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Correlation of Genetic Susceptibility in Myocardial Infaraction

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Abstract: ***Heart attack, also known as myocardial infarction (MI), remains one of the most pressing health concerns worldwide. While common risk factors such as hypertension, diabetes, smoking, and obesity explain much of the disease burden, they cannot fully account for why some individuals develop MI while others with similar lifestyles do not. This observation has directed attention toward genetic susceptibility. Over the past two decades, advances in genome-wide association studies (GWAS), family-based investigations, and candidate gene research have identified numerous genomic regions associated with coronary artery disease (CAD) and myocardial infarction [3,4,7,22]. This review summarizes current evidence regarding the genetic basis of MI, highlighting key susceptibility genes, biological pathways, polygenic risk scores, gene–environment interactions, and emerging applications in personalized cardiovascular medicine [6, 21, 24].***

Keywords: Myocardial infarction; Coronary artery disease; Genetic susceptibility; Genome-wide association studies; Polygenic risk score

1. Introduction

Heart attack continues to be one of the leading causes of death worldwide. Cardiovascular diseases account for millions of deaths annually, with myocardial infarction representing a major contributor to global mortality and morbidity [1,2]. Traditional risk factors such as unhealthy diet, smoking, obesity, physical inactivity, diabetes mellitus, and hypertension are well-established determinants of disease risk [1,2]. However, considerable variation in disease occurrence among individuals exposed to similar environmental conditions suggests a substantial genetic component [3,4].

Family history is a well-recognized independent risk factor for myocardial infarction. Individuals with affected first-degree relatives are at significantly greater risk of developing coronary artery disease themselves [15,20,23]. Advances in molecular genetics and GWAS have led to the identification of numerous susceptibility loci associated with CAD and MI, transforming our understanding of cardiovascular disease pathogenesis [3,4,7,22].

2. Genetic Basis of Heart Attack

2.1 Genome-Wide Association Studies (GWAS)

GWAS have revolutionized cardiovascular genetics by enabling systematic identification of common genetic variants associated with myocardial infarction. The most consistently replicated locus is chromosome 9p21, which has been associated with increased CAD risk across multiple populations [12–14]. Variants within this region influence nearby genes such as **CDKN2A** and **CDKN2B**, which regulate cell proliferation and vascular remodeling [3,4].

Subsequent large-scale GWAS have identified numerous additional susceptibility loci associated with coronary artery disease [5,7,22]. These studies have revealed genes involved in inflammation, lipid metabolism, endothelial function, and vascular remodeling. Among these, **ADAMTS7** has emerged as an important regulator of coronary atherosclerosis [11].

2.2 Candidate Gene Studies

Before the GWAS era, several candidate genes were implicated in cardiovascular disease susceptibility.

- **APOE:** Variants of the apolipoprotein E gene influence lipid transport and cholesterol metabolism and have been associated with premature coronary artery disease [9,19].
- **LDLR and PCSK9:** Mutations in these genes contribute to familial hypercholesterolemia, leading to markedly elevated LDL cholesterol levels and increased risk of premature myocardial infarction [8,16,17].
- **LPA:** Genetic variants affecting lipoprotein(a) levels have been strongly associated with coronary artery disease and myocardial infarction [10].
- **F5 (Factor V Leiden) and F2 (Prothrombin):** Mutations in coagulation-related genes increase thrombotic susceptibility and may contribute to acute coronary events.
- Additional lipid-associated loci have also been identified through large-scale genetic studies, further supporting the role of dyslipidemia in cardiovascular disease development [18].

2.3 Polygenic Risk Scores (PRS)

Recent studies have demonstrated that the cumulative effect of hundreds or thousands of common genetic variants can be integrated into polygenic risk scores (PRS) [6,21]. PRS have shown promise in identifying individuals at elevated risk of coronary heart disease independent of traditional clinical risk factors and family history [6,21]. These tools may facilitate earlier preventive interventions and personalized cardiovascular risk assessment.

3. Gene–Environment Interactions

Genetic risk does not operate independently of environmental exposures. Lifestyle factors such as smoking, diet, obesity, and diabetes can amplify the effects of

susceptibility variants [4]. For example, carriers of APOE variants may exhibit greater sensitivity to dietary cholesterol [19]. Similarly, individuals carrying the chromosome 9p21 risk allele who smoke or develop diabetes experience substantially increased cardiovascular risk [12–14]. These observations emphasize the importance of integrating genetic information with lifestyle modification strategies.

4. Epigenetics and Regulatory Mechanisms

In addition to inherited DNA sequence variation, epigenetic mechanisms influence susceptibility to myocardial infarction. DNA methylation, histone modification, and non-coding RNAs regulate gene expression without altering nucleotide sequences. Environmental factors such as smoking, diet, and chronic stress can induce epigenetic alterations that affect cardiovascular gene regulation and atherosclerotic progression [24,25]. Furthermore, regulatory genes such as **ADAMTS7** contribute to vascular remodeling and plaque development through complex molecular pathways [11].

5. Clinical and Public Health Implications

Understanding the genetic basis of myocardial infarction has important clinical applications.

- **Risk Prediction:** Incorporation of genetic information and polygenic risk scores can improve identification of individuals at elevated cardiovascular risk [6,21].
- **Personalized Medicine:** Individuals carrying pathogenic **PCSK9** variants may benefit from targeted lipid-lowering therapies, including PCSK9 inhibitors [16,17].
- **Preventive Strategies:** High-risk individuals identified through genetic testing may benefit from intensified lifestyle interventions and closer clinical monitoring [4,24].
- **Therapeutic Development:** Genetic discoveries are facilitating the development of novel therapeutic approaches targeting pathways involved in atherosclerosis and cardiovascular disease progression [24].

6. Future Directions

Future cardiovascular genetic research should focus on expanding studies beyond populations of predominantly European ancestry to include South Asian, African, and Indigenous populations [3,22]. Emerging technologies including multi-omics, transcriptomics, epigenomics, and systems biology approaches are expected to provide deeper insights into disease mechanisms [24]. Integration of genetic, environmental, and clinical data may ultimately enable highly personalized prevention and treatment strategies.

7. Conclusion

The study of genetic susceptibility has transformed our understanding of myocardial infarction. Variants in genes such as **APOE**, **LDLR**, **PCSK9**, **LPA**, and loci including chromosome **9p21** significantly contribute to disease risk [8,10,12–19]. Nevertheless, genetic predisposition interacts extensively with lifestyle and environmental factors [4]. Continued advances in cardiovascular genomics, polygenic risk assessment, and precision medicine hold considerable promise for improving prediction, prevention, and treatment of myocardial infarction [6,21,24].

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