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Poster presentation

B-type natriuretic peptide single nucleotide polymorphism rs198389 is highly prevalent and impacts test characteristics of common assays

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Background

BNP assays are widely used in the diagnosis and prognosis of left ventricular (LV) dysfunction and heart failure. The functional single nucleotide polymorphism rs198389 in the promoter region of the BNP gene has been associated with higher BNP levels [1-3]. The prevalence of rs198389 in the general US population is unknown. The impact on common assay test characteristics, and cardiovascular and clinical phenotypes is also unknown. The goal of this study was to determine for the first time the prevalence of rs198389 in a US general adult population and its impact on (a) three commonly used BNP assays (BNP levels, diagnostic test performance), and (b) clinical phenotype and disease prevalence.

Materials and methods

A random sample of the general population (≥ 45 years; n = 1970) from Olmsted County, MN, USA was genotyped for rs198389, BNP plasma levels (Biosite, Shionogi, and Roche NT-proBNP assays) were determined, and detailed biochemical, clinical, and echocardiographic characterizations were performed. The effect of rs198389 on plasma BNP and NT-proBNP assay test characteristics for the detection of LV dysfunction was evaluated.

Results

Genotype frequencies were in Hardy-Weinberg equilibrium (p = 0.98): TT 32.7%, TC 49.9%, and CC 17.3%. The C-allele independently predicted higher BNP in multivariate analysis (p < 0.0001 for all assays). When using previously reported genotype-unadjusted cutpoints for the detection of LV ejection fraction ≤ 40% and ≤ 50%, sensitivity increased with the number of C-alleles (approximately 10% for CC vs TT), whereas specificity decreased (approximately 10% for CC vs TT). C-alleles were associated with higher prevalence of type 2 diabetes mellitus (OR: 1.63 (CI: 1.09–2.44), p = 0.02, dominant model) and atrial fibrillation (OR: 1.63 (CI: 1.01–2.63), p = 0.04, recessive model).

Conclusion

rs198389 is common in the general US population. The C-allele is associated with higher plasma BNP and confounds the test characteristics of commonly used assays. The association of rs198389 with diabetes and atrial fibrillation needs to be confirmed and further explored.

References

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