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Article

The Influence of The *Ace* Gene I/D Polymorphism on Early Changes in The Myocardium

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Abstract: Left ventricular hypertrophy is one of the key risk factors for the development of cardiovascular complications. The onset of structural changes in the myocardium can occur as early as the subclinical phase and is dictated not only by hemodynamic loads but also by genetic predisposition. This article presents the results of a study evaluating the influence of the insertion/deletion polymorphism of the angiotensin-converting enzyme gene on early morphological and functional alterations of the left ventricular myocardium in ostensibly healthy individuals. A total of 60 subjects aged 18–40 years without clinically manifest cardiovascular pathology were examined. The findings demonstrate that carriage of the D-allele is significantly associated with an increased left ventricular mass index, thickening of the ventricular walls, and early signs of diastolic dysfunction. The obtained data confirm the significance of the ACE gene I/D polymorphism as a genetic marker of predisposition to myocardial remodeling, highlighting its promising utility within the frameworks of predictive and preventive cardiology.

Keywords: ACE gene, I/D polymorphism, left ventricular hypertrophy, myocardial remodeling.

1. Introduction

Left ventricular hypertrophy stands as one of the most critical prognostic factors for adverse outcomes in cardiovascular diseases, directly correlating with increased rates of chronic heart failure, fatal arrhythmias, and sudden cardiac death.[1] Structurally, the pathogenesis of LVH is traditionally linked to prolonged exposure to elevated arterial blood pressure. However, extensive clinical observations consistently reveal a high degree of variability in the myocardial structural response, even among individuals sharing nearly identical hemodynamic profiles.[2]

In recent years, considerable attention has been directed toward the role of genetic factors in driving myocardial remodeling. The paradigm of predictive medicine emphasizes the early identification of individuals at an elevated risk of cardiovascular pathology well before the onset of overt clinical manifestations. A primary candidate marker in this domain is the angiotensin-converting enzyme gene, which plays a fundamental role in regulating the renin-angiotensin-aldosterone system.[3]

The insertion/deletion (I/D) polymorphism of the ACE gene is characterized by the presence of an insertion, I, or absence of a 287-base-pair DNA fragment within intron 16 of the gene. This specific polymorphism directly modulates the expression levels of ACE in both plasma and tissues, which subsequently dictates the biological activity of angiotensin II—a potent stimulator of cardiomyocyte hypertrophy and myocardial fibrosis. Despite extensive research into this mechanism, empirical data regarding the impact of the ACE gene I/D polymorphism on early, subclinical cardiac changes in ostensibly healthy individuals remain limited.[4]

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2. Materials and Methods

This study enrolled 60 ostensibly healthy volunteers aged between 18 and 40 years. The strict exclusion criteria consisted of arterial hypertension, ischemic heart disease, diabetes mellitus, and congenital or acquired valvular heart defects. All participants provided written informed consent before inclusion.[5]

Genetic testing for the *ACE* gene I/D polymorphism was performed using polymerase chain reaction (PCR) assays isolated from peripheral venous blood samples. Genomic DNA amplification was carried out utilizing sequence-specific primers, and the respective genotypes (II, ID, or DD) were determined based on the molecular length of the resulting PCR fragments.[6]

A comprehensive transthoracic echocardiographic evaluation was conducted in standard views. The structural parameters measured included:

Interventricular septum thickness

Left ventricular posterior wall thickness

Left ventricular mass index

Doppler parameters of left ventricular diastolic function[7]

Resting arterial blood pressure was measured under standardized clinical conditions using a conventional sphygmomanometer.[8]

3. Results and Discussion

The distribution of the examined subjects based on their *ACE* genotypes allowed for the categorization of three distinct groups exhibiting varying degrees of genetic risk. Comparative analysis of the echocardiographic parameters revealed the presence of subclinical, structural myocardial alterations among carriers of the D-allele. These phenotypic modifications manifested in a dose-dependent manner and were most pronounced in individuals harboring the homozygous D/D genotype.[9]

These findings strongly substantiate the paradigm of genetically determined myocardial remodeling. Elevated ACE expression activity in D-allele carriers precipitates a localized increase in angiotensin II concentrations within the myocardium. Angiotensin II subsequently stimulates AT_1 receptors on cardiomyocytes and cardiac fibroblasts, activating downstream intracellular signaling cascades—such as the mitogen-activated protein kinase and transforming growth factor-beta (TGF-β) pathways. This process upregulates collagen synthesis and drives the development of interstitial fibrosis.[10]

Importantly, the observed structural alterations were documented in the absence of clinically significant arterial hypertension, highlighting the primary role of intrinsic genetic mechanisms over purely hemodynamic loads. Consequently, the insertion/deletion (I/D) polymorphism of the *ACE* gene can be considered an independent risk factor for early, subclinical myocardial remodeling.[11]

Table 1. Echocardiographic parameters stratified by ACE gene genotype[12]

Parameter	I/I	I/D	D/D
IVST *(Interventricular septum thickness, mm)*	Normal	Moderate increase	Significant increase[13]
LVPWT *(Left ventricular posterior wall thickness, mm)*	Normal	Moderate increase	Significant increase[14]
LVMI *(Left ventricular mass index)*	Normal	Elevated	Significantly elevated[15]

4. Conclusion

The insertion/deletion polymorphism of the *ACE* gene exerts a substantial influence on the development of early morphological and functional alterations within the left ventricular myocardium. Carriage of the D-allele is significantly associated with an elevated predisposition to myocardial remodeling well before the onset of clinically manifest cardiovascular pathology. Accordingly, the implementation of PCR-based genotyping of the *ACE* gene holds clinical value as a molecular screening tool within the framework of personalized preventive cardiology strategies.

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