

บทความพิเศษ

Review Article

ความก้าวหน้าของแนวทางการศึกษาทางด้านโปรตีโอมิกส์ในโรคหัวใจ

รัฐชน ชนาธิกุล¹

¹โรงเรียนปัญญาประทีป

ปัญจารีย์ สันธัญญารธรรม¹

¹โรงเรียนปัญญาประทีป

ต้นบุญ เลิศฤทธิ์เรืองสิน¹

¹โรงเรียนปัญญาประทีป

พอดิ พัทธ์พงษ์สนธิ¹

¹โรงเรียนปัญญาประทีป

ภูมิธวัชณ์ จุลพัฒน์วงศ์¹

¹โรงเรียนปัญญาประทีป

นิติศ สมานทอง²

²สถาบันพระบรมราชชนก

DOI: 10.14456/jrpsi.2026.4

Received: September 28, 2025 | Revised: November 3, 2025 | Accepted: January 8, 2026

บทคัดย่อ

โรคหัวใจและหลอดเลือด โดยเฉพาะโรคหัวใจถือเป็นปัจจัยสำคัญที่สร้างภาระด้านสุขภาพในระดับสากล แม้จะมีความก้าวหน้าทางการแพทย์และการรักษา แต่ความท้าทายหลายด้านยังคงมีอยู่ โดยเฉพาะการวินิจฉัยโรคที่ทันเวลาที่ การประเมินความเสี่ยงที่แม่นยำและการจัดการโรคที่มีประสิทธิภาพ ซึ่งการศึกษาทางโปรตีโอมิกส์ได้กลายเป็นแนวทางที่มีศักยภาพสูงในงานวิจัยโรคหัวใจและหลอดเลือด โดยช่วยให้ค้นพบตัวบ่งชี้ทางชีวภาพใหม่ๆ และเป้าหมายการรักษาที่สำคัญ ซึ่งอาจมีบทบาทในการพัฒนาทางคลินิกและเวชศาสตร์แปลผล เทคโนโลยีโปรตีโอมิกส์จึงถือเป็นเครื่องมือสำคัญที่สามารถยกระดับการแพทย์ในอนาคต ยิ่งไปกว่านั้นการบูรณาการโปรตีโอมิกส์เข้ากับแพลตฟอร์ม -omics เสริมและชี้นำสารสนเทศขั้นสูง ยังช่วยยกระดับการแบ่งชั้นของโรค สนับสนุนการพัฒนาการแพทย์แม่นยำ และช่วยให้เกิดลระยะการรักษาทันทีเร็วและตรงเป้าหมายมากขึ้น ซึ่งความก้าวหน้าเหล่านี้แสดงให้เห็นถึงศักยภาพของโปรตีโอมิกส์ในการวินิจฉัย การประเมินความเสี่ยง และการติดตามผลการรักษาที่แม่นยำยิ่งขึ้น ผ่านการศึกษาบทบาทของโปรตีโอมิกส์ที่กำลังพัฒนาในการวินิจฉัย การจัดการและการรักษาโรคหัวใจ โดยอ้างอิงจากรวบรวมที่ผ่านการทบทวนโดยผู้ทรงคุณวุฒิ ซึ่งตีพิมพ์ในช่วงปี ค.ศ. 2010 ถึง ค.ศ. 2025 ในฐานะข้อมูล Google Scholar, PubMed และ Scopus

ติดต่อผู้พิมพ์: นิติศ สมานทอง

อีเมล: nitis.sman@gmail.com

คำสำคัญ: โรคหัวใจและหลอดเลือด, โรคหัวใจ, โปรตีโอมิกส์

Advancement of Proteomic Approach in Heart Diseases

Runch Chanathitikul¹

¹Panyaprateep School

Punjaree Sintunyatham¹

¹Panyaprateep School

Tonboon Lerdlitruangsin¹

¹Panyaprateep School

Pordee Pitakpongsanit¹

¹Panyaprateep School

Bhumthawat Julpipatwong¹

¹Panyaprateep School

Nitis Smanthong²

²Praboromarajchanok Institute

Abstract

Cardiovascular diseases (CVDs), particularly heart disease (HD), represent a major contributor to the global health burden. Despite advances in medical technology and therapeutic interventions, significant challenges remain in achieving timely diagnosis, accurate risk assessment, and effective disease management. In this context, proteomics has emerged as a highly promising and transformative approach in cardiovascular research. By enabling the identification of novel biomarkers and therapeutic targets, proteomic technologies hold great potential for advancing both clinical practice and translational medicine. Furthermore, the integration of proteomics with complementary omics platforms and advanced bioinformatics has enhanced disease stratification, supported the development of precision medicine, and enabled earlier and more targeted clinical interventions. Collectively, these advancements highlight the potential of proteomics to transform cardiovascular care through more precise diagnosis, improved risk assessment, and accurate monitoring of therapeutic responses. This systematic review examines the evolving role of proteomic approaches in the diagnosis, management, and treatment of HD by analyzing peer-reviewed literature published between 2010 and 2025 across major databases, including Google Scholar, PubMed, and Scopus.

Corresponding Author: Nitis Smanthong

E-mail: nitis.sman@gmail.com

Keywords: Cardiovascular diseases, heart disease, Proteomics

Introduction

CVDs represent the leading cause of global morbidity and mortality. Globally, HD remains a primary driver of morbidity and mortality, with myocardial infarction (MI) representing a major contributor due to ischemic injury of the myocardium⁽¹⁾. These conditions encompass a broad spectrum of disorders affecting the heart and vasculature- including heart fail (HF), coronary artery disease (CAD), myocarditis, arrhythmias, and other cardiac pathologies that impact the endocardium, myocardium, pericardium, and coronary circulation, ultimately compromising cardiac output⁽²⁾. These conditions affect the heart through distinct mechanisms, ranging from impaired contractility and ischemia to inflammation, arrhythmogenesis, and vascular dysfunction. Despite significant advances in pharmacological and interventional therapies, current treatments are largely palliative, targeting symptoms rather than addressing the fundamental loss of myocardial tissue. Consequently, many patients require lifelong management, and even heart transplantation-

the definitive therapy for end-stage disease-is limited by donor shortages and post-operative complications⁽³⁾.

Given these challenges, there is a pressing need for improved strategies for early detection, risk stratification, and therapeutic intervention. Biomarker discovery offers a promising avenue to address this need by enabling early diagnosis, monitorin of cardiac dysfunction, and evaluation of therapeutic efficacy. In this context, proteomics the large scale study of protein expression, post-translational modifications, and rotein-protein interactions using mass spectrometry and other high-throughput technologies has emerged as a powerful approach in cardiovascular research^(4,5). Therefore, this review aims to highlight the advancing role of proteomic approaches in cardiovascular research, with a particular focus on heart disease (HD).

Methodology

This paper presents a systematic review of the literature examining the role of proteomic approaches in cardiovascular disease, particularly heart diseases. A structured search strategy was employed using the keywords proteomics, cardiovascular disease, heart disease, diagnosis, treatment, and management across Google Scholar, PubMed, and Scopus databases, encompassing publications from 2010 to 2025. Inclusion criteria were restricted to peer-reviewed studies, while non-English and non-scientific articles were excluded to ensure methodological rigor. Relevant findings were synthesized thematically, and study quality was appraised using standardized evaluation frameworks to enhance the validity, reliability, and relevance of the review outcomes.

Literature Review

The Impact of Heart Diseases: Issues and Consequences

CVDs account for the majority of noncommunicable diseases and remain a leading cause of global morbidity and mortality⁽⁶⁾. CVDs encompass a wide spectrum of disorders affecting the heart and blood vessels, posing substantial public health challenges and often progressing to various forms of HD. The underlying pathophysiological mechanisms of HD are diverse, involving structural abnormalities, vascular obstructions, and functional impairments within the cardiovascular system. These alterations may affect the endocardium, myocardium, pericardium, and coronary vasculature, ultimately compromising cardiac function⁽²⁾.

HD refers to a group of abnormal conditions involving the heart's muscles, valves, vessels, or electrical conduction pathways, all of which are essential for maintaining effective cardiac output. Globally, HD remains one of the primary causes of morbidity and mortality, particularly due to myocardial infarction (MI), or heart attack, which results from reduced blood flow and subsequent ischemic injury to the myocardium⁽¹⁾. In the USA, the Centers for Disease Control and Prevention (CDC) reported that HD accounts for approximately one in every five deaths annually⁽¹⁾. Similarly, in Thailand, the age-specific mortality rates for coronary heart disease and stroke are 87.1 and 123 per 100,000 population, respectively, reflecting a substantial cardiovascular burden. Epidemiological studies further underscore the growing prevalence of CVDs in Thai population. The Thai Epidemiologic Stroke (TES) study

reported a stroke prevalence of 1.88% between 2005 and 2007⁽⁷⁾. According to data from the Ministry of Public Health (2012-2021), the age-standardized hospital admission rate for ischemic heart disease (IHD) declined by 24.1% among females (from 427.5 to 390.5 per 100,000), but increased among males (from 462.7 to 485.8 per 100,000) during the same period. Notably, IHD mortality trends have risen in individuals under 60 years of age, increasing by 59.6% in males and 36.1% in females over the past decade⁽⁶⁾.

HD comprises multiple pathological entities, including HF, MI, myocarditis, sudden cardiac arrest, atrial septal defect, atrial fibrillation, coronary heart disease, angina, ventricular tachycardia, and pericarditis⁽⁸⁾. Each of these conditions affects the heart through distinct pathophysiological mechanisms. For example, HF impairs the heart's ability to pump blood effectively; MI results from arterial occlusion and subsequent ischemia; myocarditis involves inflammatory injury to the myocardium, typically of infectious origin; and sudden cardiac arrest is characterized by the abrupt cessation of cardiac activity. Atrial fibrillation arises from disorganized electrical impulses within the atria, while coronary artery narrowing leads to CAD. Angina reflects insufficient myocardial oxygen supply, ventricular tachycardia results from rapid ventricular rhythms, and pericarditis develops from inflammation of the pericardial membrane^(1,8).

Despite significant progress in pharmacological and interventional therapies, HD continues to be associated with high morbidity and mortality. Current treatment approaches remain largely palliative, focusing on symptom reduction rather than addressing the fundamental loss of myocardial tissue. Consequently, many patients require lifelong medical management, and even heart transplantation the definitive treatment for end-stage disease-faces numerous challenges, including donor shortages and postoperative complications⁽³⁾. This clinical reality imposes a considerable economic burden on patients, families, and healthcare systems. Given these limitations, there is a critical need for more effective strategies to reduce the global burden of HD. Early detection and risk stratification are essential for preventing disease progression and improving patient outcomes. A promising approach lies in the identification and validation of novel biomarkers capable of facilitating early diagnosis, monitoring cardiac dysfunction, and evaluating therapeutic efficacy. Such biomarkers have the potential to transform the diagnostic and therapeutic landscape of HD, paving the way toward more personalized and effective management strategies⁽³⁾.

The Advancing Role of Proteomic Analysis in Medical Research

Proteomic analysis focuses on the comprehensive study of the proteome, which encompasses the entire set of expressed proteins within a cell, tissue, or organ, representing the ultimate effectors of biological function⁽⁴⁾. When integrated with mass spectrometry (MS)-based high-throughput technologies, proteomics has greatly advanced the identification of novel disease biomarkers and the discovery of potential therapeutic targets. This approach also provides critical insights into the molecular pathways underlying health and disease⁽⁹⁾. Proteins play central roles in catalyzing biochemical reactions that generate diverse biomolecules-including glycans, lipids, nucleotides, metabolites, peptides, and other proteins-that are essential for structural integrity, cellular signaling, and dynamic biological responses

to internal and external stimuli. Consequently, proteomic analysis offers a detailed, context-dependent snapshot of protein and proteoform expression, structural conformations, turnover rates, and protein-protein interactions, thereby enabling a deeper understanding of complex biological systems⁽⁴⁾.

Beyond cardiovascular research, proteomic technologies have been widely applied across various medical fields. For instance, they have been used to identify molecular markers of influenza infection through machine learning (ML)-based analytical models⁽¹⁰⁾. Additionally, proteomics has advanced our understanding of host-microbe interactions, leading to the discovery of novel antigens and diagnostic markers relevant to gastrointestinal infections, autoimmune disorders, and mental health conditions. These advances have facilitated the development of innovative diagnostic, therapeutic, and preventive strategies⁽¹¹⁾.

Within cardiology, proteomic-based MS approaches provide powerful tools for characterizing protein expression patterns in cardiac tissues, enabling the identification of biomarkers that enhance diagnostic precision and inform therapeutic strategies for HD. For example, proteomic profiling can differentiate between distinct stages of HF by examining variations in left ventricular ejection fraction (LVEF), distinguishing HF with reduced ejection fraction (HFrEF) from HF with preserved ejection fraction (HFpEF). Such analyses have advanced understanding of the pathophysiological mechanisms underlying different HF subtypes, particularly HFpEF, which remains a diagnostic and therapeutic challenge⁽¹²⁾. Furthermore, targeted proteomics has demonstrated the capacity to identify predictive biomarkers for therapeutic response in sarcoidosis patients, thereby facilitating more precise treatment selection and improved clinical outcomes⁽¹³⁾.

The progression of cardiovascular proteomics has been marked by several technological milestones, including advancements in two-dimensional gel electrophoresis (2-DE), liquid chromatography (LC), MS, and the analysis of post-translational modifications (PTMs), as summarized in Figure 1. These innovations continue to refine the sensitivity, specificity, and clinical applicability of proteomic research in cardiovascular medicine⁽¹⁴⁾. (Figure 1)

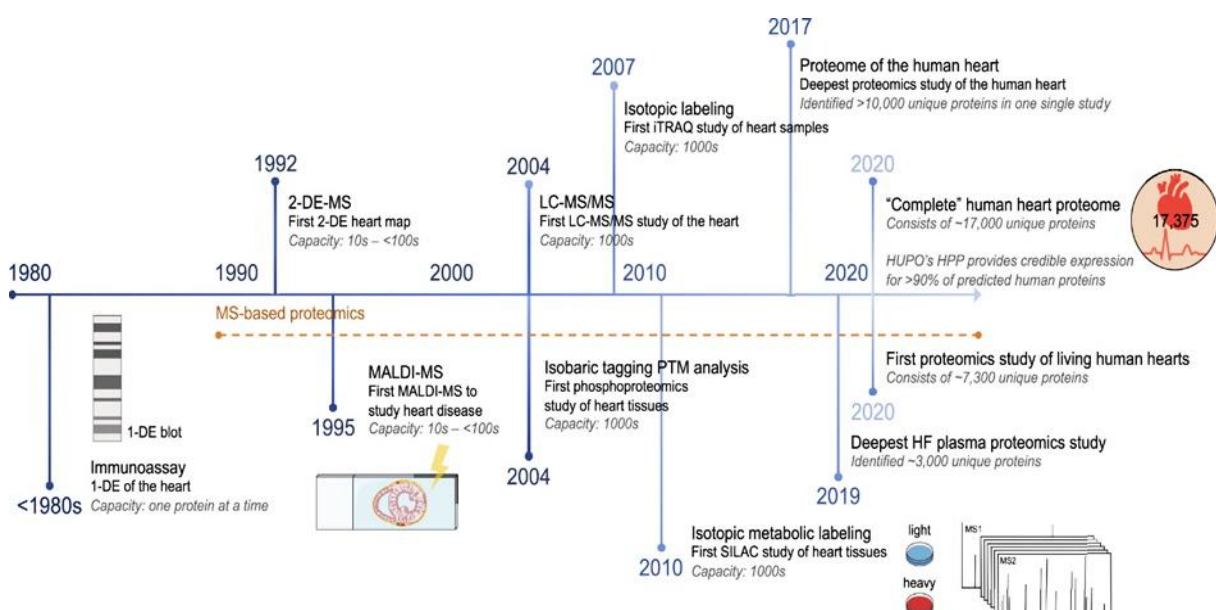


Figure 1 Schematic timeline illustrating major milestones in the evolution of cardiovascular proteomics⁽¹⁴⁾.

Biomarkers and potential mediators of HD in complicated patients with metabolic syndrome (MetS)

MetS is characterized by the coexistence of multiple obesity-associated cardiovascular risk factors, including abdominal obesity, impaired glucose tolerance, hypertriglyceridemia, reduced high-density lipoprotein (HDL) cholesterol, and hypertension. The clustering of these risk factors substantially increases both the incidence and severity of CVDs, contributing to a broad spectrum of pathological conditions, such as microvascular dysfunction, coronary atherosclerosis and calcification, cardiac dysfunction, MI and HF. Although significant advances have been made in understanding the etiology and clinical implications of MetS, the underlying pathophysiological mechanisms remain incompletely elucidated⁽¹⁵⁾. Further investigation into these mechanisms is essential to clarify how MetS contributes to adverse cardiovascular outcomes, particularly HD.

Among the components of MetS, type 2 diabetes (T2D) is a critical risk factor for CHD, significantly increasing cardiovascular mortality. Proteomic analyses have revealed key molecular mediators contributing to this elevated risk. For example, inflammatory and vascular injury-promoting proteins, including CD27, TNF- α , ICAM-1, and RAGE, are upregulated in T2D, whereas protective vascular proteins such as NRP1, VEGF, and eNOS are downregulated or functionally impaired. This imbalance between deleterious and protective molecular pathways provides a mechanistic explanation for the heightened CHD risk observed in T2D patients. Furthermore, proteomics-based profiling can be applied for screening and predicting future CHD onset in this high-risk population, enabling earlier intervention⁽¹⁶⁾. Chronic kidney disease (CKD) is another common comorbidity among patients with HF, further complicating disease management and prognosis. However, the differentiation of HF phenotypes in the context of CKD remains limited. Recent proteomic studies have identified clinical and molecular variables that help distinguish between HF with HFrEF and with HFpEF in CKD patients. Factors such as body mass index (BMI), elevated NT-proBNP levels, the use of angiotensin-converting enzyme (ACE) inhibitors, HDL, cholesterol, and a history of stroke were found to be more strongly associated with CKD patients presenting with HFrEF⁽¹⁷⁾ (Table 1). These findings highlight the utility of proteomics in refining disease classification and risk stratification in complex cardiovascular-metabolic disorders.

Table 1 The application of proteomic approaches on heart disease biomarkers of patient underlying risk conditions.

Diseases (Ref.)	Assessment/ Application	Study/ Samples	Main results/ Main findings/ Protein functions
CHD ⁽¹⁶⁾	Predicted biomarkers of CHD among patients with T2D.	2,923 plasma proteins	PCSK9: improving glycemic control and reducing cardiovascular morbidity. NRP1: target therapies for CHD risk in diabetes patients. CD27: contribute to the chronic inflammation in T2D, associated with CVDs
HF ⁽³²⁾	Predicted biomarkers of HF in CKD patients.	3,417 Participants	FCG2B: receptor for Fc region of IgG and target of Xmab5871 drug. IGFBP3: carrier for insulin-like growth factor 1. CAH6: Fc receptor-like protein 4. ASGR1: Facilitates endocytosis of plasma glycoproteins
HF ⁽³³⁾	HF-associated proteins in CKD patient.	3000 patients	FCG2B and IGFBP3: directly linked to insulin-growth factor that is responsible for several anabolic processes. CAH6: the levels of which are increased with SGLT2 inhibitor treatment. ASGR1: degrades glycoproteins important for cardio-renal-metabolic diseases.
HF ⁽³⁴⁾	Biomarkers of HF with HFrEF and HFpEF, among CKD patients.	478 patients	SAP3: served as an inter-cellular lipid transport protein. ACBP: associated with aging, kidney- and cardiovascular disease and might be a proxy for biological age. TMEDA: intracellular regulatory factor
HF ⁽³⁵⁾	Prognostic significance proteins of KI among HFpEF patients.	253 HFpEF patients	CST-C: associated with the risk of mortality in HFpEF patients. FABP3: positively correlated with the urine albumin-to-creatinine ratio in adults with type 2 diabetes. B2M: represent KI at multiple levels of the KI conditions. NGAL, KIM1: correlated with kidney tubular damage and CKD.

Table 1 The application of proteomic approaches on heart disease biomarkers of patient underlying risk conditions. (continued)

Diseases (Ref.)	Assessment/ Application	Study/ Samples	Main results/ Main findings/ Protein functions
IHD ⁽³⁶⁾	Prediction of IHD	512,000 participants	GDF15: biomarker to improve risk stratification in clinical practice for primary and secondary prevention of CVD. proBNP: marker in early detection and treatment regimens of CVD.
MI ⁽³⁷⁾	Prediction of MI	11,751 participants	CXCL16: marker of atherosclerosis progression and linked to an increased risk of MI
Left atrial remodeling (LA) ⁽³⁸⁾	Protein signatures HIV patients associated with LA	352 patients	CRTAM: immune cell adhesion and signaling. NT-proBNP: biomarker of myocardial wall stress and HI severity.
HF ⁽³⁹⁾	Cardiometabolic comorbidities proteins	Proteogenomic data	C9, LBP, ITIH4, APOM, CES1, and HS6ST2 serve as biomarkers for cardiovascular disease in patients with T2D.
HF ⁽⁴⁰⁾	Discrimination between ischemic cardiomyopathy (ISCM) and dilated cardiomyopathy (DCM)	39 tissue samples	CDC37L1: marker for differentiating HCM from DCM and ISCM patients.
HF ⁽⁴¹⁾	Biomarkers of Sinus node dysfunction (SND) in HF disease	Mice model	Chrm2: may be part of the decline in vagal control and concurrent elevated resting heart rates observed in early stages of heart failure.

Additional tool for Diagnostic test in HD patients

Cardiac diseases are among the most prevalent and morbid medical conditions worldwide, yet their pathophysiology remains only partially understood⁽⁸⁾. HF, representing the terminal stage of many cardiovascular disorders, is associated with significant morbidity and mortality⁽¹⁸⁾. Accurate diagnosis of HF requires a combination of clinical symptoms and signs along with objective evidence of underlying cardiac abnormalities. However, HF is often complicated by multiple comorbid conditions, which can obscure clinical presentation and worsen patient prognosis⁽¹⁹⁾. As a result, the development and implementation of reliable diagnostic tools are essential to enhance early disease detection, guide management strategies, and ultimately improve clinical outcomes.

Despite advances in diagnostic imaging and clinical evaluation, the prognostic markers and biological pathways associated with adverse clinical outcomes in HF remain insufficiently defined⁽²⁰⁾. This lack of precise biomarkers complicates both the diagnosis and treatment of HF. Early risk stratification and timely diagnosis of non-acute HF are essential to ensure that guideline-directed medical therapy (GDMT) is initiated promptly, thereby slowing or preventing disease progression⁽²¹⁾.

Genome-wide association studies (GWAS) have advanced the identification of genetic variants associated with HF risk. However, GWAS alone often lack tissue-specific and mechanistic insights, which are critical for understanding disease heterogeneity and guiding precision medicine approaches⁽²²⁾. To address these limitations, proteomic analyses have emerged as a powerful complementary tool, capable of identifying molecular markers and pathways involved in HF pathogenesis.

Proteomic studies have identified several promising protein-based biomarkers relevant to HF diagnosis and prognosis. For example, N-terminal pro-B-type natriuretic peptide (NT-proBNP) has become a well-established biomarker, widely used in clinical practice to support the diagnosis of HF and atrial fibrillation (AF). It is also strongly associated with adverse outcomes in patients with HF with HFpEF^(23,24). Another important biomarker is Triggering Receptor Expressed on Myeloid cells-1 (TREM-1), which, although not a direct cause of HF, acts as an inflammatory amplifier contributing to disease progression. Elevated TREM-1 levels are not only indicative of infection and sepsis but also correlate with chronic inflammatory processes, clinical frailty, and atherogenesis. In pediatric cardiology, Kawasaki disease (KD)-an acute febrile vasculitis and the leading cause of acquired heart disease in children-continues to present diagnostic challenges, as its pathogenic mechanisms remain incompletely understood. Recent proteomic investigations have identified interleukin-17A (IL-17A) as a potential early diagnostic biomarker, offering a promising avenue to improve timely and accurate diagnosis of KD⁽²⁵⁾ (Table 2).

Table 2 The application of proteomic approaches on heart disease biomarkers of patient underlying risk conditions.

Diseases	Assessment/ Application	Study/ Samples	Main results/ Main findings/ Protein functions
HF ⁽⁴²⁾	Prognostic markers of HFpEF	4,796 patients	B2M: marker of renal function. TIMP1, ADAM17, and LTBP4 were associated with HFpEF outcomes, particularly after adjustment for clinical risk factors. NT-proBNP: key markers of adverse HFpEF outcomes.
HD ⁽⁴³⁾	Markers of CAD, HF, AF and aortic stenosis (AS).	44,313 UK Biobank	PCSK9: biomarker and therapeutic target for CAD. NT-proBNP: protein-based risk scores for AF and HF.

Table 2 The application of proteomic approaches on heart disease biomarkers of patient underlying risk conditions. (continued)

Diseases	Assessment/ Application	Study/ Samples	Main results/ Main findings/ Protein functions
HF ⁽²⁰⁾	Identified marker of HF and frailty.	15,792 participants	EFEMP1: targeted for drug, prevent frailty-related cardiac dysfunction and HF. FSTL3: associated with risk of HF. TREM1: predictor of clinical frailty and atherogenesis. GDF15: marker of cardiomyopathy and in frailty.
HF ⁽¹²⁾	Proteomic patterns identification	739 patients	SLITRK6: responded to ischemic injury and adverse cardiac remodeling following myocardial infarction. It's possible to be a biomarker of HFpEF.
IHD ⁽⁹⁾	Markers of coronary artery calcification (CAC)	6 patients	C1QC: derived calcification of cardiovascular system through modulation of CTRP3.
HF ⁽¹⁹⁾	Markers of pulmonary hypertension (PH)	16 plasma samples	B2M: correlated with disease severity in PH or HF.
HF ⁽²²⁾	Markers of cardiovascular related tissues in HF patient	207,346 samples	SPON1, C2, PACAP: related to cardiomyopathy and heart failure risk for left VEF (LVEF).
Coronary microvascular dysfunction (CMD) ⁽⁴⁴⁾	Diagnostic markers of CMD	Rats	Emc1: associated with cardiac disease, primarily aortic outflow tract abnormalities. Ank1: closely associated with cardiac arrhythmias. Fbln2: a key factor in pathological remodeling after MI. Hp: a significant risk factor for acute MI and HF.
HF ⁽⁴⁵⁾	Markers of HFpEF and HFrEF among HF patients	40 patients	VCAM1, IGF2, ITIH3: associated with HFpEF development. CRP, IL6RB, PHLD, NOE1: linked to HFrEF development.
HF ⁽⁴⁶⁾	Markers of HFpEF	44 patients	All proteins are involved in metabolism and mitochondrial proteins.

Table 2 The application of proteomic approaches on heart disease biomarkers of patient underlying risk conditions. (continued)

Diseases	Assessment/ Application	Study/ Samples	Main results/ Main findings/ Protein functions
Acute MI (AMI) ⁽⁴⁷⁾	Markers of AMI	20 plasmas samples	GOT1, GOT2: key molecules of methionine and cysteine metabolism that play important roles in the mechanism of AMI.
HF ⁽⁴⁸⁾	Biomarkers of physical frailty in HF	20 patients	MMP14: an important role in the progression of cardiovascular disease, and in turn may influence the development of physical frailty.
KD ⁽²⁵⁾	Biomarkers of KD	150 patients	IL-17A: a new potential biomarker for early diagnosis of KD.
Nonischaemic cardiomyopathy (NICMP) ⁽⁴⁹⁾	Differentiation of idiopathic dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM)	Cardiac tissue	LXR: regulates the hypertrophic cardiac remodeling process with a more pronounced effect in HCM. TFEB: associated with cardiomyopathy and cardiotoxicity with DCM.
MI ⁽⁵⁰⁾	Identified protein of MI	41 patients	FXIII: a key molecule to promote the healing of cardiac wounds.
HF ⁽⁵¹⁾	Cardiometabolic proteins of HF	401 patients	C1QTNF1, CTSD, FCN2, SERPINA12, TFRC, TNFRSF10C: associated with increased risk of rehospitalization. CDH1, FABP6, TNC: associated with mortality.
HF ⁽⁵²⁾	Potential markers of HF-induced pulmonary edema (HF-PE)	10 patients	TLN1: interacted with multiple proteins and was upregulated in patients with HF-PE and can be indicator of HF-PE progression.

The discovery of improved clinical treatments for HD patients

Chronic heart failure (CHF) remains a major global health concern, characterized by high morbidity and mortality rates despite advancements in medical care. The gold standard treatment for end-stage HF is heart transplantation, typically considered after the failure of pharmacological therapy, surgical interventions, and/or cardiac resynchronization therapy. Nevertheless, even with significant progress in treatment strategies, the overall prognosis for patients with HF remains poor⁽²⁶⁾. This highlights the urgent need for novel diagnostic and therapeutic approaches to improve clinical outcomes.

Recent advances in proteomic technologies have opened new avenues for identifying disease-associated proteins that may serve as biomarkers for diagnosis, prognosis, and targeted therapy in cardiovascular diseases. Proteomics enables comprehensive analysis of protein expression patterns and signaling pathways, providing valuable insights into disease mechanisms and therapeutic responses.

For example, in CHF, treatment with Xinmailong (XML) has been shown to modulate the expression of key genes, including Col1a1, Col3a1, Cxcr2, and Mmp9, and to activate the cGMP-PKG signaling pathway, ultimately contributing to a reduction in myocardial fibrosis⁽²⁷⁾. In fulminant myocarditis (FM), the proteins S100A8/A9 have been identified as important biomarkers and potential therapeutic targets, reflecting their role in inflammatory processes⁽²⁸⁾. Similarly, in aging heart (AH), the protein Fmod has been implicated in limiting excessive collagen deposition, while CPT1b and CrAT have been linked to age-related alterations in cardiac energy metabolism⁽²⁸⁾. Moreover, in myocarditis, classical biomarkers such as lactate dehydrogenase (LDH), creatine kinase-MB (CK-MB), and cardiac troponin I (cTnI) remain essential indicators of myocardial injury⁽²⁹⁾ (Table 3).

Table 3 The application of proteomic approaches on therapeutic biomarkers of heart disease.

Diseases	Assessment/ Application	Study/ Samples	Main results/ Main findings/ Protein functions
CHF ⁽⁵³⁾	Pharmacological mechanism of Xinmailong (XML)	Rats	XML: can be used to treat CHF by modulating critical gene expression and stimulating the cGMPPKG signaling pathway.
Fulminant myocarditis (FM) ⁽⁵⁴⁾	Identification of biomarker and therapeutic target	153 patients	S100A8/A9: an essential biomarker and a promising therapeutic target for FM.
Aging heart (AH) ⁽⁵⁵⁾	The outcome of antioxidants diet for AH	Mice	Fmod: inhibited collagen fibril formation, possibly reducing extracellular matrix stiffness and thus improving diastolic function. CPT1b, CrAT: a carnitine acyltransferase these are critical to cardiomyocyte metabolism.
Myocarditis ⁽⁵⁶⁾	Determine role of T cells in myocarditis disease	Heart tissue samples	LDH, CK-MB, cTnI: markers of T cell-mediated myocardial cell injury and provide guidance in the discovery of improved clinical treatments for myocarditis.

Collectively, these examples highlight the clinical utility of proteomics in cardiovascular medicine. Beyond identifying disease-associated molecular alterations, proteomic approaches enable the discovery and validation of biomarkers that support early diagnosis, assessment of

disease severity, and the development of novel therapeutic strategies. Consequently, the integration of proteomics into cardiovascular research holds significant promise for improving the precision and effectiveness of HD management.

Future Directions of Proteomics for Heart disease

Proteomics achieves its greatest impact when integrated with complementary technologies and multi-omics approaches rather than applied in isolation. The integration of transcriptomic, proteomic, and metabolomic data enables the identification of differentially regulated molecular networks across multiple biological levels, thereby enhancing the sensitivity, accuracy, and throughput of analyses that are essential for precision medicine^(30,31).

At the transcriptomic level, recent advances in single-cell proteomics have significantly enhanced our understanding of cellular heterogeneity and disease mechanisms. By characterizing gene expression profiles at the single-cell resolution, this technology has identified distinct cardiac cell populations-including fibroblasts, endothelial cells, and immune cells-thereby providing a more granular view of cellular diversity and dynamic molecular changes within the heart under physiological and pathological conditions⁽³¹⁾.

At the metabolomic level, the comprehensive profiling of small molecules (metabolites) provides a real-time snapshot of the metabolic state of biological systems. Because metabolites represent the end products of cellular processes, their fluctuations can reveal metabolic reprogramming associated with disease onset and progression. In cardiovascular research, metabolomics has proven invaluable for elucidating the role of metabolic pathways in disease progression and for identifying novel biomarkers of risk and therapeutic response. Lipidomics, a specialized branch of metabolomics, has further advanced understanding of the contribution of specific lipid species to the pathogenesis of atherosclerosis and coronary artery disease⁽³¹⁾.

The successful application of integrative proteomics also depends heavily on advances in bioinformatics. Analytical frameworks must be capable of processing vast and complex datasets, accounting for the combinatorial diversity of PTMs, and enabling meaningful biological interpretation from high-dimensional data⁽³⁰⁾. For example, the implementation of an explainable ML-framework, such as explainable boosting machines (EBM), has demonstrated the potential of combining proteomics with computational modeling for individualized CVD risk prediction. This approach not only improves predictive accuracy but also provides transparent insights into feature importance and disease mechanisms, thereby supporting its future clinical application for risk stratification using proteomics-based blood tests⁽³¹⁾.

Discussion

CVDs remain the leading cause of morbidity and mortality worldwide, imposing substantial social and economic burdens on healthcare systems. Major cardiac conditions including HF, CAD, myocarditis, and cardiac arrhythmias, are responsible for a large proportion of these adverse outcomes. In Thailand, epidemiological data indicate a rising trend in CVD-related mortality, particularly among younger populations, despite advances in diagnostic

and therapeutic strategies. These observations highlight the ongoing challenges in early detection, risk stratification, and effective disease management.

Proteomics, the large-scale study of the entire protein complement of a cell, tissue, or organism using mass spectrometry and other high-throughput analytical techniques, has emerged as a powerful tool in cardiovascular research. Recent advances increasingly emphasize the integration of proteomics with other omics platforms-such as genomics, transcriptomics, and metabolomics-combined with ML- and advanced-bioinformatics. This multi-omics approach enhances the ability to manage complex datasets, predict individual disease risk, refine diagnostic accuracy, and implement precision medicine strategies tailored to specific patient subgroups. By enabling the comprehensive characterization of protein expression, PTMs, and signaling networks, proteomics facilitates the discovery of novel biomarkers for disease diagnosis and prognosis, provides insights into the molecular mechanisms underlying diverse cardiac pathologies, and supports the identification of therapeutic targets and markers of treatment response.

Recommendation

Building on proteomic approaches, future research on HD-related biomarkers should prioritize the systematic collection of high-quality data, rigorous and integrative multi-omics analyses within well-defined disease cohorts, and subsequent validation in large, independent populations. These steps are essential for bridging the gap between multi-omics discoveries and their translation into clinically relevant applications, advancing the development of precision medicine.

References

1. Gougheri KA, Ahmadi A, Ahmadabadi MG, Babajani A, Yazdanpanah G, Bahrami S, et al. Exosomal Cargo: Pro-angiogenic, anti-inflammatory, and regenerative effects in ischemic and non-ischemic heart diseases - A comprehensive review. *Biomed Pharmacother.* 2023;168:115801. Doi: 10.1016/j.biopha.2023.115801
2. Netala VR, Teertam SK, Li H, Zhang Z. A comprehensive review of cardiovascular disease management: cardiac biomarkers, imaging modalities, pharmacotherapy, surgical interventions, and herbal remedies. *Cells.* 2024;13(17):1471.
3. Zou E, Xu X, Chen L. Potential of plasma biomarkers for heart failure prediction, management, and prognosis: A multiomics perspective. *Heart Fail Rev.* 2024;30(1):55-67.
4. Karpov OA, Stotland A, Raedschelders K, Chazarin B, Ai L, Murray CI, et al. Proteomics of the heart. *Physiol Rev.* 2024;104(3):931-82.
5. Wu H, Pang M, Chen H, Zhuang K, Zhang H, Zhao Y, et al. Serum proteomic profiling reveals potential predictive indicators for coronary artery calcification in stable ischemic heart disease. *J Mol Histol.* 2025;56(2):110.
6. Sakboonyarat B, Rangsin R. Hospital admission and mortality rates for ischemic heart disease in Thailand: 2012-2021. *BMC Res Notes.* 2024;17(1):142.

7. Kongsakol R, Sruamsiri R, Pattanapruteep O. Health-related quality of life of Thai cardiovascular patients among smokers and non-smokers population. *J Med Assoc Thai.* 2018;101(9):1197-201.
8. Rohan D, Reddy GP, Kumar YVP, Prakash KP, Reddy CP. An extensive experimental analysis for heart disease prediction using artificial intelligence techniques. *Sci Rep.* 2025;15(1):6132.
9. Wu H, Pang M, Chen H, Zhuang K, Zhang H, Zhao Y, et al. Serum proteomic profiling reveals potential predictive indicators for coronary artery calcification in stable ischemic heart disease. *J Mol Histol.* 2025;56(2):110.
10. Zhou Y, Wang P, Zhang H, Wang T, Han S, Ma X, et al. Prediction of influenza virus infection based on deep learning and peripheral blood proteomics: A diagnostic study. *J Adv Res.* 2026;79:707-19
11. Lin CC, Chen CS. Bacterial proteome microarray technology in biomedical research. *Trends Biotechnol.* 2025;43(6):1317-27.
12. Andrzejczyk K, Kamar SA, van Ommen AM, Canto ED, Petersen TB, Valstar G, et al. Identifying plasma proteomic signatures from health to heart failure, across the ejection fraction spectrum. *Sci Rep.* 2024;14(1):14871.
13. Kraaijvanger R, Bonás MJ, Paspali I, Grutters JC, Veltkamp M, de Kleijn DPV, et al. Targeted proteomics in extracellular vesicles identifies biomarkers predictive for therapeutic response in sarcoidosis. *ERJ Open Research.* 2025;11(2):00672-2024.
14. Lee SH, Kim DH, Kuzmanov U, Gramolini AO. Membrane proteomic profiling of the heart: past, present, and future. *Am J Physiol Heart Circ Physiol.* 2021;320(1):417-23.
15. Tune JD, Goodwill AG, Sassoon DJ, Mather KJ. Cardiovascular consequences of metabolic syndrome. *Transl Res.* 2017;183:57-70.
16. Li Y, Li D, Lin J, Zhou L, Yang W, Yin X, et al. Proteomic signatures of type 2 diabetes predict the incidence of coronary heart disease. *Cardiovasc Diabetol.* 2025;24(1):120.
17. Voordes GHD, Voors AA, Hoegl A, Madsen CT, van Essen BJ, Ouwerkerk W, et al. Clinical and proteomic profiles of chronic kidney disease in heart failure with reduced and preserved ejection fraction. *Int J Cardiol.* 2024;417:132580.
18. Tankumpuan T, Asano R, Koirala B, Dennison-Himmelfarb C, Sindhu S, Davidson PM. Heart failure and social determinants of health in Thailand: An integrative review. *Heliyon.* 2019;5(5):e01658.
19. Ariyachaipanich A, Krittayaphong R, Kunjara Na Ayudhya R, Yingchoncharoen T, Buakhamsri A, Suvachittanont N. Heart failure council of Thailand (HFCT) 2019 heart failure guideline: Introduction and diagnosis. *J Med Assoc Thai.* 2019;102(2):231-9.
20. Ramonfaur D, Buckley LF, Arthur V, Yang Y, Claggett BL, Ndumele CE, et al. High throughput plasma proteomics and risk of heart failure and frailty in late life. *JAMA Cardiol.* 2024;9(7):649-58.
21. Karuna N, Tonry C, Ledwidge M, Glezeva N, Gallagher J, McDonald K, et al. Proteomic-based biomarker discovery reveals panels of diagnostic biomarkers for early identification of heart failure subtypes. *J Transl Med.* 2025;23(1):546.

22. Moore A, Venkatesh R, Levin MG, Damrauer SM, Reza N, Cappola TP, et al. Connecting intermediate phenotypes to disease using multi-omics in heart failure. *Pac Symp Biocomput.* 2025;30:504-21.
23. Patel-Murray NL, Zhang L, Claggett BL, Xu D, Serrano-Fernandez P, Healey M, et al. Aptamer proteomics for biomarker discovery in heart failure with preserved ejection fraction: The PARAGON-HF proteomic substudy. *J Am Heart Assoc.* 2024;13(13):e033544.
24. Schuermans A, Pournamdari AB, Lee J, Bhukar R, Ganesh S, Darosa N, et al. Integrative proteomic analyses across common cardiac diseases yield mechanistic insights and enhanced prediction. *Nat Cardiovasc Res.* 2024;3(12):1516-30.
25. Tu X, Chen X, Xu L, Yang C, Li J, Liu Y, et al. Serum Olink targeted proteomics identifies IL-17A as a prospective inflammatory marker for the prediction and diagnosis of kawasaki disease. *J Inflamm Res.* 2025;18:3093-3103. Doi: 10.2147/JIR.S506154
26. Haeck MLA, Hoogslag GE, Rodrigo SF, Atsma DE, Klautz RJ, Van Der Wall EE, et al. Treatment options in end-stage heart failure: where to go from here?. *Neth Heart J.* 2012;20(4):167-75.
27. Xue Y, Lv C, Jin L, Tan D, Wu D, Peng F. Study on the mechanism of Xinmailong injection against chronic heart failure based on transcriptomics and proteomics. *J Pharm Biomed Anal.* 2025;253:116529.
28. He W, Wu J, Wang D, Chen W, Yan Y, He Q, et al. Plasma proteomics identifies S100A8/A9 as a novel biomarker and therapeutic target for fulminant myocarditis. *J Adv Res.* 2025:1-14. Doi: 10.1016/j.jare.2025.06.005.
29. Ye J, Xu S, Liu X, Zhang Q, Li X, Zhang H, et al. Effect and mechanism of T lymphocytes on human induced pluripotent stem cell-derived cardiomyocytes via Proteomics. *Stem Cell Res Ther.* 2024;15(1):236.
30. Lindsey ML, Mayr M, Gomes AV, Delles C, Arrell DK, Murphy AM, et al. Transformative impact of proteomics on cardiovascular health and disease: a scientific statement from the american heart association. *Circulation.* 2015;132(9):852-72.
31. Rizi SS, Stamenkovic A, Ravandi A. Integrative omics approaches in cardiovascular disease research: current trends and future directions. *Can J Cardiol.* 2025;41(8):1642-45.
32. Dubin RF, Deo R, Ren Y, Wang J, Pico AR, Mychaleckyj JC, et al. Incident heart failure in chronic kidney disease: proteomics informs biology and risk stratification. *Eur Heart J.* 2024;45(30):2752-67.
33. Zannad F, Ferreira JP. Proteomics for understanding progression to heart failure in chronic kidney disease: promising but still not there. *Eur Heart J.* 2024;45(30):2768-70.
34. Voordes GH, Voors AA, Hoegl A, Madsen CT, van Essen BJ, Ouwerkerk W, et al. Clinical and proteomic profiles of chronic kidney disease in heart failure with reduced and preserved ejection fraction. *Int J Cardiol.* 2024;417:132580.
35. Salman O, Zhao L, Cohen JB, Dib MJ, Azzo JD, Gan S, et al. Proteomic correlates and prognostic significance of kidney injury in heart failure with preserved ejection fraction. *J Am Heart Assoc.* 2024;13(17):e033660.

36. Mazidi M, Wright N, Yao P, Kartsonaki C, Millwood IY, Fry H, et al. Risk prediction of ischemic heart disease using plasma proteomics, conventional risk factors and polygenic scores in Chinese and European adults. *Eur J Epidemiol.* 2024;39(11):1229-40.
37. Titova OE, Yuan S, Byberg L, Baron JA, Lind L, Michaëlsson K, et al. Plasma proteome and incident myocardial infarction: sex-specific differences. *Eur Heart J.* 2024;45(43):4647-57.
38. Peterson TE, Hahn VS, Moaddel R, Zhu M, Haberlen SA, Palella FJ, et al. Proteomic signature of HIV-associated subclinical left atrial remodeling and incident heart failure. *medRxiv.* 2024;24302797 Doi: 10.1101/2024.02.13.24302797
39. Loesch DP, Garg M, Matelska D, Vitsios D, Jiang X, Ritchie SC, et al. Identification of plasma proteomic markers underlying polygenic risk of type 2 diabetes and related comorbidities. *Nat Commun.* 2025;16(1):2124.
40. Tonry C, Linden K, Collier P, Ledwidge M, McDonald K, Collins BC, et al. Proteomic characterisation of heart failure reveals a unique molecular phenotype for hypertrophic cardiomyopathy. *Biomedicines.* 2024;12(8):1712.
41. Kahnert K, Soattin L, Mills RW, Wilson C, Maurya S, Sorrentino A, et al. Proteomics couples electrical remodelling to inflammation in a murine model of heart failure with sinus node dysfunction. *Cardiovasc Res.* 2024;120(8):927-42.
42. Patel-Murray NL, Zhang L, Claggett BL, Xu D, Serrano-Fernandez P, Healey M, et al. Aptamer proteomics for biomarker discovery in heart failure with preserved ejection fraction: The PARAGON-HF Proteomic Substudy. *J Am Heart Assoc.* 2024;13(13):e033544.
43. Schuermans A, Pournamdari AB, Lee J, Bhukar R, Ganesh S, Darosa N, et al. Integrative proteomic analyses across common cardiac diseases yield mechanistic insights and enhanced prediction. *Nat Cardiovasc Res.* 2024;3(12):1516-30.
44. Lu Y, Wang Y, Xin Q, Yuan R, Chen K, Chu J, et al. Metabolic and proteomic profiling of coronary microvascular dysfunction: insights from rat models. *Biomolecules.* 2024;14(10):1305.
45. Karuna N, Tonry C, Ledwidge M, Glezeva N, Gallagher J, McDonald K, et al. Proteomic-based biomarker discovery reveals panels of diagnostic biomarkers for early identification of heart failure subtypes. *J Transl Med.* 2025;23(1):546.
46. Jani VP, Yoo EJ, Binek A, Guo A, Kim JS, Aguilan J, et al. Myocardial proteome in human heart failure with preserved ejection fraction. *J Am Heart Assoc.* 2025;14(6):e038945.
47. Jiwaganont P, Roytrakul S, Thaisakun S, Sukumolanan P, Petchdee S. Investigation of coagulation and proteomics profiles in symptomatic feline hypertrophic cardiomyopathy and healthy control cats. *BMC Vet Res.* 2024;20(1):292.
48. Denfeld QE, Pavlovic NV, Lee CS, Jacobs JM, Roberts Davis M, Powell SM, et al. Plasma proteomic biomarkers of physical frailty in heart failure: a propensity score matched discovery-based pilot study. *BMC Cardiovasc Disord.* 2025;25(1):284.
49. Lee S, Jang DG, Kyoung YJ, Kim J, Kim ES, Hwang I, et al. Proteome-wide characterization and pathophysiology correlation in non-ischemic cardiomyopathies. *Korean Circ J.* 2024;54(8):468-81.

50. Zhou J, Hou HT, Chen HX, Song Y, Zhou XL, Zhang LL, et al. Plasma exosomal proteomics identifies differentially expressed proteins as biomarkers for acute myocardial infarction. *Biomolecules*. 2025;15(4):583.
51. Hubbell KT, Rao VS, Scherzer R, Shlipak MG, Ivery-Miranda JB, Bansal N, et al. Proteins associated with rehospitalization, mortality and diuretic resistance in acutely decompensated heart failure. *ESC Heart Failure*. 2025;12(5):3296-305.
52. Tan Y, Xu Z, Wang Z, Gu D. Tandem mass tag-labeling proteomics reveals TLN1 as a potential factor in cardiogenic pulmonary edema. *Int Heart J*. 2025;66(2):313-22.
53. Xue Y, Lv C, Jin L, Tan D, Wu D, Peng F. Study on the mechanism of Xinmailong injection against chronic heart failure based on transcriptomics and proteomics. *J Pharm Biomed Anal*. 2025;253:116529. Doi: 10.1016/j.jpba.2024.116529
54. He W, Wu J, Wang D, Chen W, Yan Y, He Q, et al. Plasma proteomics identifies S100A8/A9 as a novel biomarker and therapeutic target for fulminant myocarditis. *J Adv Res*. 2025;S2090-1232(25):00391-1. Doi: 10.1016/j.jare.2025.06.005
55. Angelini A, Garcia Marquez G, Malovannaya A, Fiorotto ML, Saltzman A, Jain A, et al. Sex differences in response to diet enriched with glutathione precursors in the aging heart. *J Gerontol A Biol Sci Med Sci*. 2025;80(2):glae258. Doi: 10.1093/gerona/glae258
56. Ye J, Xu S, Liu X, Zhang Q, Li X, Zhang H, et al. Effect and mechanism of T lymphocytes on human induced pluripotent stem cell-derived cardiomyocytes via proteomics. *Stem Cell Res Ther*. 2024;15(1):236.