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Editorial

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Clinical Implications of a Proteomics-Based Approach for Cardiomyopathy and Heart Failure

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▸ See the article "Proteome-wide Characterization and Pathophysiology Correlation in Non-ischemic Cardiomyopathies" in volume 54 on page 468.

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Aside from ischemic heart disease, hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), and myocarditis are common causes of non-ischemic cardiomyopathies and heart failure (HF). These diseases have heterogeneous etiologies (e.g., genetic, environmental), clinical manifestations (e.g., HF, arrhythmia, sudden cardiac death), comorbidities, and responses to therapeutic interventions. HCM typically presents with cardiac hypertrophy. However, in advanced stages, the myocardium is diffusely replaced by fibrosis, and the heart chamber size increases,[1] making it challenging to distinguish from DCM. Similarly, if myocarditis does not fully resolve and leaves sequalae, it can also be difficult to differentiate from DCM.[2] Although myocardial imaging parameters such as late gadolinium enhancement patterns, native T1 and T2 values, and extracellular volume in cardiac magnetic resonance imaging (MRI) can somewhat confirm the etiology and prognosis of cardiomyopathy,[3] there are still many cases where the etiology remains unclear.

Given the complexity of diagnosing non-ischemic cardiomyopathies and recent advancements in their treatment through precision medicine, understanding the genetic molecular pathophysiology of HF has become essential.[4] To date, hundreds of HCM- and DCM-associated mutations in up to 30 genes in the human genome have been reported. However, conventional genetics methods are thought to capture >0.1% of rare point mutations.[5] Considering that the human genome contains numerous lesions, from large chromosomal deletions and duplications to sub-microscopic changes, conventional studies of cardiomyopathies have likely overlooked the roles of many genes.[5] These undiscovered genes may be more effectively identified through systems biology supported by omics technologies, including genomics, epigenomics, transcriptomics, proteomics, and metabolomics.[5][6]

Among the omics technologies, proteomics focuses on analyzing the proteins expressed in a specific state and investigating how these proteins may change over time and under different disease conditions.[6] Proteomics allows for the simultaneous analysis of thousands of proteins, providing a comprehensive overview of protein expression, modification, and interactions within a biological system. It helps identify new biomarkers for early disease detection and personalized treatment strategies, particularly in diseases like cancer and cardiovascular disorders.[6][7] Understanding protein interactions and networks can reveal

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insights into cellular signaling pathways and metabolic processes, leading to a better understanding of cellular functions and mechanisms.[6] However, proteomics generates a vast amount of complex data, which requires sophisticated bioinformatics tools and expertise to analyze and interpret, posing a significant challenge.[7] Furthermore, results can vary based on experimental conditions and sample handling, leading to potential reproducibility problems.[7] Therefore, to utilize proteomics in real clinical settings beyond research purposes, it is crucial to overcome many technical limitations and to select and implement it with clinically meaningful indications.

Recently, several studies have utilized proteomics to offer precision medicine through precision phenotyping, differentiating etiology, and predicting prognosis in non-ischemic cardiomyopathies, such as HCM, DCM, and myocarditis. Shimada et al.[8][9] reported not only novel protein biomarkers and signaling pathways (eg, Ras-MAPK), but also the prediction of major adverse cardiovascular events in patients with HCM using plasma proteomics profiling. Tayal et al.[10] reported that proteomics was applied in machine learning approaches for the identification of three novel DCM subtypes, labeled as profibrotic metabolic, mild nonfibrotic, and biventricular impairment, using clinical, genetic, and cardiac MRI assessments. In a study by Lee et al.,[11] comparative extensive proteomic analysis of the myocardium was performed in patients with biopsy-proven non-ischemic cardiomyopathies and advanced HF including HCM, DCM, and myocarditis as well as controls. Interestingly, despite shared clinical and histopathologic findings of non-ischemic cardiomyopathies and advanced HF, such as severe ventricular systolic dysfunction and predominant myocardial fibrosis, HCM, DCM, and myocarditis each exhibit distinct proteomic expression.[11] These results demonstrate that proteomics can be beneficial in the differential diagnosis of patients with advanced HF of unknown etiology.

Taken together, proteomics can be utilized in personalized medicine for differential diagnosis, prognosis prediction, and tailored treatment planning in patients with cardiomyopathy and HF. When conducting proteomics, it is essential to consider technical issues such as sample selection, consistent experimental conditions, and the interpretation of vast amounts of data, as well as clinical issues like patient selection and number, disease stage, and integration with clinical and imaging data. Therefore, to obtain clinically meaningful results, close collaboration between data scientists and cardiologists is of utmost importance.

REFERENCES

1. Lee HJ, Kim J, Chang SA, Kim YJ, Kim HK, Lee SC. Major clinical issues in hypertrophic cardiomyopathy. *Korean Circ J* 2022;52:563-75. PUBMED | CROSSREF
2. Liu PP, Mason JW. Advances in the understanding of myocarditis. *Circulation* 2001;104:1076-82. PUBMED | CROSSREF
3. Cho JY, Cho DH, Youn JC, et al. Korean Society of Heart Failure guidelines for the management of heart failure: definition and diagnosis. *Korean Circ J* 2023;53:195-216. PUBMED | CROSSREF
4. Jung Y, Kim J, Jang H, Kim G, Kwon YW. Strategy of patient-specific therapeutics in cardiovascular disease through single-cell RNA sequencing. *Korean Circ J* 2023;53:1-16. PUBMED | CROSSREF
5. Raghow R. An 'Omics' perspective on cardiomyopathies and heart failure. *Trends Mol Med* 2016;22:813-27. PUBMED | CROSSREF
6. Michelhaugh SA, Januzzi JL Jr. Finding a needle in a haystack: proteomics in heart failure. *JACC Basic Transl Sci* 2020;5:1043-53. PUBMED | CROSSREF

7. Dupree EJ, Jayathirtha M, Yorkey H, Mihasan M, Petre BA, Darie CC. A critical review of bottom-up proteomics: the good, the bad, and the future of this field. *Proteomes* 2020;8:14. PUBMED | CROSSREF
8. Shimada YJ, Raita Y, Liang LW, et al. Comprehensive proteomics profiling reveals circulating biomarkers of hypertrophic cardiomyopathy. *Circ Heart Fail* 2021;14:e007849. PUBMED | CROSSREF
9. Shimada YJ, Raita Y, Liang LW, et al. Prediction of major adverse cardiovascular events in patients with hypertrophic cardiomyopathy using proteomics profiling. *Circ Genom Precis Med* 2022;15:e003546. PUBMED | CROSSREF
10. Tayal U, Verdonschot JA, Hazebroek MR, et al. Precision phenotyping of dilated cardiomyopathy using multidimensional data. *J Am Coll Cardiol* 2022;79:2219-32. PUBMED | CROSSREF
11. Lee S, Jang DG, Kyoung YJ, et al. Proteome-wide characterization and pathophysiology correlation in non-ischemic cardiomyopathies. *Korean Circ J* 2024;54:468-81. CROSSREF