

screening study. Furthermore, FRS does not include diabetes, obesity, red meat or saturated fat intake, or family history of colorectal cancer, all of which are relevant for the assessment of colorectal cancer risk.

In conclusion, we report an association of CVR factors and colorectal neoplasms. In this screening cohort without gastrointestinal symptoms, subjects with known CAD and high CVR had a significantly higher probability of early and advanced colorectal neoplasia compared with subjects with low CVR, presumably due to shared risk factors. Our data suggest screening colonoscopy to be indicated particularly in subjects with known CAD or high CVR to detect potentially treatable colorectal neoplasia.

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## REFERENCES

1. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and cancer. *Circulation* 2016;133:1104-14.
2. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;97:1837-47.
3. Conroy RM, Pyörälä K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J* 2003; 24:987-1003.

## The Influence of Exercise Therapy on the Heart Failure Disease Pathway



relationship between spironolactone and exercise tolerance in patients with heart failure (HF) with preserved ejection fraction. Their work has already garnered attention on the age-old adage of exercise and its relationship with disease management in HF. We would agree that exercise therapy could be a means of achieving quality of life endpoints as opposed to merely prolonging survival. Perhaps monitoring exercise tolerance along with standard biomarkers may reveal not only the progression of HF in individual patients, but also the effectiveness of exercise therapy over time.

As the management of HF is being relegated to the outpatient setting, it becomes increasingly clear that self-care is paramount in reducing readmissions and decreasing mortality rates in this population. Exercise therapy directly diminishes the levels of inflammatory biomarkers, such as tumor necrosis factor-alpha and interleukin, in the voluntary muscles of patients with HF (2). Because exercise augments cerebral perfusion (3) and directly counteracts the inflammatory response, exercise may be a cost-effective therapy in HF (4). If patients with HF were motivated to maximize self-care, a positive feedback loop could potentially arise where exercise improves executive function and affect to facilitate adherence to therapy and medication regimens.

Of course, it is not always that easy. In the United States alone, HF-associated costs will likely double from \$31 billion to \$70 billion from 2012 to 2030 (5). To add insult to injury, the aging population will in all probability increase the prevalence of and morbidity associated with HF management (5). HF has also been identified as a scourge on the international scale, discriminating not among nations of disparate resources. The onus of HF will in all likelihood continue to rise and is therefore a worldwide health concern that international bodies such as the World Health Organization are attempting to address (5).

This begs the question: Can the defeat of such a pernicious nemesis truly be carried out by exercise, which can be performed in one's own backyard? It is easy to say "yes." The true answer, however, lies in the will to act.

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We would like to thank Kosmala et al. (1) for their recent publication, which expounded on the positive

## REFERENCES

1. Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of aldosterone antagonism on exercise tolerance in heart failure with preserved ejection fraction. *J Am Coll Cardiol* 2016;68:1823-34.
2. Gielen S, Adams V, Möbius-Winkler S, et al. Anti-inflammatory effects of exercise training in the skeletal muscle of patients with chronic heart failure. *J Am Coll Cardiol* 2003;42:861-8.
3. Dorr A, Thomason LA, Koletar MM, et al. Effects of voluntary exercise on structure and function of cortical microvasculature. *J Cereb Blood Flow Metab* 2017;37:1046-59.
4. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;301:1439-50.
5. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circ Heart Fail* 2013;6:606-19.

## REPLY: The Influence of Exercise Therapy on the Heart Failure Disease Pathway



We appreciate Mr. Pan's interest in our trial of spironolactone in patients with heart failure with preserved ejection fraction (HFpEF) (1). Apart from the novel entry criteria using abnormal exercise response as a basis (which allowed more physiologic homogeneity than in previous studies), this study also used functional capacity as the primary endpoint, and it showed both a reduction of exertional filling pressure with and an improvement in exercise tolerance with spironolactone. As clinicians know only too well, the primary concern of these older patients is their impaired functional capacity, and recent guidelines emphasize the importance of this target (2). The finding of improved exercise capacity is consistent with the results of previous studies (3), which are often neglected in the dismay that we have been unable to change the outcome of HFpEF.

However, Mr. Pan is referring not just to the selection of patients and the use of exercise as an endpoint, but also to the use of exercise as therapy. We did not study this, but there is no doubt that this consistently provides functional benefit in adherent patients, including in HFpEF (4), with survival benefit being more marked in women (5). The risk of harm with this intervention is extremely low, and it is used far less than it should be. As Mr. Pan points out, the weakness is obtaining adherence, especially among frail older patients. Perhaps better surveillance using wearable devices will help to provide a solution to that problem.

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## REFERENCES

1. Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of aldosterone antagonism on exercise tolerance in heart failure with preserved ejection fraction. *J Am Coll Cardiol* 2016;68:1823-34.
2. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2016;37:2129-200.
3. Holland DJ, Kumbhani DJ, Ahmed SH, Marwick TH. Effects of treatment on exercise tolerance, cardiac function, and mortality in heart failure with preserved ejection fraction: a meta-analysis. *J Am Coll Cardiol* 2011;57:1676-86.
4. Edelmann F, Gelbrich G, Dungen H, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) Pilot Study. *J Am Coll Cardiol* 2011;58:1780-91.
5. Piña IL, Bittner V, Clare RM, et al. Effects of exercise training on outcomes in women with heart failure analysis of HF-ACTION (Heart Failure-A Controlled Trial Investigating Outcomes of Exercise Training) by sex. *J Am Coll Cardiol HF* 2014;2:180-6.

## Effect of Aldosterone Antagonism on Exercise Tolerance in Heart Failure With Preserved Ejection Fraction



A randomized placebo-controlled study, STRUCTURE (SpironolacTone in myocardial dysfunction with reduced ExeRcisE capacity) (1), performed in subjects with heart failure with preserved ejection fraction and an increased E/e' response to exertion, has shown improvement in exercise duration after 6 months of spironolactone treatment. A particularly laudable aspect of this study is that exclusion of subjects with atrial arrhythmias and ischemic heart disease resulted in less heterogeneity among subjects compared with previous studies. However, there are unanswered questions related to the general applicability of the study findings to patient management and the mechanism underlying the treatment benefit.

One possibility for improved exercise tolerance with spironolactone is that diuresis caused a reduction in left atrial (LA) pressure at rest and during exertion, in which case the use of a diuretic with mineralocorticoid receptor antagonism (MRA) may have no additional