EDITORIAL

Correlation between Nutritional State and Prognosis of Heart Failure, with a Focus on the Immune System

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The number of patients with congestive heart failure is increasing worldwide, and the prognosis of these patients is poorer than that of patients with malignancy. Pharmacological therapy for heart failure involving β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists improves the prognosis of patients with heart failure who show reduced ejection fraction; however, the effect of these therapies on the prognosis of malnourished patients called cardiac cachexia is unclear. Cardiac cachexia is a complex pathophysiological condition caused by impaired absorption of nutrients from the intestine because of mucosal edema, muscle catabolism, and chronic inflammation induced by heart failure. Patients with cardiac cachexia need advanced nutritional intervention and cardiac rehabilitation in addition to standard pharmacological therapy for improving their general condition. Moreover, early detection of malnutrition is needed to rapidly achieve intervention goals and to improve the outcomes of malnourished patients. Previously reported scoring systems such as mini-nutritional assessment and geriatric nutritional index are efficient for determining the nutritional state of patients with heart failure; however, these scoring systems involve multiple questions and calculations for patient assessment. In the acute phase of heart failure treatment, easy and rapid scoring systems are needed to assess the risk of heart failure in patients for smooth translational intervention.

Nishi, et al examined the utility of controlling nutritional status (CONUT) scoring system to assess the relationship between malnutrition and short-term prognosis of heart failure. The CONUT scoring system is a simple scoring system that requires the determination of serum albumin level, serum total cholesterol level, and total lymphocyte count. CONUT scores are classified as follows: scores 0-1, normal; scores 2-4, slight malnutrition; scores 5-8, moderate malnutrition; and scores 9-12, severe malnutrition. High CONUT scores indicate malnutrition and poor long-term prognosis of patients with cardiovascular diseases. Interestingly, the study by Nishi, et al. showed that CONUT scores were directly correlated with the logarithmic change in serum brain natriuretic peptide level. This result suggests that CONUT scores can be used as an index for monitoring heart failure.

However, it is unclear as to why malnutrition is associated with the poor prognosis of patients with heart failure. CONUT scores simply represent protein synthesis ability and white blood cell proliferation capacity, suggesting that the immune-metabolic state might determine the prognosis of patients with heart failure. Low lymphocyte count is also associated with high mortality in patients with heart failure and those with acute myocardial infarction. In general, malnutrition state such as cardiac cachexia represses anabolic metabolism and induces macrophage dysfunction in the presence of a protein disorder. Moreover, malnutrition represses lymphocyte function and proliferation. For example, repression of effector T cells such as Th1 and Th17 cells is considered to be one of the causes of immunosuppressive state of malnutrition, and this state is provoked in low serum leptin level during malnutrition. In addition, tissue macrophages play an important role in maintaining homeostasis in various organs, including the heart. The heart contains two types of tissue macrophages, namely, Ly6C hi and Ly6C lo macrophages at least. Ly6C hi macrophages are inflammatory macrophages, and Ly6C lo macrophages are tissue-repairing macrophages that are predominantly present in the heart at the steady state. During inflammation or tissue damage, Ly6C hi monocytes, which are inflammatory monocytes, are recruited to the heart where they differentiate into Ly6C hi cardiac macrophages. These cells exert a cardio-protective effect in the heart during acute tissue injury. These macrophages are under control of T cells and impairment of T cells reduces macrophage function. For example, elimination of regulator T cells (Treg) that have the ability to resolve inflammation, causes cardiac macrophages to lose their ability to repair injured heart tissue and accelerate cardiac remodeling during myocardial infarction in mice. In patients with heart failure with reduced ejection fraction
Fraction, the peripheral blood Th17/Treg ratio increases. This also indicates the proportion of Treg to inflammatory Th17 cells is important in heart failure. Deregulated inflammation has a deleterious effect on heart failure. On the contrary, in a malnourished state, the Th17/Treg ratio decreases. Although elevating the proportion of Treg appears to be beneficial to the heart through the cardioprotective function of Ly6Clo cardiac macrophages, the prognosis of malnourished heart failure patients is poor. Based on these observations, the existence of only Treg is not sufficient to compensate for heart failure.

The imbalance of T cell function induced by malnutrition might deregulate the function of cardiac macrophages in patients with heart failure. In obesity, serum fatty acid levels increase, which in turn induces low-grade inflammation because of the production of inflammatory cytokines by immune cells that induce cardiovascular diseases. This low grade inflammation also activates Ly6Clo cardiac macrophages through the activation of effector T cells. Although excess accumulation of Ly6Clo cardiac macrophages induces tissue damage, these macrophages are also necessary for stress adaptation. In contrast, in malnourished heart failure patients, a decreased lymphocyte count and Th17/Treg ratio cause the interruption of Ly6Clo macrophage recruitment during sudden cardiac stress such as pressure overload. This might lead to decompensated heart failure and a worsening of the prognosis. T cell function is also impaired in malnourished patients. Moreover, T cell dysfunction decreases the recruitment of monocytes and macrophages to the heart and leads to macrophage dysfunction in these patients. This may explain one of the mechanisms of the obesity paradox.

If the nutritional state determines immune system function, we should pay more attention to our nutritional state to prevent cardiovascular and infectious diseases. Moreover, nutritional intervention may be an option for treating patients with heart failure.

Disclosures

Conflicts of interest: The authors declare that they do not have any conflicts of interest related to this study.

References

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