Korean Circ J. 2018 Nov;48(11):1025-1027
https://doi.org/10.4070/kcj.2018.0218
pISSN 1738-5520·eISSN 1738-5555

kcj
Korean Circulation Journal

Editorial

Prolonged Intensive Exercise: When the Right Ventricle Goes Wrong

Yoonjee Park, MD and Eung Ju Kim, MD, PhD

Division of Cardiology, Department of Internal Medicine, Korea University Guro Hospital, Seoul, Korea

▸ See the article "Exercise induced Right Ventricular Fibrosis is Associated with Myocardial Damage and Inflammation" in volume 48 on page 1014.

Received: Jul 2, 2018
Accepted: Jul 4, 2018

Correspondence to
Eung Ju Kim, MD, PhD
Division of Cardiology, Department of Internal Medicine, Korea University Guro Hospital, 148, Gurodong-ro, Guro-gu, Seoul 08308, Korea.
E-mail: withnoel@empal.com

ORCID iDs
Eung Ju Kim
https://orcid.org/0000-0003-2322-6267

Conflict of Interest
The authors have no financial conflicts of interest.

Author Contributions
Conceptualization: Kim EJ; Writing - original draft: Park Y; Writing - review & editing: Kim EJ.

The contents of the report are the author's own views and do not necessarily reflect the views of the *Korean Circulation Journal*.

Appropriate physical activity is beneficial for cardiovascular health, but just how much, exactly, is "appropriate"? How can we decide when the duration or intensity of physical activity is "too much"? Since numerous guidelines have recommended moderate endurance exercise to maintain cardiovascular health, a growing population has been incorporating regular exercise into their daily lifestyle, some of them performing high intensity approaching that of an athlete's. Observational studies on athletes, who maintain exercise highest in intensity and duration regularly for years, have reported a phenomenon of left ventricular changes as well as right ventricular structural change and fibrosis associated with arrhythmia — the so called 'athlete's heart.' Non-prospective or short-term prospective studies assessing acute structural and functional changes in the ventricles after a short duration of exercise were mostly inconclusive as to the clinical significance of this condition, as some resulted in premature cardiac death while the majority appeared to be benign.[1)2)]

Accumulative evidences show that exercise is more closely associated with the right ventricle (RV) rather than the left ventricle (LV). The nature of this relationship — whether causative or not, and if so, 1-sided or interactive — has not been well established. In this issue of the journal, Rao et al.[3)] demonstrate that exercise induced myocardial fibrosis takes place exclusively in the RV, accompanied by local inflammation and myocardial damage.

The difference between RV and LV in their developmental,[4)] biochemical[5)] or physical[6)] properties has been investigated by many, and some have reported that the RV shows an exaggerated response to various stimuli.[7)8)] Importantly, the RV undergoes greater workload during exercise[6)] while having lesser means of adaptation and is susceptible to damage compared to the LV, possibly leading to eccentric remodeling and fibrosis.[9)]

Rao and colleagues[3)] show the linkage between myocardial damage, fibrosis and localized inflammation all induced by prolonged, intense exercise but not by moderate exercise. Thoughtful comparison was done between groups which differed in the duration and intensity of exercise, while the frequency of exercise was controlled uniformly. Time-dependent fibrosis based on collagen volume fraction, myocardial damage proven by serum cardiac Troponin I and microstructure examination through light and electronic microscopy, and increased expression

of local inflammatory molecules were all demonstrated in the RV and not the LV, exclusively in high intensity exercised group of mice.[3] Direct correlation between cardiac biomarkers and myocardial fibrosis has not been demonstrated previously, and this finding hints that exercise induced myocardial fibrosis is indeed not entirely harmless.

The authors also discuss the tool of assessing myocardial fibrosis in animal and human studies. Although cardiac magnetic resonance imaging (MRI) may be helpful in quantifying focal myocardial fibrosis, it has revealed heterogeneous findings in athletic hearts and its role in diffuse fibrosis is unknown.[10] An accurate and noninvasive method of localizing and quantifying myocardial fibrosis needs to be validated for future prospective studies.

Once reproduced and validated through larger animal or human studies, several aspects of this study would give insight for future studies. First, the correlation between inflammation and structural change after exercise seen in this study may be further linked with RV functional changes, which has been partly demonstrated.[8] Second, whether these changes are reversible, and whether it would affect soft and hard clinical endpoints should be evaluated. Third, the authors have shown a potential role of local inflammation in the structural changes induced by exercise. Elucidating the molecular pathway may lead to preventive pharmacological intervention for populations at risk.

This study revealed the potential harmful effect of long-term extreme physical exercise. Meanwhile, it also documented that moderate exercise is not related to significant myocardial fibrosis, damage and inflammation. This finding could support the recommendation of moderate exercise as an important and safe therapy for cardiovascular health.

REFERENCES

1. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people. *N Engl J Med* 1988;318:129-33.
PUBMED | CROSSREF
2. La Gerche A, Burns AT, Mooney DJ, et al. Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes. *Eur Heart J* 2012;33:998-1006.
PUBMED | CROSSREF
3. Rao Z, Wang S, Bunner WP, Chang Y, Shi R. Exercise induced right ventricular fibrosis is associated with myocardial damage and inflammation. *Korean Circ J* 2018;48:1014-24.
CROSSREF
4. Fukui H, Chiba A, Miyazaki T, et al. Spatial allocation and specification of cardiomyocytes during zebrafish embryogenesis. *Korean Circ J* 2017;47:160-7.
PUBMED | CROSSREF
5. Jacques D, Descorbeth M, Abdel-Samad D, Provost C, Perreault C, Jules F. The distribution and density of ET-1 and its receptors are different in human right and left ventricular endocardial endothelial cells. *Peptides* 2005;26:1427-35.
PUBMED | CROSSREF
6. La Gerche A, Heidbüchel H, Burns AT, et al. Disproportionate exercise load and remodeling of the athlete's right ventricle. *Med Sci Sports Exerc* 2011;43:974-81.
PUBMED | CROSSREF
7. Waskova-Arnostova P, Elsnicova B, Kasparova D, et al. Right-to-left ventricular differences in the expression of mitochondrial hexokinase and phosphorylation of Akt. *Cell Physiol Biochem* 2013;31:66-79.
PUBMED | CROSSREF
8. Molina CE, Johnson DM, Mehel H, et al. Interventricular differences in β-adrenergic responses in the canine heart: role of phosphodiesterases. *J Am Heart Assoc* 2014;3:e000858.
PUBMED | CROSSREF

https://doi.org/10.4070/kcj.2018.0218

9. Arbab-Zadeh A, Perhonen M, Howden E, et al. Cardiac remodeling in response to 1 year of intensive endurance training. *Circulation* 2014;130:2152-61.
PUBMED | CROSSREF

10. van de Schoor FR, Aengevaeren VL, Hopman MT, et al. Myocardial fibrosis in athletes. *Mayo Clin Proc* 2016;91:1617-31.
PUBMED | CROSSREF