Association of High-Sensitivity Cardiac Troponin T and N-Terminal Pro–Brain-Type Natriuretic Peptide With Left Ventricular Structure: J-HOP Study

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Although both high-sensitivity cardiac troponin T (Hs-cTnT) and N-terminal pro–brain-type natriuretic peptide (NT-proBNP) levels are higher among patients with cardiac structural abnormalities than among those with apparently normal hearts, there is considerable overlap between the groups. The authors evaluated 1336 patients who had ≥1 cardiovascular risk factors, underwent echocardiography, and had Hs-cTnT and NT-proBNP measured and excluded patients with left ventricular (LV) dysfunction. The patients in the highest Hs-cTnT category in quintiles had an increased likelihood of abnormal relative wall thickness compared with those in the lowest category (odds ratio, 1.66; 95% confidence interval, 1.17–2.36; $P<.01$). However, no such association was found in the category of NT-proBNP. The patients in the highest NT-proBNP category had an increased likelihood of abnormal LV diastolic dimension/body surface area compared with those in the lowest category (odds ratio, 2.11; 95% confidence interval, 1.17–3.79; $P<.05$). However, no such association was found in the category of Hs-cTnT. The data suggest that the measurement of Hs-cTnT and NT-proBNP might provide information on cardiac structural abnormalities. *J Clin Hypertens (Greenwich).* 2014;16:354–361. ©2014 Wiley Periodicals, Inc.

Left ventricular (LV) hypertrophy assessed by echocardiography is an ominous prognostic sign and an independent risk factor for cardiovascular disease, both in the general population and in hypertensive patients.[1,2] LV hypertrophy occurs as pressure overload hypertrophy or volume overload hypertrophy. Pressure overload usually elicits concentric hypertrophy, with increased wall thickness and unaltered or decreased diameter, whereas volume overload triggers eccentric hypertrophy with increased LV diameter and unaltered or decreased wall thickness.[3,4]

A high-sensitivity assay of cardiac troponin T (Hs-cTnT) and N-terminal pro–brain-type natriuretic peptide (NT-proBNP) have been reported to be associated with cardiac structural or functional abnormalities and can be used in this way in both general populations and patients with heart failure and coronary artery disease at increased risk for future cardiovascular events.[5–7] In asymptomatic patients, although Hs-cTnT and NT-proBNP levels are higher among patients with cardiac structural or functional abnormalities than among those with apparently normal hearts, there is considerable overlap between the groups.[5] In fact, some papers have reported that not only measurement of Hs-cTnT but also NT-proBNP could independently provide prognostic and risk-assessment information in general populations and cardiovascular patients.[6,8]

To better understand the information provided by the hs-cTnT and NT-proBNP, we investigated the relationship between these two biomarkers and echocardiographic indices of LV structure from a robust number of ambulatory patients without LV dysfunction.

METHODS

Patients

The patients in this paper were among the participants in the Japan Morning Surge-Home Blood Pressure (J-HOP) study.[9] The protocol of the J-HOP study has been registered on the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) Web site under the trial number UMIN 000000894. Briefly, the J-HOP study is a prospective observational study to evaluate predictive values of home blood pressure (BP) for cardiovascular events in Japanese patients with any of the following cardiovascular risk factors: hypertension, impaired glucose tolerance or diabetes, dyslipidemia, smoking habit (including chronic obstructive pulmonary disease), chronic renal disease, atrial fibrillation, metabolic syndrome, and sleep apnea syndrome. Exclusion criteria in the J-HOP study were a recent history of cardiovascular and cerebrovascular events (within 6 months), current hemodialysis treatment, chronic inflammatory disease, and malignancy. The patients in this paper were enrolled in this study between January 2005 and June 2010 by physicians. The institutional review board of the Jichi Medical University School of Medicine approved this study, and written informed consent was obtained from all participants of the J-HOP study.

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In the present study, diabetes was defined as fasting glucose levels ≥126 mg/dL and/or glycated hemoglobin levels ≥6.1 mg/dL or treated diabetes. Hyperlipidemia was defined as total cholesterol levels ≥240 mg/dL or treated hyperlipidemia. Alcohol drinkers were defined as those who were reported consuming ≥20 g/d. History of cardiovascular disease was defined as those who had angina pectoris, myocardial infarction, heart failure, aortic dissection, or stroke. Sleep apnea syndrome was defined as an apnea-hypopnea index of ≥15 events per hour, as measured by overnight sleep polysomnography. To estimate renal function, the estimated glomerular filtration rate (eGFR) was derived using the following equation: eGFR (mL/min/1.73 m^2)=194×age (years)$^{-0.287}$×serum creatinine (mg/dL)$^{-1.094}$ (if women×0.739).[10]

Among the 4019 patients recruited for the J-HOP study, 1606 patients gave informed consent and participated in the echocardiography examination. Among the 1606 patients for whom echocardiography was performed, to evaluate the relationship between biomarkers (Hs-cTnT and NT-proBNP) and echocardiographic indices of LV structure, we first excluded patients who had no measurement of biomarkers (n=177). Second, we excluded patients who did not have measurements of LV mass index (LVMI), relative wall thickness (RWT), and ejection fraction (EF) (n=17) of 1429 patients who had echocardiography performed and data of biomarkers. Finally, we analyzed 1336 patients, because we excluded patients with systolic dysfunction (EF <55%; n=76) of 1412 patients with both data of echocardiographic indices of LV structure and biomarkers.

BP Measurement

Office BP was measured by a digital oscillometric BP monitoring device (HEM-5001; Omron Healthcare Co, Ltd, Kyoto, Japan) after the patients had been seated for 2 minutes and was calculated as the mean of 3 consecutive measurements. Self-measured home BP values were obtained using the same device as in the clinic (HEM-5001). The patients were instructed to place the cuff on the same arm throughout the measurement and to measure their BPs in a sitting position after at least 2 minutes of rest. Morning BP was measured within 1 hour after waking, after urination, and before breakfast. Evening BP was measured just before going to bed and at least 60 minutes after taking a bath. These methods are based on Japanese home BP guidelines.[11] Three home BP readings were taken at 15-second intervals in a sitting position in both the morning and evening for 14 days. The mean home BP was defined as the average of all readings for each individual.

Biomarker Assays

Blood samples were collected in the morning in a fasting state at enrollment. Using the stored serum samples, Hs-cTnT was measured using a highly sensitive assay on an automated platform (Elecsys-2010 Troponin Ths STAT; Roche Diagnosis, Tokyo, Japan), with a lower detection limit of 3 pg/mL and a reported 99th percentile value in apparently healthy individuals of 14 pg/mL. The lower limit of detection of NTproBNP is 5 pg/mL. The intracoefficients/intercoefficients of variation were 2.02%/3.02% for Hs-cTnT and 1.93%/3.13% for NT-proBNP.

Echocardiography

Echocardiography was performed at each participating institute. The two-dimensional M-mode or B-mode image was recorded using an ultrasound machine according to the guidelines of the American Society of Echocardiology and the European Association of Echocardiography.[12] The LV mass was obtained using the formula validated by the American Society of Echocardiology: LVM=0.8 x (1.04 [(LVIDd+PWTd +SWTd)^3−(LVIDd)^3])+0.6 g, where LVIDd is LV internal diameter in diastole, PWTd is posterior wall thickness in diastole, and SWTd is septal wall thickness in diastole. LVMI was calculated as LV mass/body surface area (BSA). RWT was calculated using the formula (2×PWTd)/(LVIDd). LV hypertrophy was defined as an LVMI >115 g/m^2 and >95 g/m^2 in both men and women, respectively. A normal reference range in LVIDd/BSA was defined by <32 mm in women and <31 mm in men. Concentric LV hypertrophy (LVH) was defined as the presence of LVH and an RWT >0.42. Eccentric LVH was defined as the presence of LVH and an RWT ≤0.42. Concentric remodeling was defined as the presence of an RWT >0.42, but without LVH. Normal LV geometry was considered the absence of LVH and an RWT ≤0.42. These measurements and definitions were based on the guidelines of the American Society of Echocardiology and the European Association of Echocardiography.[12]

Statistical Analysis

Data are expressed as mean (±standard deviation), percentage or median (25th–75th percentile). Hs-cTnT and NT-proBNP data had skewed distributions and so were analyzed after being subjected to natural logarithmic transformation. For the analysis of Hs-cTnT as a categorical variable, our population was subdivided into 4 a priori–determined categories: those with undetectable Hs-cTnT levels and those with Hs-cTnT levels ≥3 pg/mL were divided into tertiles. For the analysis of NT-proBNP as a categorical variable, we combined the lowest quintile with the second quintile after dividing into quintiles of NT-proBNP levels, because there were 576 patients with undetectable Hs-cTnT, which was almost equal to the population of two quintiles of NT-proBNP (n=535). One-way analysis of variance was performed to detect differences among categories, and Tukey's honestly significant differences test for multiple pairwise comparisons of the means among groups. The χ^2 statistic was used to compare categorical variables among categories. Analysis of covariance was used to

analyze the relationship of LV structure to each group while statistically controlling for confounding factors, and the Bonferroni test was used for multiple pairwise comparisons. Multiple logistic regression analysis was performed to estimate and test the independent effects of Hs-cTnT or NT-proBNP on LVIDd/BSA, RWT, and LVMI. Age, sex, body mass index (BMI), current smoking, drinking, diabetes, dyslipidemia, use of antihypertensive drug, history of cardiovascular disease (CVD), eGFR, office systolic BP (SBP) and diastolic BP (DBP), and home SBP and DBP were used as adjustments. Differences/associations with a P value <.05 were considered statistically significant. All analyses were performed with SPSS version 18.0J statistical software (SPSS Inc, Chicago, IL).

RESULTS

Patient Characteristics

Table I presents the clinical characteristics, BP parameters, and echocardiographic profiles of the patients divided by categories of Hs-cTnT. The prevalence of undetectable Hs-cTnT was 43.1%. The median Hs-cTnT was 7.0 pg/mL in the patients with detectable Hs-cTnT. Higher Hs-cTnT was significantly associated with higher age, NT-proBNP, and home SBP; higher prevalence of diabetes and CVD; and lower eGFR, office DBP, and home DBP. Table II presents the clinical characteristics, BP parameters, and echocardiographic profiles of the patients divided by categories of NT-proBNP. The median NT-proBNP was 57.1 pg/mL. Higher NT-proBNP was significantly associated with higher age, Hs-cTnT, and home SBP; higher prevalence of smoking CVD, atrial fibrillation, and sleep apnea syndrome; and lower BMI, BSA, eGFR, and office and home DBP.

Association Between LV Structure and Hs-cTnT

In Table I, across Hs-cTnT categories, LVMI and RWT increased. LVMI in the highest category was significantly higher than any other categories. The second and third category was significantly higher in the LVMI than the lowest category. RWT in the highest category was significantly higher than the lowest and second categories, and the second and third categories were significantly higher in RWT than the lowest category. After adjustment for age, sex, BMI, smoking, alcohol, diabetes, dyslipidemia, history of CVD, atrial fibrillation, sleep apnea syndrome, the use of antihypertensive drugs, eGFR, clinic SBP and DBP, and home SBP and DBP, LVMI in the highest category was significantly higher than in the lowest category. After adjustment for similar confounders, RWT in the highest category was significantly higher than in the lowest category. As shown in Table III, the patients in the second to highest category of Hs-cTnT had higher risk of abnormal LVH and those in the highest category had higher risk of abnormal RWT after adjusting for confounders. However, this association was not found in patients with abnormal LVIDd/BSA.

Association Between LV Structure and NT-proBNP

In Table II, across NT-proBNP categories, LVIDd/BSA, LVMI, and RWT increased. LVIDd/BSA in the highest category was significantly higher than the lowest and second categories. The second and third category was significantly higher in LVIDd/BSA than the lowest category. LVMI in the highest category was significantly higher than any other categories. The third category was significantly higher in LVMI than the lowest category. RWT in the highest category was significantly higher than in the lowest and second category. After adjustment for age, sex, BMI, smoking, alcohol, diabetes, dyslipidemia, history of CVD, atrial fibrillation, sleep apnea syndrome, the use of antihypertensive drugs, eGFR, clinic SBP and DBP, and home SBP and DBP, LVIDd/BSA in the highest category was significantly higher than in the lowest category. After adjustment for similar confounders, LVMI in the highest category was significantly higher than any other categories. However, the association was not found in RWT. As shown in Table III, the patients in the third and highest categories of NT-proBNP had higher risk of abnormal LVIDd/BSA and LVH after adjusting for confounders. This association was not found in those with abnormal RWT, while the prevalence of abnormal RWT increased across categories.

DISCUSSION

The important findings of this study were that (1) after dividing the patients into categories by Hs-cTnT, patients in the highest category had higher likelihood of abnormal RWT than the patients with undetectable Hs-cTnT, and this association was not found in those with abnormal LVIDd/BSA; (2) after dividing the patients into categories by NT-proBNP, the patients in third and highest categories had higher likelihood of abnormal LVIDd/BSA than those in the lowest category, and this association was not found in patients with abnormal RWT; (3) the patients in the second to highest categories of Hs-cTnT had higher risk of LVH than the patients in the lowest category, and the patients in the highest category of NT-proBNP had higher risk of LVH than those in the lowest category.

The possible mechanism responsible for higher Hs-cTnT associated with increased LV wall, ie, high RWT, has not yet been elucidated. Cardiac troponins are established biomarkers of myocardial injury that are commonly used in the diagnosis of acute coronary syndromes.[13–15] However, the mechanisms responsible for the release of very low levels of cardiac troponins in patients without acute coronary syndrome are unconfirmed. For chronic troponin leakage, increased demand ischemia or cardiomyocyte apoptosis in volume or pressure overloaded hearts plays an important role.[7,16] LVH is divided in two phenotypes, concentric hypertrophy caused by pressure overload hypertrophy and eccentric hypertrophy caused by volume overload hypertrophy. A prior study reported that concentric hypertrophy was linked to a substantial reduction in

TABLE I. Characteristics of Patients Divided by Categories of Hs-cTnT

General Characteristics	All Patients (N=1336)	Hs-cTnT Category, pg/mL <3.0 (n=576)	3.0–5.0 (n=270)	5.1–9.0 (n=257)	≥9.1 (n=233)	*P* Value
Age, y	65±11	61±10	66±11[a]	69±9.1[a,d]	72±10[a,d,g]	<.001
Men, %	49.9	39.8	50.4	54.1	51.5	<.001
Body mass index, kg/m^2	24.5±3.6	24.4±3.7	24.3±3.8	25.0±3.5	24.5±3.3	0.108
Body surface area, m^2	1.61±0.19	1.62±0.18	1.61±0.20	1.63±0.18	1.59±0.18	.120
Current smokers, %	11.8	9.7	13.7	11.3	9.4	.312
Habitual drinkers, %	23.3	23.4	25.9	25.3	17.6	.118
Hyperlipidemia, %	65.9	64.9	66.3	61.9	72.1	.107
Diabetes, %	24.9	21.0	23.0	28.8	32.2	.003
History of CVD, %	19.4	14.4	17.0	25.3	27.9	<.001
eGFR, mL/min/1.73 m^2	71.4±17.5	77.8±15.5	72.9±14.7[a]	67.5±16.3[a,d]	58.0±18.1[a,d,f]	<.001
Atrial fibrillation, %	5.1	4.0	3.7	6.6	7.7	.069
Sleep apnea syndrome, %	4.4	4.7	3.0	5.8	3.9	.416
Use of antihypertensive medication, %	82.7	77.6	84.4	85.2	90.6	<.001
NT-proBNP, pg/mL	57.1 (28.6–112.3)	39.2 (19.7–68.3)	56.5[a] (29.3–106.8)	72.7[a,d] (38.6–127.6)	143.9[a,d,f] (64.9–297.0)	<.001
BP parameters, mm Hg						
Office SBP	140±16	140±16	141±16	140±17	142±19	.418
Office DBP	80±11	83±10	80±10[c]	79±11[a]	76±12[a,d]	<.001
MEave in SBP	135±14	133±13	136±14[c]	136±14[b]	141±17[a,d,g]	<.001
MEave in DBP	76±9.6	77±9.1	76±9.4	75±9.4[b]	74±11[a]	<.001
Echocardiographic profiles						
LVIDd, mm	45.8±5.3	45.7±4.5	46.0±5.0	45.9±5.4	45.7±5.4	.779
LVIDd/BSA, mm/m^2	28.6±3.5	28.4±3.1	28.9±3.8	28.4±3.7	29.0±3.9	.086
LVIDd/BSA after adjusted, mm/m^2	–	28.6 (28.3–28.8)	28.9 (28.5–29.2)	28.5 (28.1–28.8)	28.6 (28.2–29.1)	.446
LVM, g	158±45	150±40	159±42[c]	163±45[a]	173±53[a,e]	<.001
LVM index, g/m^2	98±25	92±22	99±24[a]	100±24[a]	108±24[a,d,f]	<.001
LVM index after adjusted, g/m^2	–	95 (93–97)	99 (96–102)	98 (95–101)	103[a] (100–106)	.001
Relative wall thickness	0.43±0.09	0.41±0.08	0.43±0.09[c]	0.44±0.09[a]	0.46±0.09[a,d]	<.001
Relative wall thickness after adjusted	–	0.42 (0.41–0.43)	0.43 (0.42–0.44)	0.43 (0.42–0.44)	0.47[b] (0.43–0.46)	.016
LVEF, %	72±7.5	73±7.5	72±7.4	72±7.3	72±7.9	.218
LV geometric category						
Normal	35	44	34	29	19	<.001
Concentric remodeling	31	29	30	33	33	
Concentric hypertrophy	23	16	25	23	36	
Eccentric hypertrophy	12	11	12	15	12	

Abbreviations: BP, blood pressure; BSA, body surface area; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; Hs-cTnT, high-sensitivity cardiac troponin T; LV, left ventricular; LVIDd, left ventricular internal diameter in diastole; LVEF, left ventricular ejection fraction; LVM, left ventricular index; MEave, the average of morning and evening value at home; NT-proBNP, N-terminal pro–brain-type natriuretic peptide; SBP, systolic blood pressure. Data are shown as mean±standard deviation, median (25%–75%), or percentage. *P* values were calculated by analysis of variance and Tukey's honestly significant differences or χ^2 test. Values are expressed as mean (95% confidence interval) and *P* values were obtained using analysis of covariance, and the Bonferroni test was used for multiple pairwise comparisons or percentages: categories sum up to 100% vertically. [a]$P \leq 0.001$, [b]$P < 0.01$, and [c]$P < 0.05$ vs the lowest category. [d]$P \leq 0.001$, and [e]$P < 0.01$ vs the second category. [d]$P \leq 0.001$, and [f]$P \leq 0.001$, and [g]$P < 0.01$ vs the third category.

coronary flow reserve in hypertensive patients with normal coronary arteries. Therefore, impairment of coronary microcirculation might predispose patients to a higher incidence and severity of myocardial ischemia, which, in turn, leads to a higher Hs-cTnT level.[17] Another study reported that the efficiency of oxygen utilization in the myocardium as measured by echocardiography and position emission tomography was lower in patients with concentric hypertrophy than in patients with normal LV geometry, while this association was not found in eccentric hypertrophy.[18] Thus, there is a significant difference in myocardial ischemia between concentric hypertrophy caused by pressure overload hypertrophy and eccentric hypertrophy caused by volume overload hypertrophy. Pressure overload caused by hypertension of the left ventricle results in an increment in LV mass with a high RWT, in which the increase in RWT often manifests before there is a detectable

TABLE II. Characteristics of Patients Divided by Categories of NT-proBNP

General Characteristics	All Patients (N=1336)	NT-proBNP Category, pg/mL ≤23.16 (n=535)	43.32–71.01 (n=267)	71.02–141.00 (n=267)	≥141.01 (n=267)	*P* Value
Age, y	65±11	60±11	66±10[a]	69±9.7[a,b]	72±10[a,b,c]	<.001
Men, %	49.9	53.8	41.6	38.6	45.7	<.001
Body mass index, kg/m^2	24.5±3.6	25.1±3.6	24.3±3.3[d]	24.1±3.5[e]	23.8±3.8[a]	<.001
Body surface area, m^2	1.61±0.19	1.67±0.19	1.60±0.16[a]	1.56±0.18[a]	1.56±0.18[a]	<.001
Current smokers, %	11.8	15.7	6.7	7.5	8.2	<.001
Habitual drinkers, %	23.3	27.7	25.5	14.6	21	<.001
Hyperlipidemia, %	65.9	68.4	62.2	65.2	65.2	.351
Diabetes, %	24.9	25.2	22.8	25.8	25.1	.858
History of CVD, %	19.4	15.0	17.6	20.2	29.2	<.001
eGFR, mL/min/1.73 m^2	71.4±17.5	77.2±16.1	72.3±15.8[a]	68.2±16.3[a,f]	62.0±18.7[a,b,g]	<.001
Atrial fibrillation, %	5.1	1.5	3.7	2.2	16.5	<.001
Sleep apnea syndrome, %	4.4	6.5	2.2	3.4	3.4	.018
Use of antihypertensive medication, %	82.7	81.3	81.3	83.5	86.1	.328
Hs-cTnT, pg/mL	7.0 (4.0–8.0)	5.0 (4.0–8.0)	7.0 (4.0–10.0)	6.5 (5.0–9.3)	10.0 (6.0–17.0[a,b,g]	<.001
BP parameters						
Office SBP, mm Hg	140±16	139±15	140±15	143±18[e]	141±20	.006
Office DBP, mm Hg	80±11	83±10	81±10[d]	79±11[a]	76±12[a,b,c]	<.001
MEave in SBP, mm Hg	135±14	133±12	134±14	138±14[a,h]	139±18[a,b]	<.001
MEave in DBP, mm Hg	76±9.6	78±8.5	76±9.2[d]	75±9.9[a]	73±11[a,f]	<.001
Echocardiographic profiles						
LVIDd, mm	45.8±5.3	45.8±4.8	45.7±5.0	45.7±4.7	46.1±5.5	.665
LVIDd/BSA, mm/m^2	28.6±3.5	27.6±3.2	28.7±3.3[a]	29.5±3.6[a]	29.8±3.8[a,h]	<.001
LVIDd/BSA after adjusted, mm/m^2	–	28.2 (27.9–28.4)	28.6 (28.2–28.9)	28.9 (28.6–29.3)	29.3 (28.8–30.0)[a]	<.001
LVM, g	158±45	155±41	153±41	156±40	172±55[a,b,g]	<.001
LVM index, g/m^2	98±25	93±21	95±23	99±22[a]	110±30[a,b,g]	<.001
LVM index after adjusted, g/m^2	–	94 (92–96)	96 (93–99	98 (96–101)	107 (104–110[a,b,g]	<.001
Relative wall thickness	0.43±0.09	0.42±0.08	0.42±0.09	0.43±0.09	0.45±0.10[a,b]	<.001
Relative wall thickness after adjusted	–	0.42 (0.42–0.43)	0.42 (0.41–0.43)	0.43 (0.42–0.44)	0.44 (0.43–0.45)	.130
LVEF, %	72±7.5	73±7.1	72±7.9	72±7.5	72±7.9	.126
LV geometric category						
Normal	35	41	36	32	23	
Concentric remodeling	31	35	32	25	26	
Concentric hypertrophy	23	16	17	29	37	
Eccentric hypertrophy	12	8	15	14	15	

Abbreviations: BP, blood pressure; BSA, body surface area; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; Hs-cTnT, high-sensitivity cardiac troponin T; LV, left ventricular; LVEF, left ventricular ejection fraction; LVIDd, left ventricular internal diameter in diastole; LVM, left ventricular mass index; MEave, the average of morning and evening value at home; NT-proBNP, N-terminal pro–brain-type natriuretic peptide; SBP, systolic blood pressure. Data are expressed as mean±standard deviation, median [25%–75%], or percentage. *P* values were calculated by analysis of variance and Tukey's honestly significant differences or χ^2 test, obtained using patients with detectable Hs-cTnT (n=760). Mean (95% confidence interval) and *P* values were obtained using analysis of covariance, and the Bonferroni test was used for multiple pairwise comparisons. Values are expressed as percentages: categories sum up to 100% vertically. [a]*P*≤.001, [d]*P*<.05, and [e]*P*≤.01 vs the lowest category; [b]*P*≤.001, [f]*P*<.05, and [h]*P*≤.01 vs second category; and [c]*P*<.05 vs third category.

increase in LV mass. It is also possible that the development of concentric hypertrophy may indicate an early stage of transition to overt systolic dysfunction as seen in animal models of pressure-overload hypertrophy.[19]

In this study, NT-proBNP was significantly associated with LVIDd/BSA, but not with RWT. It has been revealed that NT-proBNP plays an important role in the regulation of body fluid and BP in response to volume expansion. In clinical conditions, it has been reported that plasma NT-proBNP levels are considerably elevated in heart failure and that plasma NT-proBNP levels are inversely correlated with LVEF and positively correlated with LV end-systolic and end-diastolic volumes in patients with heart failure.[20] Our study confirms the findings from previous studies.

TABLE III. Association Between Hs-cTnT or NTproBNP and Left Ventricular Structure

	Hs-cTnT Category, pg/mL				
	<3.0 (n=576)	3.0–5.0 (n=270)	5.1–9.0 (n=257)	≥9.1 (n=233)	*P* Value
Prevalence of LVIDd/BSA, mm/m^2 (>33 in women and 32 in men)	9.5	13.7	12.1	17.2	.021
Odds of LVIDd/BSA, mm/m^2 (>33 in women and >32 in men)	1.00	0.97 (0.57–1.64)	1.06 (0.60–1.86)	1.16 (0.67–1.99)	
Prevalence of RWT >0.42	44.8	54.8	56	68.7	<.001
Odds of RWT >0.42	1.00	1.33 (0.93–1.85)	1.31 (0.93–1.85)	1.66 (1.17–2.36)[a]	
Prevalence of LVH	27.1	36.3	37.7	48.5	<.001
Odds of LVH	1.00	1.44(1.00–2.07)[b]	1.47 (1.01–2.15)[b]	1.69 (1.16–2.45)[a]	
	NT-proBNP Category, pg/mL				
	≤23.16 (n=535)	43.32–71.01 (n=267)	71.02–141.00 (n=267)	≥141.01 (n=267)	*P* Value
Prevalence of LVIDd/BSA, mm/m^2 (>33 in women and 32 in men)	5.0	12.4	17.8	21	<.001
Odds of LVIDd/BSA, mm/m^2 (>33 in women and >32 in men)	1.00	1.71 (0.98–2.98)	2.03 (1.17–3.52)[b]	2.11 (1.17–3.79)[b]	
Prevalence of RWT >0.42	50.7	48.3	53.9	62.2	.005
Odds of RWT >0.42	1.00	0.96 (0.70–1.31)	0.97 (0.70–1.35)	1.40 (0.96–2.03)	
Prevalence of LVH	23.6	31.8	43.1	51.7	<.001
Odds of LVH	1.00	1.32 (0.93–1.87)	1.78 (1.24–2.55)[a]	2.34 (1.57–3.48)[c]	

Abbreviations: BSA, body surface area; Hs-cTnT, high-sensitivity cardiac troponin T; LVH, left ventricular hypertrophy; LVIDd, left ventricular internal diameter in diastole; NT-proBNP, N-terminal pro–brain-type natriuretic peptide; RWT, relative wall thickness. Prevalence is expressed as percentage. [a]*P*<.01, [b]*P*<.05, and [c]*P*<.001 vs the lowest category. Adjusted by age, sex, body mass index, smoking, alcohol, diabetes, dyslipidemia, history of cardiovascular disease, atrial fibrillation, sleep apnea syndrome, use of antihypertensive drugs, estimated glomerular filtration rate, clinic systolic and diastolic blood pressure, and home systolic and diastolic blood pressure.

Both Hs-cTnT and NT-proBNP were significantly associated with LVMI. This finding should be interpreted in the context of prior studies investigating Hs-cTnT, which suggested that the increase in Hs-cTnT is paralleled and mediated to a greater extent by indices of heart failure, such as lower LVEF and increased NT-proBNP.[6,8] Prior studies have described the association between Hs-cTnT or NT-proBNP and LV structure. In a general population, Hs-cTnT was independently associated with cardiac structure, although further adjustment for levels of NT-proBNP resulted in more substantial attenuation of hazard ratios.[5] In heart failure patients, Hs-cTnT has been reported to be closely associated with NT-proBNP.[20] Taken together, NT-proBNP and Hs-cTnT provide partly overlapping information concerning cardiac structural and functional abnormalities.

Hs-cTnT was associated with wall thickness affected by pressure overload, but NT-proBNP was not. Although BP level was an important component of pressure overload, both Hs-cTnT and NT-proBNP were associated with SBP at home measurement. Recently, we have also reported that these biomarkers were associated with morning SBP more than evening SBP at home measurement. These conflicting findings may partly be explained by the fact that pressure overload to LV might be regulated by not only absolute BP level but also BP variability. BP variability assessed by ambulatory BP monitoring and day-to-day variability assessed by home BP measurement could have given additional information, showing the relationship between these indices of BP variability and LVH in previous studies.[21,22]

STUDY LIMITATIONS AND STRENGTHS

There are some limitations of this study. First, the possibility of selection bias needs to be considered when generalizing the present findings, because of the patients who had echocardiography performed, only 33.2% were analyzed. Second, this report is a cross-sectional analysis of the cardiac structural correlates of circulating Hs-cTnT and NT-proBNP levels. As such, this analysis does not establish a causal or mechanistic link among elevated Hs-cTnT level, NT-proBNP level, and LV structural abnormalities. Recently, a study has reported the early detection of LV hypertrophy using ^{18}F-FDG positron emission tomography imaging in a mouse model.[23] Noninvasive new technology might help physicians offer new methods of discrimination of LVH. LVH itself may be related to the increased Hs-cTnT and NT-proBNP levels in patients with LVH. Neeland and colleagues[24] recently reported that there was a different distribution of Hs-cTnT or NT-proBNP among patients with LVH, and that the patients with elevated biomarkers had higher risk of cardiovascular death than those without among patients with LVH. Third, Hs-cTnT and NT-proBNP were correlated with each other in the patients with detectable Hs-cTnT (data not shown), which confirms the notion that each biomarker may reflect partially overlapping. However,

the results of this study support that each biomarker might be considered a useful marker for discrimination of LVH.

CONCLUSIONS

Our study benefited from a robust number of ambulatory patients undergoing Hs-cTnT and NT-proBNP measurements and echocardiography, and supported the conclusion that Hs-cTnT could be significantly associated with pressure overload LV hypertrophy shown by a concentric LV change with increased RWT. On the other hand, NT-proBNP was significantly associated with volume overload LV hypertrophy shown by an increment of LVMI with increased LV diameter.

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