VOL. 4, NO. 1, 2024
ISSN 2772-3747

Letters

RESEARCH LETTER

Association Between B-Type Natriuretic Peptide Deficiency and Left Ventricular Concentric Hypertrophy in Subclinical Individuals

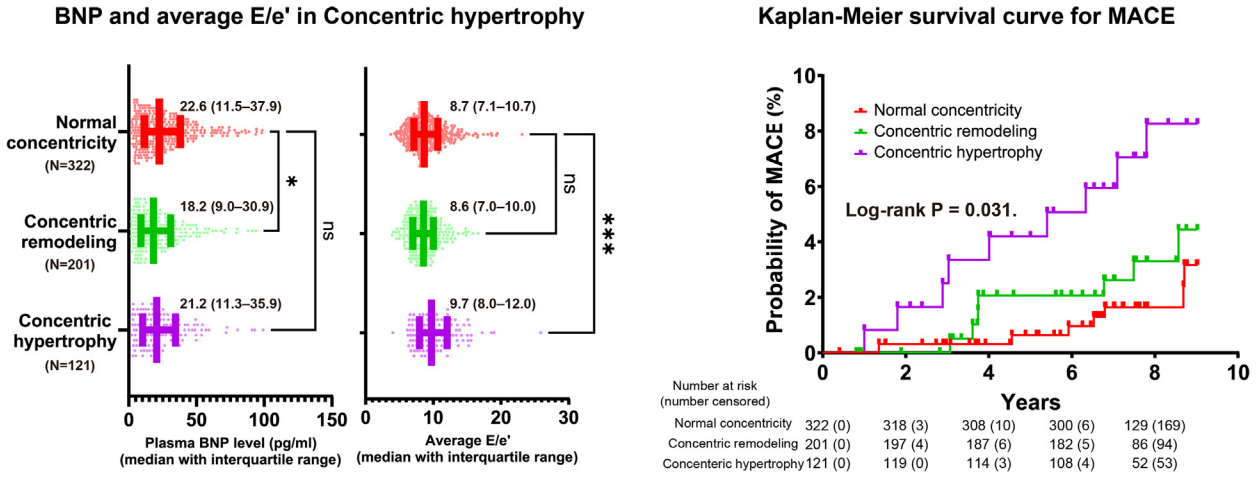
Higher natriuretic peptide (NP) levels are frequently linked to left ventricular hypertrophy (LVH)[1] because elevated left ventricular (LV) filling pressure promotes LVH and NP production.[2] However, some individuals show unexpectedly low NP levels under elevated LV filling pressure, suggesting an "endocrine deficiency of NPs."[3] Recently, an association was found between lower plasma B-type natriuretic peptide (BNP) levels and LV concentric remodeling in a subclinical cohort,[4] with animal studies supporting this link.[5] We examined the association among plasma BNP levels, LV geometry, and major adverse cardiovascular event (MACE) risk in a subclinical population.

We retrospectively investigated participants from the Arita-cho Health Check Program (n = 1,632, from June 2005 to July 2008). After excluding those with cardiovascular diseases, BNP ≥100, or LV ejection fraction <50%, 1,197 asymptomatic participants were categorized using their relative wall thickness into the normal and abnormal LV concentricity groups. LV concentricity propensity score was obtained by fitting a logistic regression model for age, sex, body mass index, blood pressure, heart rate, estimated glomerular filtration rate, Doppler echocardiographic parameters (peak E- and A-wave velocity, deceleration time, and septal and lateral e'), and medical history (hypertension, dyslipidemia, and diabetes mellitus). The groups were matched 1:1 using the nearest neighbor method with a 0.2-caliper restriction. Ultimately, 644 patients were analyzed, with each group comprising 322 participants (267 men; median age 67 years). Abnormal concentricity was a relative wall thickness ≥0.42; LVH was an LV mass index >115/95 in men and women.[6] The primary composite endpoint was MACE, including cardiovascular mortality, acute myocardial infarction, stroke, and hospitalization for heart failure. Statistical analyses were performed using SPSS version 26.0. Values were expressed as median (IQR). This study obtained the necessary approvals (M28-077-3 and M14-025-6) and adhered to the Declaration of Helsinki, the guidelines of the human research ethics committees, and Food and Drug Administration guidelines, including patient consent where appropriate.

In the matched cohort, the abnormal group had lower BNP levels (18.6 pg/mL [IQR: 10.1-32.4 pg/mL] vs 22.5 pg/mL [IQR: 11.5-37.9 pg/mL]; $P = 0.040$) and a larger LV mass index (94.9 g/m^2 [IQR: 78.9-110.7 g/m^2] vs 89.6 g/m^2 [IQR: 75.9-105.8 g/m^2]; $P = 0.010$) than the normal group. We subdivided the abnormal group into the concentric remodeling and concentric hypertrophy (CH) groups and evaluated the average ratio between early mitral inflow velocity and early diastolic mitral annular velocity (E/e′), a noninvasive estimation of LV filling pressure.[6] Although the CH group had a higher average E/e′ (9.7 [IQR: 8.0-12.0] vs 8.7 [IQR: 7.1-10.7]; $P < 0.001$) than the normal group, their BNP levels were comparable ($P = 0.670$) (Figure 1). The CH group had elevated LV filling pressure without a proportional increase in BNP levels, suggesting a BNP deficiency. Multivariable logistic regression analysis showed that normal BNP levels and abnormal E/e′[6] increased CH risk (adjusted OR: 1.589; 95% CI: 1.006-2.509; $P = 0.047$ and adjusted OR: 1.617; 95% CI: 1.042-2.508; $P = 0.032$, respectively) (adjusted for age, sex, obesity [body mass index ≥27.5 kg/m^2], systolic blood pressure, heart rate, estimated glomerular filtration rate, medical history, and plasma BNP levels or average E/e′). Within a median follow-up of 7.8 years, 23 patients experienced MACE, with elevated rates in the CH group (log-rank $P = 0.031$) (Figure 1, right). In conclusion, CH was associated with higher LV filling pressure without a proportional increase in plasma BNP levels and a poor prognosis in a subclinical health check population. However, invasive cardiac examination with simultaneous

JACC: ASIA, VOL. 4, NO. 1, 2024
JANUARY 2024:87–88

FIGURE 1 Association Among Plasma BNP Levels, Left Ventricular Geometry, and MACE Risk



(Left) Comparison of plasma B-type natriuretic peptide (BNP) levels and average ratio between early mitral inflow velocity and early diastolic mitral annular velocity (E/e') by left ventricular geometry. *$P < 0.05$ and *** $P < 0.001$, Kruskal-Wallis test followed by the Dunn-Bonferroni post hoc test. (Right) Kaplan-Meier analysis of major adverse cardiovascular events (MACE).

measurement of NP levels under hemodynamic stress is warranted to clarify the clinical significance of BNP deficiency.

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https://doi.org/10.1016/j.jacasi.2023.10.002

This work was supported by grants from the Osaka Medical Research Foundation for Intractable Disease (28-2-6) and the Japan Arteriosclerosis Prevention Fund, grants from the Japan Heart Foundation, and Grants-in-Aid from the Japan Society for the Promotion of Science (JP18K15910 and 22H03066). The authors thank Yoshiaki Matsuo (Mayor of Arita-cho) and Yoko Okumoto (Health and Welfare Division, Arita-cho) for operating the program.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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