Int J Heart Fail. 2022 Apr;4(2):91-94
https://doi.org/10.36628/ijhf.2022.0010
pISSN 2636-154X·eISSN 2636-1558

International Journal of Heart Failure
IJHF

Editorial

Check for updates

The Paradox in Defining Obesity in Patients With Heart Failure

Se-Eun Kim, MD, and Chan Joo Lee, MD, PhD

Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea

OPEN ACCESS

Received: Apr 19, 2022
Accepted: Apr 21, 2022
Published online: Apr 25, 2022

Correspondence to
Chan Joo Lee, MD, PhD
Division of Cardiology, Department of Internal Medicine, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Email: zanzu@yuhs.ac

Copyright © 2022. Korean Society of Heart Failure
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs
Se-Eun Kim
https://orcid.org/0000-0002-9824-1069
Chan Joo Lee
https://orcid.org/0000-0001-5362-478X

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

Author Contributions
Conceptualization: Lee CJ; Writing - original draft: Kim SE, Lee CJ.

Dubbed by the World Health Organization (WHO) as a disease that requires long-term treatment in 1995, obesity has emerged as a "new infectious disease of the 21st century".[1] According to the WHO, the global prevalence of obesity tripled in 2016 from 1975. In 2017, the Centers for Disease Control and Prevention named obesity as the most common chronic disease afflicting 42% of the U.S. population.[2][3] In Korea, the proportion of adults with a body mass index (BMI) ≥25 kg/m^2 has been increasing rapidly, the prevalence of obesity was 38.3% in 2020.[4]

Obesity causes several health problems, either independently or in association with other diseases.[5] As obesity is associated with several metabolic disorders, such as insulin resistance, dyslipidemia, inflammation, and endothelial dysfunction, it is a well-known risk factor in the development of atherosclerotic cardiovascular disease.[6][7] It increases the risk of heart failure (HF), arrhythmia, and even sudden cardiac death by altering central hemodynamics, cardiac structure, and ventricular function.[8][9]

However, there have been many reports that BMI-defined obesity was significantly associated with a low mortality risk in chronic diseases as coronary artery disease, diabetes, and renal failure.[10-13] This observation defies the previously accepted notion that obesity is a risk factor for various diseases, including cardiovascular disease, leading to the conceptualization of the "Obesity Paradox".

A meta-analysis of 9 observational studies (n=28,209) showed that patients with HF who are overweight and obese had a 16% and 33% lower risk of death, respectively, compared with patients with HF and a normal BMI.[14] A post-hoc analysis of candesartan use in the reduction of mortality and morbidity and a randomized study of 7,599 patients with HF also confirmed the obesity paradox.[15] However, the obesity paradox has not been universally observed when taking into account etiology, gender, and comorbidity, and ethnicity. In particular, people living in East Asian countries have relatively lower BMI than those living in Westerncountries.[16] Using a registry of 4,146 patients with acute HF in Korea, Hwang et al. observed an ascending mortality risk in patients with overweight (BMI, 23–25 kg/m^2), ideal body weight (BMI, 18.5–23 kg/m^2), and underweight (BMI <18.5 kg/m^2) compared to those with severe obesity (BMI ≥30 kg/m^2).[17] The inverse relationship between mortality risk and BMI was consistent when parameters, such as age, sex, hypertension, diabetes, atrial fibrillation, ischemic heart disease, and type of HF, were considered, reaffirming the obesity paradox in the East Asian population.

Generated by xmlinkpress

Several hypotheses attempt to explain the obesity paradox in patients with HF. In general, patients with high BMI have greater energy reserve, muscle mass, and high blood pressure, so it is easier to increase guideline-directed medications to their target dose, which may affect the prognosis in this population Some studies suggest that the impact of increased fat or lean mass on neuro-hormonal, inflammatory, and adipokine physiology was protective.[9)18-21)] Consequently, obese patients are less responsive to renin-angiotensin-aldosterone system, which is implicated in worsening HF.[9)18)22)]

Adipose tissue plays two roles: it serves as an efficient energy reservoir; but it also leads to a chronic inflammatory condition in metabolic syndrome.[23)24)] BMI does not accurately measure the impact of adipose tissue on the pathophysiology of HF. Epicardial fat, a marker of visceral adiposity, is associated with atrial fibrillation, left ventricular hypertrophy, and onset of HF.[25)] A recent study for patients with HF mildly reduced ejection fraction and HF with preserved ejection fraction reported that obese patients with an increased epicardial adipose tissue (EAT) had a worse prognosis compared with obese patients with low EAT.[26)] Therefore, in HF prognostication, it seems to be reasonable to consider the distribution and function of adipose tissue rather than obesity determined by BMI.

Furthermore, obese patients may be more physically fit than non-obese patients in general. This may be attributed to a greater contribution of muscle mass in BMI. Inflammatory cytokines play a role in metabolic disorders, decreased muscle mass, and deteriorated muscle strength. HF is known to induce and sustain a chronic inflammatory state. This may explain the reduced muscle mass in patients with HF, thereby affirming the obesity paradox.[19)] In the study by Hwang et al.,[17)] 92% of underweight patients had low muscle mass. In non-underweight patients, low muscle mass was associated with increased mortality. Muscle serves as a metabolic and functional reservoir in the body. Cachexia and sarcopenia are known to negatively affect the prognosis of patients with HF, a catabolic disease. Lower extremity muscle strength increases the risk of hospitalization for HF.[19)27-29)] Therefore, a generally better prognosis in patients with HF and BMI-defined obesity may be attributed to a greater muscle mass in these patients.

The conflicting views of the role of obesity in HF and other conditions continue to be controversial. On one hand, obesity increases the risk of HF; on the other hand, it has a protective role in HF. The current approach to diagnosis and risk stratification (i.e., BMI measurement) may not have captured the protective and risk factors that explain the obesity paradox. BMI does not accurately reflect or estimate body composition; therefore, it does not predict the risk attributed to excess fat. Muscle mass may play a role in HF and in the mechanism of the obesity paradox.

In conclusion, we have to consider that underweight and/or sarcopenic patients with HF may have poor clinical outcomes. Therefore, it is necessary to revisit the present definition and classification of obesity and to find new diagnostic or classification criteria that can be used to better predict risk. Further studies on the clinical usefulness of interventions, such as increasing muscle mass in patients with HF and low muscle mass, are warranted.

REFERENCES

1. James WP. WHO recognition of the global obesity epidemic. Int J Obes 2008;32 Suppl 7:S120-6.
PUBMED | CROSSREF

2. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet 2017;390:2627-42.
PUBMED | CROSSREF
3. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. NCHS Data Brief 2020;(360):1-8.
PUBMED
4. Nam GE, Kim YH, Han K, et al. Obesity fact sheet in Korea, 2019: prevalence of obesity and abdominal obesity from 2009 to 2018 and social factors. J Obes Metab Syndr 2020;29:124-32.
PUBMED | CROSSREF
5. Jastreboff AM, Kotz CM, Kahan S, Kelly AS, Heymsfield SB. Obesity as a disease: The Obesity Society 2018 position statement. Obesity (Silver Spring) 2019;27:7-9.
PUBMED | CROSSREF
6. Després JP. Body fat distribution and risk of cardiovascular disease: an update. Circulation 2012;126:1301-13.
PUBMED | CROSSREF
7. Abel ED, Litwin SE, Sweeney G. Cardiac remodeling in obesity. Physiol Rev 2008;88:389-419.
PUBMED | CROSSREF
8. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. Circulation 2021;143:e984-1010.
PUBMED | CROSSREF
9. Lavie CJ, Alpert MA, Arena R, Mehra MR, Milani RV, Ventura HO. Impact of obesity and the obesity paradox on prevalence and prognosis in heart failure. JACC Heart Fail 2013;1:93-102.
PUBMED | CROSSREF
10. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Woo MA, Tillisch JH. The relationship between obesity and mortality in patients with heart failure. J Am Coll Cardiol 2001;38:789-95.
PUBMED | CROSSREF
11. Park J, Ahmadi SF, Streja E, et al. Obesity paradox in end-stage kidney disease patients. Prog Cardiovasc Dis 2014;56:415-25.
PUBMED | CROSSREF
12. Uretsky S, Messerli FH, Bangalore S, et al. Obesity paradox in patients with hypertension and coronary artery disease. Am J Med 2007;120:863-70.
PUBMED | CROSSREF
13. Costanzo P, Cleland JG, Pellicori P, et al. The obesity paradox in type 2 diabetes mellitus: relationship of body mass index to prognosis: a cohort study. Ann Intern Med 2015;162:610-8.
PUBMED | CROSSREF
14. Oreopoulos A, Padwal R, Kalantar-Zadeh K, Fonarow GC, Norris CM, McAlister FA. Body mass index and mortality in heart failure: a meta-analysis. Am Heart J 2008;156:13-22.
PUBMED | CROSSREF
15. Haass M, Kitzman DW, Anand IS, et al. Body mass index and adverse cardiovascular outcomes in heart failure patients with preserved ejection fraction: results from the Irbesartan in Heart Failure with Preserved Ejection Fraction (I-PRESERVE) trial. Circ Heart Fail 2011;4:324-31.
PUBMED | CROSSREF
16. Jee SH, Sull JW, Park J, et al. Body-mass index and mortality in Korean men and women. N Engl J Med 2006;355:779-87.
PUBMED | CROSSREF
17. Hwang IC, Choi HM, Yoon YE, et al. Body mass index, muscle mass, and all-cause mortality in patients with acute heart failure: the obesity paradox revisited. Int J Heart Fail 2022;4:95-109.
CROSSREF
18. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. J Am Coll Cardiol 2009;53:1925-32.
PUBMED | CROSSREF
19. Soto ME, Pérez-Torres I, Rubio-Ruiz ME, Manzano-Pech L, Guarner-Lans V. Interconnection between cardiac cachexia and heart failure-protective role of cardiac obesity. Cells 2022;11:1039.
PUBMED | CROSSREF
20. von Haehling S, Horwich TB, Fonarow GC, Anker SD. Tipping the scale: heart failure, body mass index, and prognosis. Circulation 2007;116:588-90.
PUBMED | CROSSREF
21. von Haehling S, Doehner W, Anker SD. Nutrition, metabolism, and the complex pathophysiology of cachexia in chronic heart failure. Cardiovasc Res 2007;73:298-309.
PUBMED | CROSSREF

22. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms. Circ Res 2015;116:991-1006.
PUBMED | CROSSREF
23. Goyal A, Nimmakayala KR, Zonszein J. Is there a paradox in obesity? Cardiol Rev 2014;22:163-70.
PUBMED | CROSSREF
24. Bays HE. Adiposopathy is "sick fat" a cardiovascular disease? J Am Coll Cardiol 2011;57:2461-73.
PUBMED | CROSSREF
25. Packer M. Disease-treatment interactions in the management of patients with obesity and diabetes who have atrial fibrillation: the potential mediating influence of epicardial adipose tissue. Cardiovasc Diabetol 2019;18:121.
PUBMED | CROSSREF
26. van Woerden G, van Veldhuisen DJ, Manintveld OC, et al. Epicardial adipose tissue and outcome in heart failure with mid-range and preserved ejection fraction. Circ Heart Fail 2022;15:e009238.
PUBMED | CROSSREF
27. Lee CJ, Ryu HY, Chun KH, et al. Association of muscular fitness with rehospitalization for heart failure with reduced ejection fraction. Clin Cardiol 2021;44:244-51.
PUBMED | CROSSREF
28. Davos CH, Doehner W, Rauchhaus M, et al. Body mass and survival in patients with chronic heart failure without cachexia: the importance of obesity. J Card Fail 2003;9:29-35.
PUBMED | CROSSREF
29. Saitoh M, Ishida J, Doehner W, et al. Sarcopenia, cachexia, and muscle performance in heart failure: review update 2016. Int J Cardiol 2017;238:5-11.
PUBMED | CROSSREF