minimal weight loss, is encouraging and provides the practitioner and the adult with overweight/obesity additional options for successful treatment [1]. Therefore, if a patient increases PA and achieves moderate weight loss, this may be ideal. However, much can be achieved with increases in PA and CRF without much weight loss, which is generally associated with improvements in cardiometabolic risk, which is a powerful message for patients [1].

Additionally, substantial evidence suggests that focusing on improving CRF, which is largely driven by PA and exercise, and reducing visceral/ectopic adiposity, may be more important, as these are the key drivers of cardiometabolic diseases and adverse outcomes in patients with overweight and obesity [5]. Indeed, reductions in visceral fat do not always equate to substantial weight loss; but, are associated with lower CVD risk.

We have published extensively on the "obesity paradox" in CVD, including coronary heart disease (CHD), where CHD patients with obesity had a better short- and medium-term prognosis [2, 6–8]. However, PA and CRF modifies the obesity paradox in CHD. Among nearly 10,000 patients with CHD followed for nearly 15 years, those within the upper two tertiles of CRF had better survival regardless of BMI, BF, or WC when compared with individuals with low CRF [6]. In the latter, survival followed a strong obesity paradox based on BMI, % BF, and WC. Those having the lowest values for these body composition parameters had a worse prognosis than those with higher values; similar findings occurred for CVD mortality. In the Nord-Trøndelag Health Study (HUNT), individuals with overweight or mild obesity and CHD had better survival rates than their lean counterparts; however, it appears the survival benefit of obesity disappears after 5 years of follow up. Furthermore, they showed that all levels of PA in patients with CHD resulted in improved survival regardless of BMI [7]. Additionally, the obesity paradox was only noted in those who did not meet their PA requirements. In a second analysis from this study, we assessed changes in weight and PA over time and showed that changes in PA were much more important than changes in weight for predicting all-cause mortality and CVD mortality [8]. In fact, there was no group where weight loss, which included voluntary and nonvoluntary, lowered mortality. In those with "normal" BMI, weight gain was associated with lower mortality, whereas weight loss was associated with higher mortality. Without exception, these studies demonstrated that in adults with CHD, PA and CRF markedly altered the relationship between adiposity and subsequent outcomes [2, 6–8]. These studies are consistent with the Ahmadi et al. [4] data suggesting that PA and CRF are more important than adiposity for long-term prognosis.

Finally, we are still in the COVID-19 era, where obesity is certainly associated with worse COVID-19 outcomes (Fig. 1) [2, 9]. The site of the coronavirus entry into cells is at the angiotensin 2 (ACE2) receptor, and there is evidence that adipocytes have even higher ACE2 receptor content then do the lungs, so excess adipose tissue

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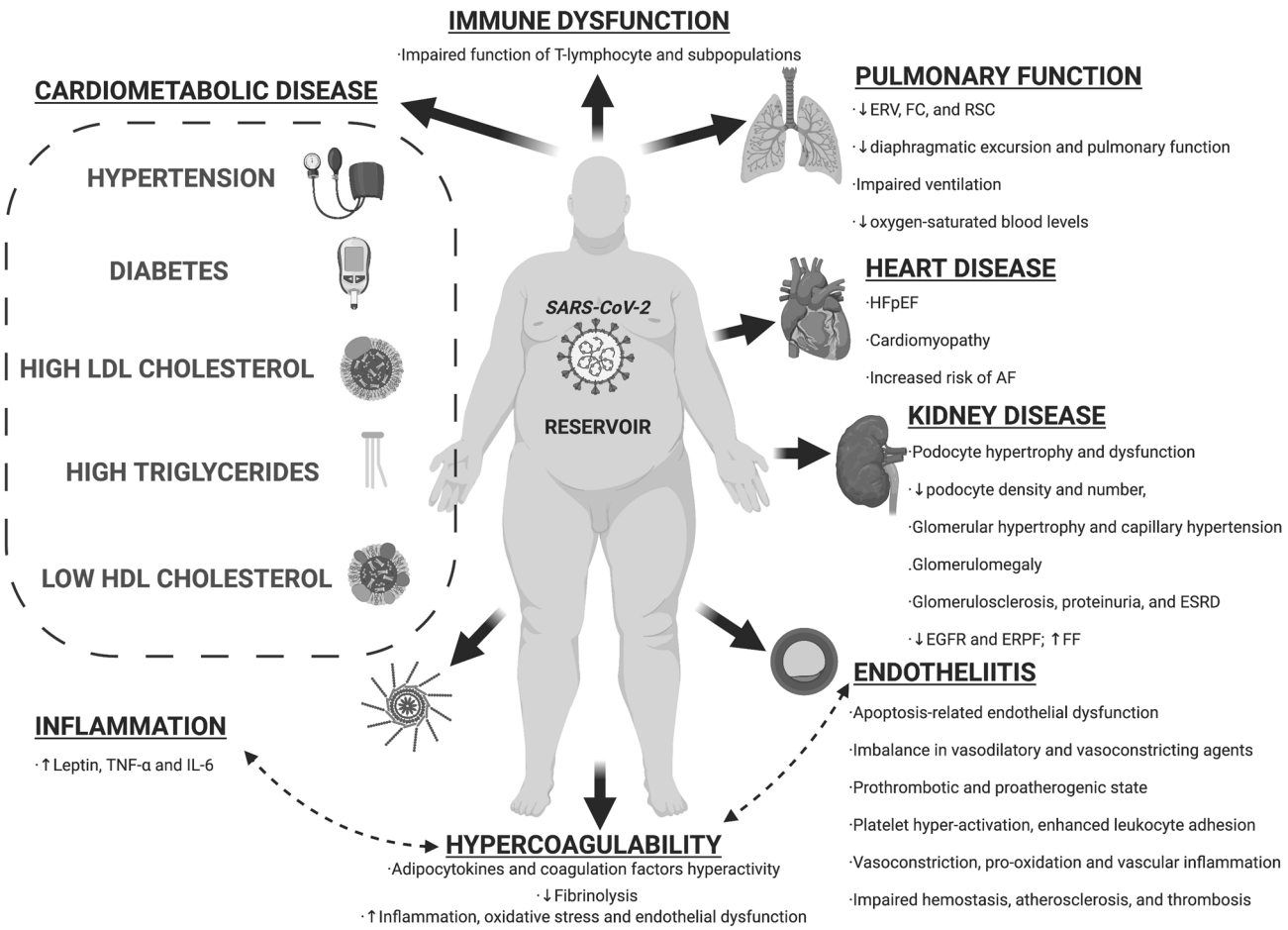

Fig. 1 Potential obesity implications and mechanisms in coronavirus disease 2019 (COVID-19) infection. AF atrial fibrillation, eGFR estimated glomerular filtration rate, ERPF effective renal plasma flow, ERV expiratory reserve volume, FC functional capacity, FF filtration fraction, HDL high-density lipoprotein, HFpEF heart failure with preserved ejection fraction, IL-6 interleukin 6, LDL low-density lipoprotein, RSC respiratory system compliance, SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, TNF-α tumor necrosis factor α. Reproduced with permission from Sanchis-Gomar F et al. *Mayo Clin Proc* 2020; 95(7): 1445–1453 [2].

may serve as a reservoir for the coronavirus in patients with obesity. However, there is also evidence that higher PA [10] and high levels of CRF [3, 11] are also associated with better COVID-19 outcomes. Therefore, in a perfect world, overall health and survival would be best with maintaining both a healthy weight and PA/CRF throughout the life span, but this is certainly not the case in our present society, where most adults gain weight and reduce PA, exercise and CRF over time. As suggested by the current paper by Ahmadi et al. [4] and other evidence [1–3, 5–11], maintaining or increasing PA/CRF may be even more important than changes in adiposity for long-term health and survival.

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COMPETING INTERESTS

Dr. Lavie has previously served as a Speaker and Consultant for PAI Health on their PAI (Personalized Activity Intelligence) applications. Dr. Neeland has served as a Consultant/Speaker for Boehringer Ingelheim/Lilly Alliance, Nestle Health Sciences, and Bayer Pharmaceuticals. Dr. Ross has no disclosures.

ADDITIONAL INFORMATION

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