OPEN ACCESS Freely available online

Journal of Clinical and Experimental Cardiology

Mini Review

New Thinking on the Diagnosis and Treatment of Septic Cardiomyopathy

Di Chen[1], Honglei Li[1], Shitao Huang[1], Zhongya Huang[1], Yibo Sun[1], Liping Liu[1,2*]

[1]Department of Cardiology, The First Clinical College of Lanzhou University, Lanzhou, China; [2]Department of Emergency Critical Care Medicine, The First Hospital of Lanzhou University, Lanzhou, China

ABSTRACT

Myocardial inhibition due to sepsis is common, and unlike left ventricular dysfunction in the traditional sense, right ventricular dysfunction is associated with long-term prognosis in patients with sepsis. There is no consensus on the pathogenesis of SCM, and mitochondrial dysfunction has been the focus of research in recent years. Failure to accurately evaluate the cardiac function of patients with Septic Cardiomyopathy (SCM) is the main reason for the high mortality of patients, so it is of great significance to explore the diagnosis and treatment of SCM to improve the prognosis of SCM.

Keywords: Septic cardiomyopathy; Pathogenesis; Diagnosis; Treatment

INTRODUCTION

Septic Cardiomyopathy (SCM) is a major cause of death in patients with sepsis and septic shock [1]. Recently, numerous studies have focused on the pathogenesis, diagnosis, and treatment of SCM, making it difficult for clinicians to accurately assess the severity of myocardial injury and select appropriate treatment. This article summarizes the recent research on SCM at home and abroad, and further elaborates the latest progress in the pathogenesis, diagnosis and treatment of SCM, so as to provide references for the early diagnosis and treatment of patients with SCM.

LITERATURE REVIEW

Septic Cardiomyopathy (SCM) is an early and reversible myocardial injury in septic shock, it is a serious complication of sepsis and septic shock [2]. A meta-analysis showed a prevalence of 20% and mortality of up to 80% for septic cardiomyopathy [3]. Current research suggests that men, age, high lactic acid and congenital heart disease are risk factors for the disease [1]. Due to the lack of specificity of clinical manifestations, doctors often use echocardiography to distinguish, which is manifested as: Left/right ventricular dilation, Left Ventricular Ejection Fraction (LVEF) decrease, ventricular compliance increase, filling pressure decrease, survivors can recover heart function within 7-10 days [4]. Cardiac Magnetic Resonance Imaging (MRI) shows myocardial edema or metabolic abnormalities, which are completely different from myocardial ischemia and necrosis [5]. In terms of hemodynamics, there are five different types of SCM, in which 23% of patients show left ventricular systolic function preservation, aortic blood flow increased; 22% of patients presented with right ventricular failure; nearly 19% of patients still had persistently low blood volume [6].

The pathophysiological mechanism of SCM is complex. A large number of studies have shown that the inflammatory response directly causes myocardial inhibition and activates the host immune system together with inflammatory factors to produce excess oxygen free radicals, leading to myocardial dysfunction. In addition, due to the excessive activation of sympathetic nerves in SCM patients, a large amount of catecholamines are secreted, and the myocardial response to catecholamines is weak, which impels cardiac function and reduces the filling time of myocardium during diastole [7]. In addition to the mechanisms identified above, recent studies have suggested that mitochondrial dysfunction is an important cause of the development of SCM, and oxidative phosphorylation, mitochondrial autophagy, and energy metabolism disorders can all cause mitochondrial damage [8]. Mitochondrial Permeability Transition Pore (mPTP) is a channel transporting Reactive Oxygen Species (ROS) and Ca^{2+} in the Inner Mitochondrial

Correspondence to: Liping Liu, Department of Emergency Critical Care Medicine, The First Hospital of Lanzhou University, Lanzhou, China, E-mail: 3448923751@qq.com

Received: 21-Aug-2024, Manuscript No. JCEC-24-33570; **Editor assigned:** 23-Aug-2024, PreQC No. JCEC-24-33570 (PQ); **Reviewed:** 06-Sep-2024, QC No. JCEC-24-33570; **Revised:** 13-Sep-2024, Manuscript No. JCEC-24-33570 (R); **Published:** 20-Sep-2024, DOI:10.35248/2155-9880.24.15.905

Citation: Chen D, Li H, Huang S, Huang Z, Sun Y, Liu L (2024). New Thinking on the Diagnosis and Treatment of Septic Cardiomyopathy. J Clin Exp Cardiolog. 15:905.

Membrane (IMM), in the state of inflammation, the excessive production of ROS and NO and Ca^{2+} overload can increase the permeability of IMM, reduce the mitochondrial membrane potential, and cause the coupling of oxidative phosphoric acid and the decrease of ATP [9]. Mitochondrial autophagy is a way of removing damaged mitochondria in order to facilitate the absorption of nutrients and maintain Adenosine Triphosphate (ATP) levels, the PINK/Parkin pathway is a classical pathway of mitochondrial autophagy, and 1A/1B Light Chain 3 (LC3) is a key protein in the formation of autophagy and a key indicator for the evaluation of mitochondrial autophagy [10]. A basic study demonstrated that the expression of autophagy related molecules PINK/Parkin and LC3B-II/LC3B-I increased in myocardial mitochondria of sepsis mice, but decreased in the late stage, indicating that in the early stage of sepsis, the body can up-regulate the level of mitochondrial autophagy to remove excess mitochondria to protect the heart. However, in the later stage, continuous oxidative stress may cause serious myocardial damage, which weakens the expression of autophagy [11]. The energy metabolism of SCM is mainly glycolysis, accompanied by elevated lactic acid, macrophages can promote their transformation into M1 type through glycolysis, which aggravates the inflammatory response. When mitochondrial autophagy or aerobic glycolysis occurs in cardiomyocytes, the damage of ROS to cardiomyocytes can be alleviated [12]. Therefore, reducing myocardial aerobic glycolysis and inhibiting lactic acid production can protect myocardial ATP and enhance immunity.

DISCUSSION

At present, there is a lack of clear diagnostic criteria for SCM. Earlier studies proposed Myocardial Performance Index (MPI), a new index derived from cardiac Doppler to evaluate cardiac systolic and diastolic functions, including cardiac Isovolumic Contraction Time (IVCT), Isovolumic Relaxation Time (IVRT) and cardiac Ejection Time (ET), in this prospective clinical study, MPI improved in 20 of 47 patients with sepsis and worsened in only 13 patients, but there was no difference in baseline data, demonstrating that the lower the MPI, the better the heart function, unlike LVEF, it is not associated with ventricular and afterload, again demonstrating the value of MPI for the prognosis of patients with SCM [13]. However, due to the small sample size of the experiment, further verification is needed. In 1967, it was reported that Mitral Ring Plane Systolic Pressure Shift (MAPSE) is a marker of left ventricular longitudinal function and is more sensitive than LVEF, recent studies have proved that MAPSE ≤ 1.2 cm is related to left ventricular systolic dysfunction, which has better clinical practicability [14]. Lactic acid is a commonly used marker for mitochondrial disorders, but it is not specific. Hubens, et al., proposed that Fibroblast Growth Faction-21 (FGF-21) and Growth Differentiation Faction-15 (GDF-15) are the latest markers of mitochondrial dysfunction, and FGF-21 protects mitochondrial function by regulating lipid and glucose metabolism. GDF-15 modulates activation of transcription factor 4 to enhance immune cell function and mitigate the development of SCM [15].

The main treatment of SCM is fluid resuscitation and vasoactive drugs. In 2023, Melatonin (MLT) was shown to regulate mitochondrial homeostasis and prevent SCM in mice with sepsis, Mammalian sterile 20-like kinase 1 (Mst1) overexpresses in SCM and increases Jun N-terminal Kinase (JNK) activity. MLT can inhibit Mst1 transcription and protect mitochondria by decreasing JNK activity, MLT alleviates mitochondrial damage and maintains mitochondrial membrane potential through ERK-BAP31 pathway [16]. The NOD-Like Receptor Protein 3 (*NLRP3*) inflammasome plays an important role in the pathogenesis of SCM, and Vaccarin can promote *NLRP3* palmitoylation, inhibit pro-inflammatory factors and protect SCM [17]. Similarly, Angiopoietin-Like Protein 2 (*ANGPTL2*) silencing can inhibit *NLRP3* inflammasome, protect cardiac function and reduce the level of markers of myocardial injury [18]; NSC228155 was injected into mice to model sepsis, and it was found that NSC228155 can alleviate myocardial damage, activate mitochondrial autophagy, correct metabolic disorders, and improve cardiac function [19]. These are some of the latest discoveries about potential treatments for SCM.

CONCLUSION

SCM is a common disease in Intensive Care Unit (ICU) and a hot topic of recent research. The diagnostic indicators of SCM lack standard, the key lies in the differential diagnosis with other cardiovascular diseases. There have been a lot of studies on the pathogenesis of SCM, but mitochondrial disorders still need to be verified. It is hoped that the pathophysiological mechanism of SCM will be closely related to treatment in future studies, which will help improve the prognosis of SCM. This will be a new challenge for researchers.

REFERENCES

1. Lukić I, Mihić D, Varžić SC, Relatić KS, Zibar L, Loinjak D, et al. Septic cardiomyopathy. Rev Cardiovasc Med. 2024;25(1):23.
2. Carbone F, Liberale L, Preda A, Schindler TH, Montecucco F. Septic cardiomyopathy: From pathophysiology to the clinical setting. Cells. 2022;11(18):2833.
3. Hasegawa D, Ishisaka Y, Maeda T, Prasitlumkum N, Nishida K, Dugar S, et al. Prevalence and prognosis of sepsis-induced cardiomyopathy: A systematic review and meta-analysis. J Intensive Care Med. 2023;38(9):797-808.
4. Pruszczyk A, Zawadka M, Andruszkiewicz P, LaVia L, Herpain A, Sato R, et al. Mortality in patients with septic cardiomyopathy identified by longitudinal strain by speckle tracking echocardiography: An updated systematic review and meta-analysis with trial sequential analysis. Anaesth Crit Care Pain Med. 2024;43(2):101339.
5. Silvis MJ, Kaffka genaamd Dengler SE, Odille CA, Mishra M, Van der Kaaij NP, Doevendans PA, et al. Damage-associated molecular patterns in myocardial infarction and heart transplantation: The road to translational success. Front Immunol. 2020;11:599511.
6. Geri G, Vignon P, Aubry A, Fedou AL, Charron C, Silva S, et al. Cardiovascular clusters in septic shock combining clinical and echocardiographic parameters: A post hoc analysis. Intensive Care Med. 2019;45:657-667.
7. Saiyang X, Qingqing W, Man X, Chen L, Min Z, Yun X, et al. Activation of Toll-like receptor 7 provides cardioprotection in

septic cardiomyopathy-induced systolic dysfunction. Clin Transl Med. 2021;11(1):266.

8. Tan Y, Zhang Y, He J, Wu F, Wu D, Shi N, et al. Dual specificity phosphatase 1 attenuates inflammation-induced cardiomyopathy by improving mitophagy and mitochondrial metabolism. Mol Metab. 2022;64:101567.
9. Li Y, Yu J, Li R, Zhou H, Chang X. New insights into the role of mitochondrial metabolic dysregulation and immune infiltration in septic cardiomyopathy by integrated bioinformatics analysis and experimental validation. Cell Mol Biol Lett. 2024;29(1):21.
10. Wang Y, Jasper H, Toan S, Muid D, Chang X, Zhou H. Mitophagy coordinates the mitochondrial unfolded protein response to attenuate inflammation-mediated myocardial injury. Redox Biol. 2021;45:102049.
11. Song J, Fang X, Zhou K, Bao H, Li L. Sepsis-induced cardiac dysfunction and pathogenetic mechanisms (Review). Mol Med Rep. 2023;28(6):1-2.
12. Ni D, Lin X, Deng C, Yuan L, Li J, Liu Y, et al. Energy metabolism: From physiological changes to targets in sepsis-induced cardiomyopathy. Hellenic J Cardiol. 2024;1109-9666(24): 114-123.
13. Nizamuddin J, Mahmood F, Tung A, Mueller A, Brown SM, Shaefi S, et al. Interval changes in myocardial performance index predict outcome in severe sepsis. J Cardiothorac Vasc Anesth. 2017;31(3):957-964.
14. Huang SJ, Ting I, Huang AM, Slama M, McLean AS. Longitudinal wall fractional shortening: An M-mode index based on Mitral Annular Plane Systolic Excursion (MAPSE) that correlates and predicts Left Ventricular Longitudinal Strain (LVLS) in intensive care patients. Crit Care. 2017;21:1-1.
15. Hubens WH, Vallbona-Garcia A, de Coo IF, van Tienen FH, Webers CA, Smeets HJ, et al. Blood biomarkers for assessment of mitochondrial dysfunction: An expert review. Mitochondrion. 2022;62:187-204.
16. Taha AM, Mahmoud AM, Ghonaim MM, Kamran A, AlSamhori JF, AlBarakat MM, et al. Melatonin as a potential treatment for septic cardiomyopathy. Biomed Pharmacother. 2023;166:115305.
17. Fujimura K, Karasawa T, Komada T, Yamada N, Mizushina Y, Baatarjav C, et al. *NLRP3* inflammasome-driven IL-1β and IL-18 contribute to lipopolysaccharide-induced septic cardiomyopathy. J Mol Cell Cardiol. 2023;180:58-68.
18. Li J, Wan T, Liu C, Liu H, Ke D, Li L. ANGPTL2 aggravates LPS-induced septic cardiomyopathy *via NLRP3*-mediated inflammasome in a *DUSP1*-dependent pathway. Int Immunopharmacol. 2023;123: 110701.
19. Jiang Y, Li Y, Zhang Y, Hu D, Zhang S, Wang C, et al. NSC228155 alleviates septic cardiomyopathy *via* protecting mitochondria and inhibiting inflammation. Int Immunopharmacol. 2023;116: 109847.