The Association between Blood Pressure Variability and Vascular dementia: A Two-sample Mendelian Randomization Study

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Introduction

This study aims to explore the causal relationship between blood pressure variability (BPV) and vascular dementia by applying a mendelian randomization (MR) study using summary data of the genome-wide association studies based on UK biobank and FinnGen datasets.

Methods

The genetic instruments were chosen from BPV GWAS based on UK Biobank data. The estimates between those genetic variables and dementia were extracted from the FinnGen project. The following exclusion criteria were applied for SNPs: (1) confounding SNPs by searching hypertension and artery stiffness GWAS; (2) significant SNPs that are associated with dementia in the datasets; (3) palindromic SNPs with an effect allele frequency between 0.4 and 0.7. Proxy SNPs were manually selected for some SNPs. (4) only SNPs with linkage disequilibrium r2 < 0.01 were selected as genetic instruments, also known as independent SNPs. The effect/reference alleles were checked to ensure the consistency of the base pair between BPV and dementia GWAS, which is also known as data harmonization. After data harmonization, four MR methods were employed to measure the causal effect: IVW-MR with random effect, IVW-MR with fixed effect, MR-Egger, and weighted median MR.

Results

Finally, six independent SNPs were chosen as instrument variants for SBPV, and five for DBPV. The results showed that SBPV has a significant causal effect on vascular dementia, with OR for per 5-unit increase in SBPV of 2.85,2.36, and 2.07 for MR-Egger, weighted median, and IVW-MR, respectively (Table 1). In contrast, no significant result was found for DBPV.

Table 1. Summary of the MR Analysis of BPV and Vascular Dementia (5-unit increase in BPV)

Exposure	SNP	OR (95% CI)
SBPV		
MR Egger	5	**2.85 [1.08, 7.52]**
IVW (fixed effects)	5	**2.07 [1.18, 3.63]**
IVW (random effects)	5	**2.07 [1.21, 3.54]**
Weighted median	5	**2.36 [1.17, 4.76]**
DBPV		
MR Egger	5	1.02 [0, 407.63]
IVW (fixed effects)	5	0.90 [0.44, 1.83]
IVW (random effects)	5	0.90 [0.47, 1.73]
Weighted median	5	1.04 [0.42, 2.57]

Conclusion

This MR study suggested that systolic blood pressure variability is a causal risk factor for vascular dementia, while the evidence from diastolic blood pressure variability is still uncertain. Hypertension treatment should focus on both blood pressure level and blood pressure stability.

Keywords: Blood pressure variability, cognitive function, mendelian randomization

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