EDITORIAL POINT OF VIEW

Can Visceral Adiposity Predict Paradoxical Prognostic Implications on Lethal Arrhythmic Events in Chronic Heart Failure Patients with Impaired Cardiac Sympathetic Activity?

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The sympathetic nervous system of the heart is critically involved in the controlling cardiovascular homoeostasis by regulation of cardiac contractility, conduction, heart rate and peripheral vasoconstriction (1). Myocardial imaging with ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG), an analogue of norepinephrine, is useful for detecting abnormalities of cardiac sympathetic nerve activity (CSNA) in heart failure patients (2). This imaging modality has been reported as the useful prognostic value for pump failure death (3, 4), or sudden death due to lethal arrhythmia (5, 6) in these patients.

Visceral adiposity and cardiac events

Visceral adiposity has been reported to be the main contributor to metabolic dysregulation, the independent risk factor for cardiovascular disease (7). Therefore, visceral adipose tissue area obtained from computed tomography is helpful for management of obese patients with cardiovascular risk (8). However, since malnutrition or underweight is known to be associated with poor clinical outcomes in patients with heart failure, these obese patients may have better outcomes. Furthermore, the association between visceral adiposity and sudden cardiac death is not well understood.

Relationship among visceral adiposity, cardiac sympathetic nervous function and cardiac events

In this issue of *Annals of Nuclear Cardiology*, Doi et al. (9) reported an interesting study as it evaluates whether visceral adiposity is predictive for paradoxical prognostic implications between heart failure mortality and fatal arrhythmic events in chronic heart failure patients with impaired CSNA. In the patients of this study, the less visceral fat areas resulted in higher overall and heart failure mortality. In contrast, more visceral adiposity resulted in higher sudden death risk. The assessment of CSNA was useful for the predictor of both heart failure mortality and sudden death risk, as in the previous reports (3-6). The study has shown for the first time that the relationship between visceral adiposity and heart failure mortality was paradoxical for that between visceral adiposity and fatal arrhythmic events. Their data indicate that excessive physical activity relative to their impaired systemic and/or cardiac functional reserve may induce atherosclerotic or ischemic events, leading to fatal arrhythmic events rather than left ventricular pump failure progression in obese patients with heart failure. In addition, CSNA could predict cardiac event risk without being affected by visceral adiposity, overcoming so-called “obesity paradox” (10).

Chronically increased systemic sympathetic activity in heart failure brings changes in myocardial metabolic substrates. It leads to increased lipolysis of adipose tissue, which promotes myocardial fatty acid (FA) transport and metabolism, intracellular accumulation of lipid materials, and lipotoxicity (11). Although Doi et al. (9) could not show the dynamic relationships between lipolysis and CSNA, the underlying pathophysiological link between lipid metabolism and sympathetic innervation could be outlined. Interestingly, some researchers tried to revert the metabolic shift to glycolysis in heart failure. Representatively, Tuunanen et al. (12) used trimetazidine (TMZ), which inhibits 3-ketoacyl-CoA thiolase (mitochondrial enzyme converting acetylCoA to 3-ketoacylCoA). In their prospective randomized study with 19

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patients with dilated cardiomyopathy, TMZ-treated group (n= 7) showed significant differences in functional improvement and FA metabolism rate, as compared to controls (n＝12). According to the study by Doi et al. (9), even in patients with preserved CSNA, decreased visceral adiposity is associated with an increased cardiac event risk. Metabolic modulation may play a role in this group of patients. In contrast, even in patients with visceral adiposity (tertile 3), decreased CSNA was associated with an increased cardiac event risk. In this group of patient, preventive intervention (e. g. implantable cardioverter-defibrillator implantation) may be an optimal treatment option. Future studies linking the treatment options with metabolism/sympathetic nerve activity are warranted.

Although the data of the study by Doi et al. is very interesting, there are some limitations necessary to be considered. The level of plasma norepinephrine and its spillover were not measured in the study. As these variables are predictive for adverse outcome in failing human heart (1), it would be interesting to evaluate the relation between plasma norepinephrine levels (or its spillover) and visceral adiposity. Moreover, the study evaluated one-time evaluation of ^{123}I-MIBG scintigraphy. Since this imaging method has been well known to improve after medical treatments (13, 14), several reports have demonstrated that serial ^{123}I-MIBG scintigraphic studies are more useful for predicting prognosis and managing heart failure than a one-time scan in these patients (15, 16).

Conclusions

Despite these study limitations, the study by Doi et al. (9) contributes significantly to the current literature as it provides evidence that visceral adiposity can be predictive for paradoxical prognostic implications between heart failure mortality and lethal arrhythmic events. In the future, additional studies are needed to clarify the relationship between visceral adiposity and heart failure mortality was paradoxical for that between visceral adiposity and lethal arrhythmic events in multicenter studies, including large groups of patients.

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Conflicts of interest

None.

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