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Inflammatory and Cardiac Biomarkers in Obstructive and Non-Obstructive Hypertrophic Cardiomyopathy: A Review

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ABSTRACT

Background: Hypertrophic cardiomyopathy (HCM) is a genetically determined cardiac disorder characterized by asymmetric left ventricular hypertrophy, with or without left ventricular outflow tract obstruction. Inflammatory cytokines and cardiac biomarkers have been increasingly implicated in its pathogenesis, disease progression, and clinical outcomes. Interleukins (IL-1, IL-6), tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), and natriuretic peptides such as B-type natriuretic peptide (BNP) and its precursor fragment NT-proBNP provide valuable insights into myocardial stress and systemic inflammation.

Material and Methods: This review compiles evidence from studies assessing serum concentrations of IL-1, IL-6, TNF-α, CRP, BNP, and NT-proBNP in obstructive hypertrophic cardiomyopathy (OHCM), non-obstructive HCM (NOHCM), and healthy controls. PubMed, Scopus, and Embase were searched for articles published up to 2022 using keywords "Hypertrophic Cardiomyopathy," "Obstructive," "Cytokines," "BNP," and "Inflammation." Comparative analyses from observational studies, case–control cohorts, and experimental models were reviewed.

Conclusion: Evidence suggests that patients with OHCM and NOHCM exhibit significantly higher circulating levels of pro-inflammatory cytokines and natriuretic peptides compared to healthy controls. OHCM patients generally display greater biomarker elevation, reflecting higher hemodynamic stress and inflammatory activation. Elevated IL-6 and TNF-α correlate with myocardial fibrosis, while BNP and NT-proBNP are strongly associated with symptom severity, arrhythmic risk, and progression to heart failure. Understanding these biomarker profiles may aid in risk stratification, therapeutic monitoring, and potential incorporation of anti-inflammatory strategies in HCM management.

KEYWORDS: Hypertrophic cardiomyopathy, Obstructive HCM, IL-6, TNF-α, CRP, BNP, NT-proBNP and Inflammation

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INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiac disorder, with a prevalence of approximately 1 in 500 individuals in the general population (1). It is characterized by left ventricular hypertrophy that occurs in the absence of abnormal loading conditions such as hypertension or valvular disease (2). Clinically, HCM can be classified into obstructive hypertrophic cardiomyopathy (OHCM), defined by left ventricular outflow tract obstruction, and non-obstructive hypertrophic cardiomyopathy (NOHCM), in which obstruction is absent (3). Both forms are associated with increased risk of sudden cardiac death, arrhythmias, and progression to heart failure (4).

Beyond genetic predisposition, there is growing recognition that inflammatory pathways and neurohormonal activation significantly contribute to disease pathophysiology (5). Pro-inflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), have been implicated in myocardial remodeling, fibrosis, and altered contractility (6). Elevated systemic inflammation is thought to exacerbate ventricular stiffness and diastolic dysfunction, both hallmarks of HCM (7).

C-reactive protein (CRP), an acute-phase reactant, is also elevated in HCM patients and correlates with left ventricular hypertrophy and adverse outcomes (8). Similarly, biomarkers of myocardial stress such as B-type natriuretic peptide (BNP) and its N-terminal prohormone fragment (NT-proBNP) are widely used in clinical practice to assess cardiac function, filling pressures, and heart failure progression (9). In HCM, both BNP and NT-proBNP levels are consistently elevated and linked with symptom severity, arrhythmic events, and mortality (10).

Several studies have shown that OHCM patients, who experience higher left ventricular outflow gradients, tend to have greater biomarker elevation than NOHCM counterparts (11). This observation suggests that inflammatory and neurohormonal activation may be more pronounced in obstructive physiology due to increased wall stress and ischemia (12). Healthy controls consistently exhibit lower levels of these markers, supporting the pathological role of these pathways in HCM (13).

Understanding the comparative biomarker profile between OHCM, NOHCM, and healthy controls is crucial for clarifying disease mechanisms, refining risk stratification, and identifying therapeutic targets. This review synthesizes current evidence on serum levels of IL-1, IL-6, TNF-α, CRP, BNP, and NT-proBNP in HCM subgroups, aiming to highlight their diagnostic, prognostic, and therapeutic implications.

DISCUSSION

Inflammatory cytokines and cardiac stress markers are increasingly recognized as critical contributors to the pathogenesis and clinical progression of hypertrophic cardiomyopathy (HCM). Patients with obstructive HCM (OHCM) generally exhibit higher levels of these biomarkers compared to those with non-obstructive HCM (NOHCM) and healthy controls, underscoring the importance of mechanical and hemodynamic stress in driving inflammatory activation (3,6).

Pro-inflammatory Cytokines:

IL-1 and IL-6 are central mediators of inflammation and fibrosis. Elevated IL-6 levels in OHCM patients have been correlated with the degree of myocardial hypertrophy and severity of diastolic dysfunction (7). IL-1, though less studied, appears to contribute to maladaptive myocardial remodeling, promoting fibroblast proliferation and collagen deposition (8). TNF-α, another critical cytokine, is implicated in adverse ventricular remodeling and arrhythmogenesis, with higher concentrations reported in OHCM than NOHCM (9).

C - reactive protein (CRP):

CRP serves as a systemic marker of inflammation. Elevated CRP levels in HCM patients correlate with adverse outcomes, including progression to heart failure and arrhythmic complications (10). Evidence suggests that OHCM patients, in particular, have higher CRP concentrations compared to NOHCM, reflecting a heightened inflammatory burden secondary to increased wall stress and microvascular ischemia (11).

BNP and NT-proBNP:

BNP and NT-proBNP are well-established indicators of myocardial stretch and pressure overload. Their elevation in HCM is consistent with impaired ventricular compliance and elevated filling pressures (12). OHCM patients often exhibit markedly higher natriuretic peptide levels, correlating with the severity of obstruction and symptom burden (13). These markers also provide prognostic information, predicting adverse outcomes such as atrial fibrillation, sudden cardiac death, and progression to end-stage heart failure (9, 12).

Comparisons with Healthy Controls:

Healthy individuals consistently demonstrate significantly lower levels of these biomarkers, reinforcing their pathological role in HCM. The marked differences highlight the potential for incorporating biomarker evaluation into clinical practice for early disease detection and monitoring (4,5).

Clinical Implications:

The integration of inflammatory cytokine and natriuretic peptide assessment may refine risk stratification in HCM. Elevated IL-6 and TNF-α could potentially identify patients at higher risk for fibrosis-related complications, while BNP and NT-proBNP remain invaluable for assessing functional impairment. Furthermore, the recognition of inflammation as a driver of disease progression raises the possibility of exploring anti-inflammatory therapies, alongside conventional interventions such as septal myectomy, alcohol septal ablation, or pharmacological agents (6,10).

CONCLUSION

Hypertrophic cardiomyopathy is a complex genetic and inflammatory cardiac disorder characterized by significant heterogeneity in clinical presentation and outcomes. Comparative evaluation of biomarkers reveals that patients with obstructive HCM exhibit markedly higher levels of IL-1, IL-6, TNF-α, CRP, BNP, and NT-proBNP compared to non-obstructive HCM patients and healthy controls. These elevations reflect enhanced myocardial stress, systemic inflammation, and maladaptive remodeling.

The consistent association of elevated biomarkers with adverse structural and functional changes suggests their potential utility in refining risk stratification, predicting complications, and guiding therapeutic interventions. BNP and NT-proBNP, in particular, remain robust indicators of symptom burden and disease progression, while IL-6 and TNF-α may provide insights into fibrosis and arrhythmic risk.

Thus, incorporating biomarker profiling into clinical management could bridge the gap between genetic predisposition and clinical expression, providing a more comprehensive approach to diagnosis, prognosis, and individualized therapy in hypertrophic cardiomyopathy.

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. 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
3. 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
4. Kubo T, Kitaoka H, Okawa M, Hirota T, Hayato K, Yamasaki N, et al. Clinical impact of atrial fibrillation in patients with hypertrophic cardiomyopathy. Circ J. 2009;73(9):1599-605. PMID: 19690344
5. Kuusisto J, Kärjä V, Sipola P, Kholová I, Peuhkurinen K, Jääskeläinen P, et al. Low-grade inflammation and the phenotypic expression of 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. Geske JB, Sorajja P, Nishimura RA, Ommen SR. Evaluation of left ventricular outflow gradient: echocardiographic methods and clinical relevance for hypertrophic cardiomyopathy. J Am Coll Cardiol. 2011;57(3):325-32. PMID: 21232663
13. 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