The Role of Genetic Polymorphisms in Modulating Beta-Blocker Response: A Comprehensive Review

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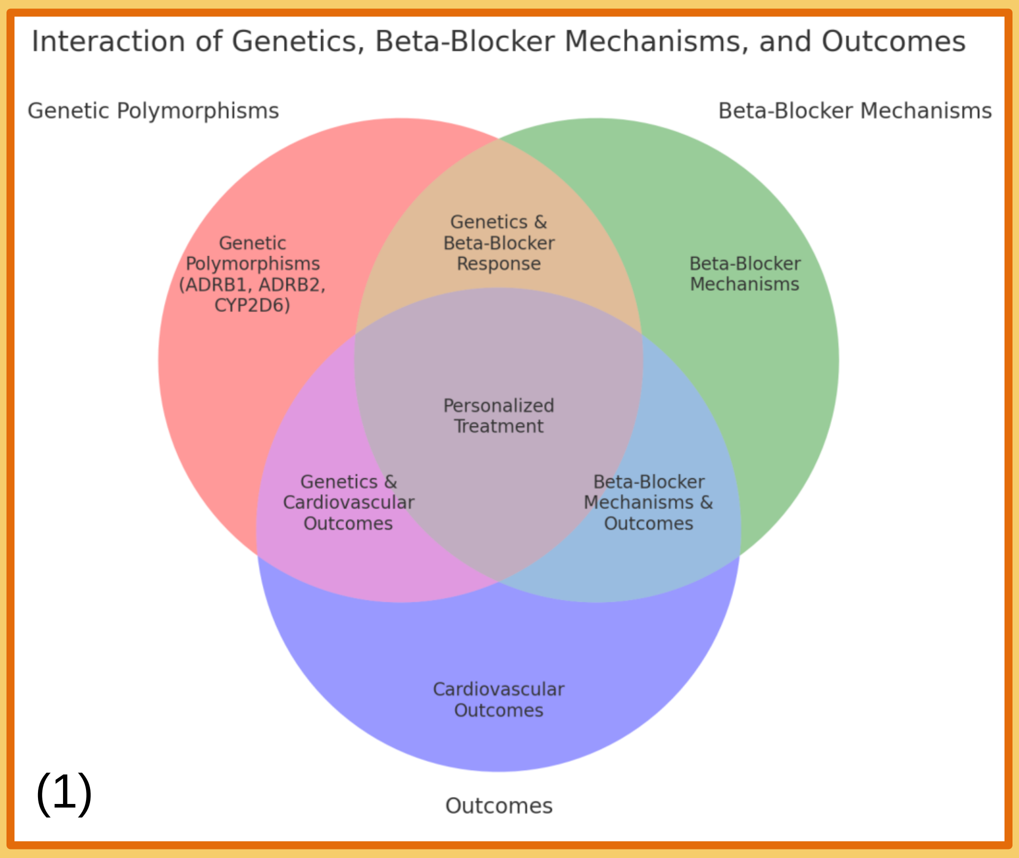
Introduction and Aims

Introduction:
Beta-blockers are central to managing cardiovascular diseases, such as hypertension, heart failure, and arrhythmias, due to their ability to reduce heart rate, blood pressure, and improve cardiac function. However, patient responses to these medications can vary widely, leading to differences in efficacy and adverse effects. Recent research has identified genetic polymorphisms in receptor genes like ADRB1 and ADRB2, as well as metabolic pathway genes like CYP2D6, as key determinants of these variations. These genetic differences influence drug-receptor interactions, drug metabolism, and overall therapeutic outcomes. Understanding these genetic variations is crucial for optimizing treatment efficacy, minimizing adverse effects, and promoting personalized medicine in cardiovascular care.

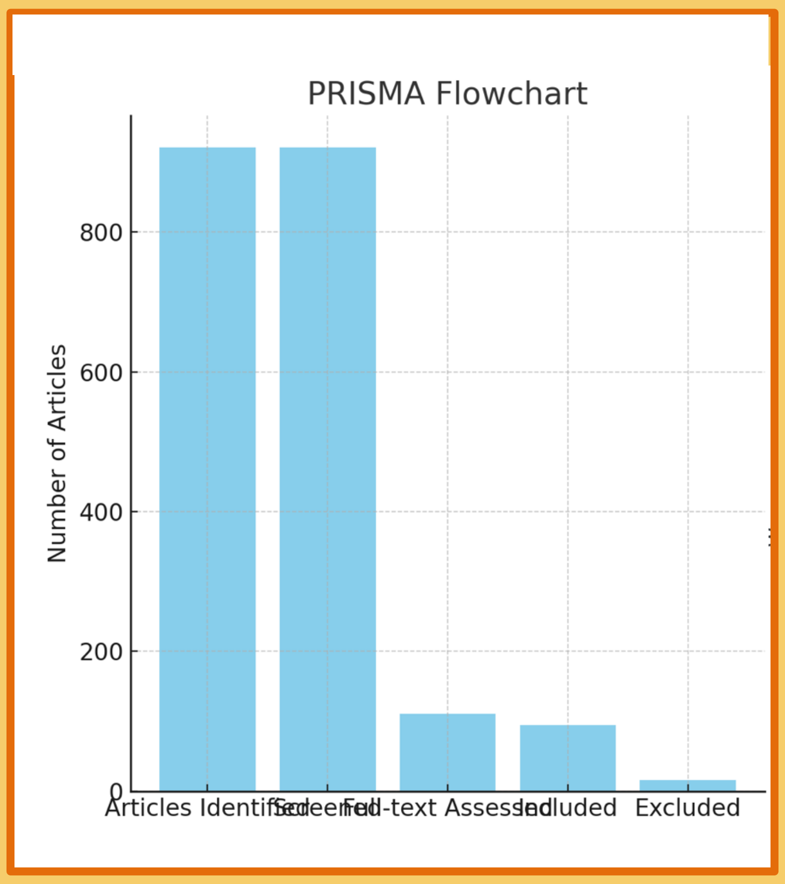
Aims:
1. To assess how **ADRB1**, **ADRB2**, and **CYP2D6** polymorphisms influence beta-blocker efficacy and safety.
2. To identify specific genetic variants linked to therapeutic outcomes and adverse effects.
3. To promote the integration of pharmacogenetics into clinical practice for improved cardiovascular care.



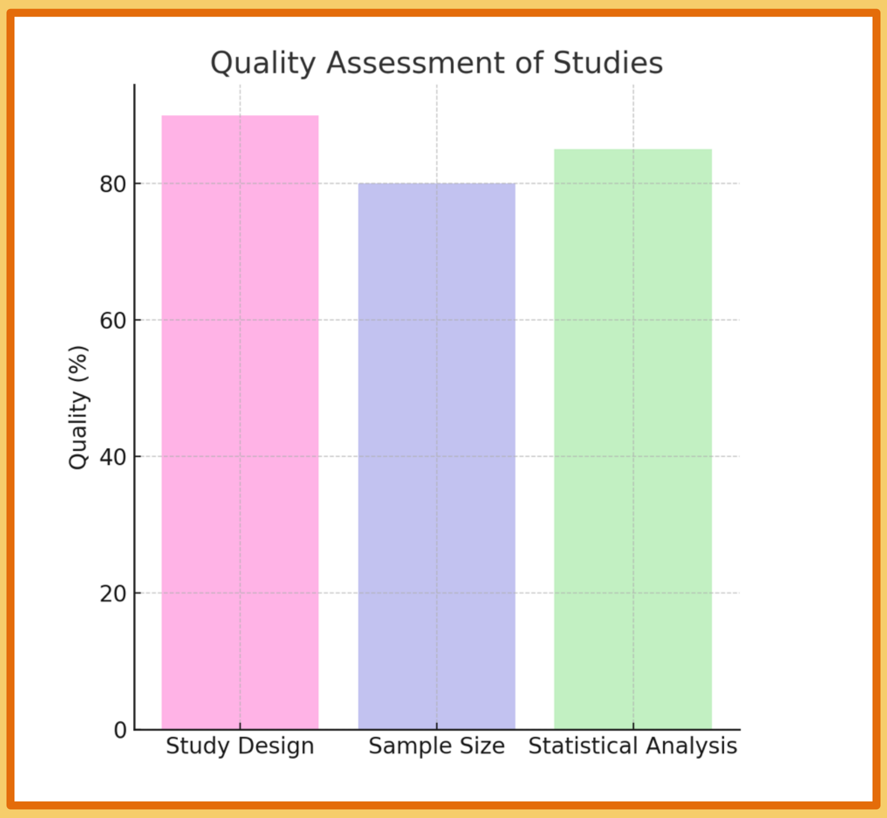
Methods

A systematic review was conducted using three major online databases: PubMed, Scopus, and Web of Science. Search terms included "genetic polymorphisms," "beta-blockers," "ADRB1," "ADRB2," and "CYP2D6." The initial search resulted in 921 articles, which were screened for relevance. After the removal of duplicates, 111 full-text articles were assessed based on eligibility criteria, which focused on genetic polymorphisms influencing beta-blocker response in human populations.

Of these, 95 studies met the inclusion criteria and were included in the final analysis. A quality assessment of the included studies was performed using a modified Cochrane Risk of Bias (RoB1) tool, evaluating study design, sample size, data reporting, and statistical analysis. Studies that did not meet the required quality standards were excluded from the final analysis.



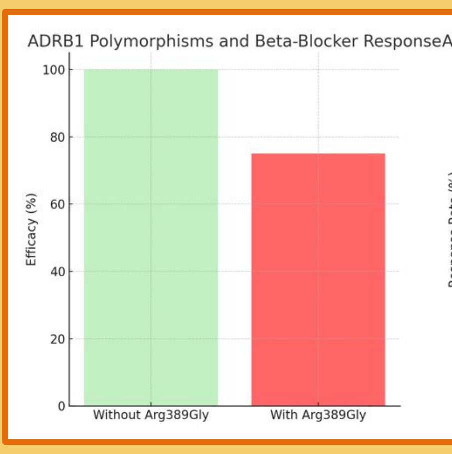
2- PRISMA Flowchart



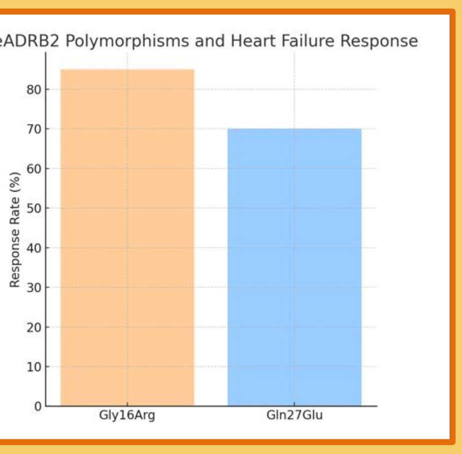
3- Quality Assessment of Studies

Results

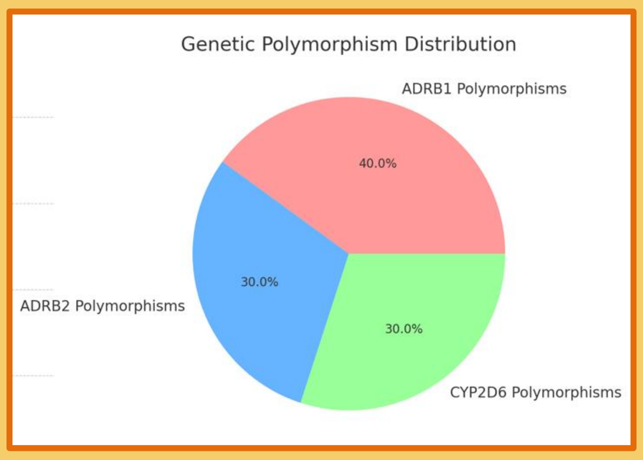
Of the 95 included studies, 40% focused on ADRB1 polymorphisms, 30% on ADRB2 variants, and 30% on CYP2D6 metabolism. Key findings revealed that the Arg389Gly variant in ADRB1 was linked to a 25% reduction in beta-blocker efficacy in hypertensive patients, while Gly16Arg and Gln27Glu variants in ADRB2 were associated with differential responses in heart failure. CYP2D6 polymorphisms significantly impacted drug metabolism, altering plasma levels and clinical outcomes.



4- ADRB1 Polymorphisms



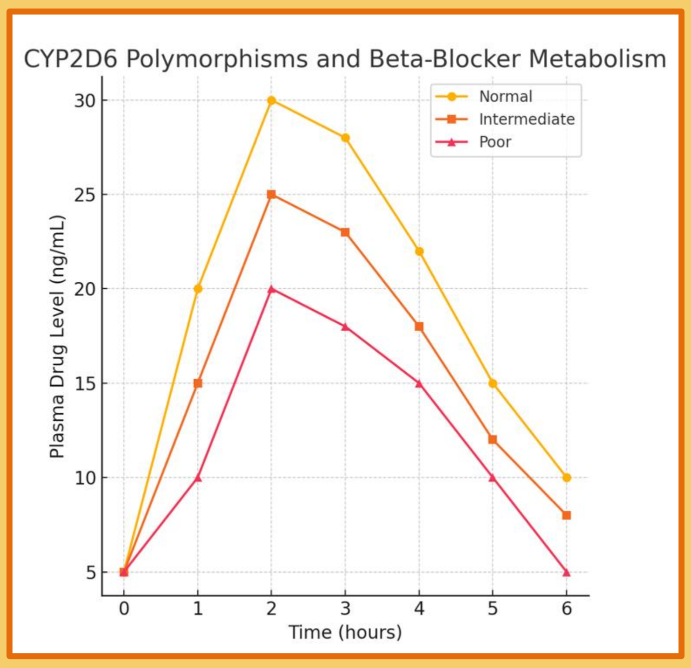
5- ADRB2 Polymorphisms



6- Distribution of Genetic Polymorphisms

Conclusion

Genetic polymorphisms in ADRB1, ADRB2, and CYP2D6 substantially influence the efficacy and safety of beta-blockers. Incorporating pharmacogenomic data into clinical practice can enhance therapeutic outcomes by personalizing treatments based on genetic profiles. Future research should validate these findings through large-scale trials and develop actionable pharmacogenomic guidelines.



7- CYP2D6 Metabolism