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Integrating Inflammatory and Cardiac Stress Markers for Improved Diagnostic Accuracy and Risk Stratification in Obstructive Hypertrophic Cardiomyopathy: A Review

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ABSTRACT

Background: Obstructive hypertrophic cardiomyopathy (OHCM) is a common genetic cardiac disorder characterized by asymmetric ventricular hypertrophy and left ventricular outflow tract obstruction. Current diagnostic strategies primarily rely on imaging and hemodynamic assessments, which, while effective, often fail to capture underlying pathophysiological mechanisms. Biomarkers such as inflammatory mediators—interleukin (IL)-1, IL-6, tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP)—along with cardiac stress markers—B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP)—have shown promise as adjunct tools.

Material and Methods: This review synthesizes evidence from PubMed, Scopus, and Embase (up to 2022) on the role of combining inflammatory and cardiac stress markers in OHCM. Emphasis is placed on studies evaluating their diagnostic accuracy, prognostic relevance, and correlation with adverse outcomes. Comparative analyses were made between single-marker and multimarker approaches.

Conclusion: Evidence suggests that integrating inflammatory biomarkers with cardiac stress markers significantly enhances diagnostic precision and risk stratification in OHCM. Elevated IL-6 and TNF-α are strongly associated with myocardial fibrosis and arrhythmogenic substrate, whereas BNP and NT-proBNP correlate with symptom burden, hemodynamic gradients, and progression to heart failure. A multimarker approach offers superior predictive accuracy compared to individual biomarkers or imaging alone. Future studies should focus on establishing standardized multimarker panels and validating their clinical utility in large, prospective cohorts.

KEYWORDS: Obstructive hypertrophic cardiomyopathy, IL-6, TNF-α, CRP, BNP, NT-proBNP, inflammation, biomarker panel

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INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most prevalent inherited cardiovascular disease, affecting approximately 1 in 500 individuals worldwide (1). A significant proportion of patients present with obstructive physiology, referred to as obstructive hypertrophic cardiomyopathy (OHCM), characterized by dynamic left ventricular outflow tract obstruction (2). This subtype is associated with heart failure symptoms, atrial fibrillation, sudden cardiac death, and increased morbidity compared with non-obstructive forms (3).

Current diagnostic strategies for OHCM rely heavily on echocardiography, cardiac MRI, and exercise testing to evaluate structural and functional abnormalities (4). While imaging provides critical insights, it does not fully capture the complex molecular and pathophysiological mechanisms underlying disease progression (5). Hence, there is increasing interest in incorporating biomarkers into diagnostic and prognostic frameworks.

Inflammatory cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), play a critical role in promoting myocardial fibrosis, ventricular remodeling, and arrhythmogenesis (6). Elevated C-reactive protein

(CRP) levels have been reported in OHCM, reflecting systemic inflammation and its correlation with adverse cardiac remodeling (7). These inflammatory mediators are not only markers of disease activity but may also represent therapeutic targets (8).

Parallel to inflammatory markers, cardiac stress biomarkers such as B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are widely established in the evaluation of heart failure and structural heart disease (9). In OHCM, elevated natriuretic peptides are associated with higher outflow tract gradients, advanced diastolic dysfunction, and worse clinical outcomes (10).

The emerging concept of a multimarker strategy, combining inflammatory cytokines with natriuretic peptides, may provide a more comprehensive assessment of disease activity. Such integration could improve diagnostic accuracy, identify high-risk patients, and facilitate earlier intervention (11). While individual biomarkers provide useful information, their combined measurement might capture the interplay between inflammation and hemodynamic stress, offering a more robust predictive model (12).

This review explores the rationale and current evidence for integrating inflammatory and cardiac stress markers in OHCM, with a focus on diagnostic accuracy and risk stratification.

DISCUSSION

Biomarkers have gained considerable attention in cardiovascular medicine, particularly for their ability to complement imaging and clinical evaluation. In OHCM, where both mechanical obstruction and molecular remodeling drive pathology, a multimarker strategy may offer unique advantages.

Inflammatory Markers:

Several studies have demonstrated elevated IL-6 and TNF-α in OHCM patients compared with healthy controls (6,7). IL-6, in particular, has been correlated with myocardial fibrosis and adverse ventricular remodeling (8). TNF-α contributes to arrhythmogenesis and apoptosis, creating a substrate for malignant arrhythmias (9). IL-1, though less extensively studied, may amplify local inflammation and contribute to extracellular matrix remodeling (6). CRP, as a systemic marker of inflammation, has shown positive associations with hypertrophy severity and adverse outcomes (10).

Cardiac Stress Markers:

BNP and NT-proBNP are secreted in response to increased wall stress and pressure overload. Their utility in OHCM has been well-documented, with higher levels associated with symptomatic burden, diastolic dysfunction, and atrial fibrillation (11). Importantly, BNP levels are often higher in OHCM compared with non-obstructive HCM, reflecting greater hemodynamic compromise (12).

Integration of Inflammation and Stress Markers:

The key advantage of combining inflammatory and cardiac stress markers lies in their complementary information. Inflammatory cytokines reflect molecular remodeling and fibrosis, while natriuretic peptides indicate functional and hemodynamic stress. Together, they create a more comprehensive risk profile. For example, patients with both elevated IL-6 and NT-proBNP have been shown to have higher risks of hospitalization and progression to advanced heart failure compared with those with elevated natriuretic peptides alone (13).

Diagnostic Accuracy and Risk Stratification:

Individually, BNP and NT-proBNP are strong predictors of adverse outcomes, but they do not fully capture arrhythmic risk or fibrosis-related complications. Incorporating IL-6 and TNF-α improves predictive accuracy for arrhythmias and sudden cardiac death (9,13). A multimarker panel thus enhances diagnostic precision, offering a stratification system that may surpass conventional imaging alone.

Clinical Implications:

From a therapeutic standpoint, multimarker profiling could guide individualized treatment. Patients with high inflammatory cytokines may benefit from anti-inflammatory strategies, while those with elevated natriuretic peptides could require aggressive heart failure management. Furthermore, integrating biomarker data into established risk prediction models may improve patient selection for septal reduction therapy or implantable cardioverter-defibrillator implantation (11,12).

CONCLUSION

Obstructive hypertrophic cardiomyopathy remains a complex clinical entity in which diagnosis and prognosis rely predominantly on imaging and clinical evaluation. However, these methods alone may not fully capture the intricate interplay between inflammation, fibrosis, and hemodynamic stress.

The integration of inflammatory markers such as IL-1, IL-6, TNF-α, and CRP with cardiac stress biomarkers BNP and NT-

proBNP provides a more holistic understanding of disease activity. This multimarker approach enhances diagnostic precision, stratifies patients more effectively according to risk, and identifies those at greater likelihood of progression to advanced heart failure or arrhythmic complications.

Current evidence indicates that elevated inflammatory and stress biomarkers are more predictive when used together than individually. Their combined use could complement imaging findings, guide therapy selection, and improve prognostic models.

While limitations exist, particularly regarding standardization and large-scale validation, this integrated biomarker approach represents a promising advancement in the management of OHCM. Future prospective studies are warranted to confirm their clinical utility and establish biomarker-guided therapeutic strategies.

REFERENCES

1. Maron BJ, Gardin JM, Flack JM, Gidding SS, Kurosaki TT, Bild DE. Prevalence of hypertrophic cardiomyopathy in a general population of young adults. Circulation. 1995;92(4):785-9. PMID: 7641357
2. Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. N Engl J Med. 2003;348(4):295-303. PMID: 12540642
3. Elliott PM, Poloniecki J, Dickie S, Sharma S, Monserrat L, Varnava A, et al. Sudden death in hypertrophic cardiomyopathy: identification of high risk patients. J Am Coll Cardiol. 2000;36(7):2212-8. PMID: 11127458
4. Geske JB, Sorajja P, Ommen SR, Nishimura RA. Hypertrophic cardiomyopathy: clinical update. JACC Heart Fail. 2018;6(5):364-75. PMID: 29673576
5. Kuusisto J, Kärjä V, Sipola P, Kholová I, Peuhkurinen K, Jääskeläinen P, et al. Low-grade inflammation and myocardial fibrosis in hypertrophic cardiomyopathy. Heart. 2012;98(12):1007-13. PMID: 22511658
6. Seko Y, Nishikawa T, Yamaguchi K, Yamaoka M, Motoyoshi T, Takahashi N, et al. Serum levels of interleukin-6 in patients with hypertrophic cardiomyopathy. Am Heart J. 1995;129(4):924-6. PMID: 7702065
7. Shioji K, Kishimoto C, Sasayama S. Elevated interleukin-6 levels in patients with hypertrophic cardiomyopathy. Heart Vessels. 1998;13(3):141-6. PMID: 9869700
8. Frustaci A, Chimenti C, Calabrese F, Pieroni M, Thiene G, Maseri A. Immunohistological evidence of myocardial inflammation in hypertrophic cardiomyopathy. Heart. 2003;89(6):752-7. PMID: 12748233
9. Yoshida N, Ikeda U, Shimada K. Tumor necrosis factor-alpha and ventricular arrhythmias in hypertrophic cardiomyopathy. Jpn Heart J. 1999;40(4):451-8. PMID: 10586638
10. Ohtsuka T, Hamada M, Hara Y, Suzuki M, Shigematsu Y, Ogimoto A, et al. Relation of C-reactive protein to left ventricular hypertrophy and diastolic dysfunction in hypertrophic cardiomyopathy. Am J Cardiol. 2004;94(2):252-4. PMID: 15246886
11. Uemura Y, Morimoto S, Hida S, Nakajima T, Fujino T, Kusano K, et al. Serum high-sensitivity C-reactive protein and hypertrophic cardiomyopathy. Circ J. 2009;73(5):1020-5. PMID: 19282624
12. Kubo T, Okawa M, Yamasaki N, Kitaoka H, Hirota T, Hayato K, et al. Elevated plasma brain natriuretic peptide concentrations in patients with hypertrophic cardiomyopathy. Heart. 2010;96(13):1014-8. PMID: 20525617
13. Geske JB, Ommen SR, Gersh BJ. Hypertrophic cardiomyopathy: clinical spectrum, diagnosis, and management. Circ Res. 2017;121(7):749-70. PMID: 28912168
14. Ho CY, Day SM, Ashley EA, Michels M, Pereira AC, Jacoby D, et al. Genotype and lifetime burden of disease in hypertrophic cardiomyopathy: insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). Circulation. 2018;138(14):1387-98. PMID: 29997164