Clinical Meaning of the Ratio of Brachial Pre-Ejection Period to Brachial Ejection Time in Patients with Left Ventricular Systolic Dysfunction

Comparison with B-type Natriuretic Peptide

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Summary

An increase in the ratio of the brachial pre-ejection period to brachial ejection time [pre-ejection period (PEP)/ET] is correlated with a decrease of left ventricular ejection fraction (LVEF). The current study was designed to test the hypothesis that the change value (Δ) of PEP/ET is a useful indicator of Δ LVEF in patients with left ventricular systolic dysfunction.

We consecutively enrolled 104 patients with left ventricular systolic dysfunction (LVEF < 45%). PEP/ET, B-type natriuretic peptide (BNP), and LVEF were evaluated at baseline and at 6-month follow-up. Compared with the baseline measurements, the 6-month values of Δ LVEF, Δ BNP, and Δ PEP/ET were $9.8\% \pm 9.0\%$ (from $36.3\% \pm 9.2\%$ to $46.3\% \pm 12.5\%$, $P < 0.001$), -168.5 ± 255.4 (from 271.4 ± 282.5 to 104.1 ± 129.6 , $P < 0.001$), and -0.060 ± 0.069 (from 0.413 ± 0.097 to 0.358 ± 0.079 , $P < 0.001$), respectively. There were significant correlations between LVEF and PEP/ET and between LVEF and BNP in both the initial ($r = -0.316$, $P = 0.001$ and $r = -0.598$, $P < 0.001$, respectively) and 6-month follow-up ($r = -0.307$, $P = 0.003$ and $r = -0.701$, $P < 0.001$, respectively). The Steiger's Z test showed that BNP had a significantly stronger correlation with LVEF compared with the correlations between LVEF and PEP/ET in both the initial and 6-month studies ($Z = 2.471$, $P = 0.013$ and $Z = 3.575$, $P < 0.001$, respectively). There were also significant correlations between Δ LVEF and Δ PEP/ET ($r = -0.515$, $P < 0.001$) and between Δ LVEF and Δ BNP ($r = -0.581$, $P < 0.001$); however, there was no difference between the correlations for Δ LVEF and Δ PEP/ET versus Δ LVEF and Δ BNP (Steiger's $Z = 0.600$, $P = 0.545$).

In patients with left ventricular systolic dysfunction not only Δ BNP but also Δ PEP/ET could be a simple indicator of predicting change of LVEF.

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Key words: Heart failure, Left ventricular ejection fraction, Ankle-brachial index device

Studies have reported that decreased left ventricular systolic function is significantly correlated with an increased risk of future cardiovascular events.^{1,2)} Echocardiography is considered the gold standard for evaluation of left ventricular systolic dysfunction; however, limited availability and high cost prohibit it from being used in a general screening and serial follow up.^{3,4)} Several studies have analyzed the assessment of B-type natriuretic peptide (BNP) levels for ruling out heart failure, and have raised expectations about left ventricular systolic dysfunction in clinical follow-up.^{5,6)}

An ankle-brachial index (ABI)-form device has been developed to measure blood pressure and pulse waves using an automated oscillometric method. This device calcu-

lates the brachial pre-ejection period (PEP) and brachial ejection time (ET) by analyzing the signals from the electrocardiogram, phonocardiogram and brachial pressure volume waveform.⁷⁾ A previous cross-sectional study reported that PEP over ET (PEP/ET) was significantly correlated with left ventricular ejection fraction (LVEF), and this could be a useful parameter in the prediction of left ventricular systolic dysfunction in a single moment.⁸⁾ However, there has been no study evaluating the relationship between the change value of PEP/ET (Δ PEP/ET) and changes of LVEF (Δ LVEF) in patients with heart failure. The aim of the present study was to investigate whether Δ PEP/ET is a useful predictor of Δ LVEF in patients with newly-diagnosed heart failure.

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Methods

Patients: All patients in this study were newly diagnosed with heart failure and they had left ventricular systolic dysfunction, defined as impaired LVEF of $\leq 45\%$, regardless of ischemic and non-ischemic origin, and none of the patients had previously been treated for heart failure. The exclusion criteria included age of > 65 years, atrial fibrillation, significant valvular heart disease (greater than a moderate degree), complete left bundle branch block, ABI of < 0.9 , inadequate visualization on echocardiography, and inability to follow up. In cases of acute coronary syndrome and acute heart failure, the patients were evaluated in stable condition one or two days before discharge. To evaluate the relationship between the changes in PEP/ET, BNP, and LVEF, all of these measurements were evaluated at baseline and at 6-month follow up. This study was approved by the institutional review board of the Hallym University and all patients gave written informed consent to participate in this study.

Assessment of brachial PEP and ET: The PEP and ET were measured in a quiet, temperature-controlled room with an ABI-form device (Colin VP2000, Komaki, Japan), which automatically and simultaneously measures blood pressure in both arms and ankles using oscillometric method.^{7,8)} The ET was automatically measured from the foot to the dirotic notch of the pulse volume waveform. Total electromechanical systolic interval (QS2) was measured from the onset of the QRS complex on the electrocardiogram to the first high-frequency vibration of the aortic component of the second heart sound on the phonocardiogram. The PEP was also automatically calculated by subtracting the ET from the QS2. The values of ABI and brachial-ankle pulse wave velocity (baPWV) were also measured; the measurement method is reported and validated in previous studies.⁷⁻⁹⁾

Echocardiographic assessment: Comprehensive echocardiographic images were obtained using a commercially available Vivid 7 machine (GE Medical Systems, Milwaukee, WI, USA) echocardiographic system. Echocardiography was performed according to the guidelines of the American Society of Echocardiography recommendations.¹⁰⁾ Mitral flow recorded with pulsed Doppler was placed between the tips of the mitral valves. The ratio between early (E) and late (A) mitral inflow was calculated (E/A), and the E-wave deceleration time was measured. Tissue spectral Doppler recordings were performed in the septal annular plane. The early diastolic medial mitral annular velocity (E') was measured and the E/E' ratio was calculated for the septal wall. Measurements were made online, recorded digitally, and interpreted off-line by echocardiography physicians blinded to the clinical data. The LVEF was quantified by the modified Simpson's rule using two-dimensional echocardiography images from the apical four- and two-chamber views.

Measurements of plasma BNP: Plasma BNP levels were measured directly with validated and commercially available immunoassay kits (Architect BNP, Abbott Laboratories, IL, USA).

Statistical analysis: Statistical analysis was performed using SPSS 22.0 (SPSS, Inc., Chicago, IL, USA). Data are

expressed as percentages or as mean $\pm$ standard deviation. Comparisons between index and follow-up measures were tested with the paired *t*-test or Wilcoxon's signed rank test, as appropriate. Correlations between variables were evaluated with Spearman's rank correlation. The differences between correlations involving a common variable were tested using Steiger's *Z* test to account for the dependency of the correlations. To determine whether there is an additional advantage to using the combined parameter Δ PEP/ET plus Δ BNP (Δ PEP/ET&BNP) over Δ BNP in predicting Δ LVEF, Δ PEP/ET&BNP was formulated as Δ BNP added to Δ PEP/ET*1000. The PEP/ET*1000 was used to tune in the number of digits between BNP and PEP/ET. The multivariable linear regression analysis was evaluated with the associated variables to assess independent correlates of the Δ LVEF. All statistical tests were two-sided, and a *P*-value of < 0.05 was considered statistically significant.

Results

We consecutively screened 120 patients with LVEF $\leq 45\%$ between January 2014 and May 2015. Sixteen of these patients were excluded due to atrial fibrillation ($n = 3$), ABI < 0.9 ($n = 2$), significant valvular heart disease ($n = 4$), complete left bundle branch block ($n = 2$), inadequate echocardiographic imaging ($n = 1$), or refusal to participate in the study ($n = 4$). A total of 104 patients were included in the final analysis. During the study period nine patients (8.7%) were lost to follow-up, meaning a total of 95 patients finished the study. In this study, 82 of 104 patients had ischemic heart failure. Among them, 73 patients had acute myocardial infarction and all of them underwent emergency percutaneous coronary intervention (PCI). Nine patients had chronic ischemic heart failure due to multi-vessel disease. Five patients had undergone PCI, two had undergone coronary artery bypass graft (CABG) operation, and two were treated with only medical therapy because they refused PCI or CABG. The baseline clinical characteristics are shown in Table I.

The results of the initial and 6-month follow-up findings of echocardiographic, BNP, and ABI data are described in Table II. The Δ PEP was -0.9 ± 14.5 and Δ ET was 40.0 ± 33.1 . The values of Δ LVEF, Δ BNP, and Δ PEP/ET were $9.8\% \pm 9.0\%$, -168.5 ± 255.4 , and -0.060 ± 0.069 , respectively. Table III shows the correlations between LVEF, PEP/ET and BNP. In both the initial and 6-month follow-up studies, there were significant correlations between LVEF and PEP/ET and between LVEF and BNP. In both the initial and 6-month evaluations, however, Steiger's *Z* test showed that BNP had a significantly stronger correlation with LVEF compared with the correlations between LVEF and PEP/ET. There was a significant correlation between Δ LVEF and Δ PEP/ET ($r = -0.515$, $P < 0.001$; Figure 1A), which was stronger than the correlation between Δ LVEF and Δ PEP ($r = -0.320$, $P = 0.002$) and between Δ LVEF and Δ ET ($r = 0.310$, $P = 0.002$). There was also a significant correlation between Δ LVEF and Δ BNP ($r = -0.581$, $P < 0.001$) (Figure 1B). However, there was no difference in the correlations between Δ LVEF and Δ PEP/ET versus Δ LVEF and Δ BNP (r

Table I. Baseline Clinical Characteristics

Variable	Value (<i>n</i> = 104)	Initial (<i>n</i> = 104)	6-month (<i>n</i> = 95)	<i>P</i>
Age, years	58 ± 9			
Male, <i>n</i> (%)	82 (78.8)			
History of smoking, <i>n</i> (%)	56 (53.8)			
Hypertension, <i>n</i> (%)	48 (46.2)			
Dyslipidemia, <i>n</i> (%)	53 (51.0)			
Diabetes, <i>n</i> (%)	34 (32.7)			
Family history of CHD, <i>n</i> (%)	10 (9.6)			
Body mass index, kg/m ²	24.4 ± 3.1			
Systolic blood pressure, mmHg	122 ± 22			
Diastolic blood pressure, mmHg	74 ± 11			
Heart rate, beats/minute	78 ± 10			
Ischemic heart failure, <i>n</i> (%)	82 (78.8)			
Acute myocardial infarction	73 (70.2)			
Chronic multi-vessel disease	9 (8.6)			
Non-ischemic heart failure, <i>n</i> (%)	22 (21.2)			
Laboratory data				
Hemoglobin (mg/dL)	14.4 ± 1.5			
Fasting blood sugar (mg/dL)	118 ± 41			
Creatinine (mg/dL)	0.8 ± 0.3			
Total cholesterol (mg/dL)	200 ± 38			
Triglyceride (mg/dL)	141 ± 70			
HDL-C (mg/dL)	45 ± 11			
LDL-C (mg/dL)	119 ± 37			
Medication				
Aspirin, <i>n</i> (%)		85 (81.7)	77 (81.0)	1.000
Statin, <i>n</i> (%)		88 (84.6)	78 (82.1)	0.500
ACE-inhibitor, <i>n</i> (%)		69 (66.3)	62 (65.3)	1.000
Beta-blocker, <i>n</i> (%)		95 (91.3)	84 (88.4)	0.453
Nitrate, <i>n</i> (%)		49 (47.1)	40 (42.1)	0.289
Loop diuretics, <i>n</i> (%)		47 (45.2)	39 (41.0)	0.219
Aldosterone, <i>n</i> (%)		42 (40.4)	38 (40.0)	0.625
Digoxin, <i>n</i> (%)		10 (9.6)	8 (8.4)	1.000

ACE indicates angiotensin converting enzyme; CHD, coronary heart disease; HDL-C, high density lipoprotein cholesterol; and LDL-C, low density lipoprotein cholesterol.

= -0.515, $P < 0.001$ versus $r = -0.581$, $P < 0.001$; Steiger's $Z = 0.600$, $P = 0.545$). There was a significant correlation between Δ LVEF and Δ PEP/ET&BNP ($r = -0.630$, $P < 0.001$; Figure 2). However, the combined parameters of Δ PEP/ET&BNP did not show a stronger correlation with Δ LVEF compared with Δ BNP alone ($r = -0.630$, $P < 0.001$ versus $r = -0.581$, $P < 0.001$; Steiger's $Z = 0.496$, $P = 0.620$). In patients with non-ischemic heart failure ($n = 22$), Δ PEP/ET&BNP was more strongly correlated with Δ LVEF than it was in the 82 patients with ischemic heart failure ($r = -0.765$ versus $r = -0.524$, all $P < 0.001$).

In this study, compared with the initial study, there were significant changes in heart rate (HR), systolic blood pressure, and diastolic blood pressure, and the Δ HR, Δ SBP, and Δ DBP values were -13.2 ± 11.1 /minute, 3.8 ± 21.1 mmHg, and 2.8 ± 12.3 mmHg, respectively (Table II). In addition, PEP and ET may be affected by changes in heart rate and blood pressure.^{8,11} Therefore, the multi-variable linear regression analysis was evaluated to assess independent correlates of the Δ LVEF, including Δ HR, Δ SBP, Δ DBP, Δ BNP, and Δ PEP/ET. The analysis showed that the Δ BNP and Δ PEP/ET were independently correlated with Δ LVEF (Table IV).

Discussion

The present study demonstrated that Δ PEP/ET could be a simple indicator of predicting Δ LVEF in patients with decreased LVEF, and this is similar to the relationship between Δ BNP and Δ LVEF. To the best of our knowledge, this is the first report to demonstrate a significant correlation between Δ PEP/ET from the ABI-form device and Δ LVEF.

Decreased left ventricular systolic function was reported to predict poor CV outcomes.^{1,2} Therefore, assessment of changes in left ventricular function treated after medical or revascularization procedures is an important clinical issue in patients with left ventricular systolic dysfunction.¹² In this study, most echocardiographic parameters, including LVEF, as well as HR and BNP, were improved because most patients who had ischemic heart failure underwent reperfusion therapy and all patients were treated with optimal medical therapy.

BaPWV-derived PEP/ET automatically obtained from an ABI-form device may be helpful in estimating left ventricular systolic function. The prolongation of PEP could be caused by a diminished rate of left ventricular pressure rise during isovolumic contraction.¹³ Therefore, when left ventricular systolic function decreases, the PEP value will

Table II. Results of Initial and 6-month Follow-up Echocardiography, BNP, and ABI

	Initial (<i>n</i> = 104)	6-month (<i>n</i> = 95)	<i>P</i>
LVEF (%)	36.3 ± 9.2	46.3 ± 12.5	< 0.001
LVMI (g/m ²)	100.0 ± 30.3	97.1 ± 23.3	0.112
LVEDd (mm)	51.1 ± 7.0	49.5 ± 7.0	0.096
LVESd (mm)	39.0 ± 8.9	37.7 ± 9.1	0.148
E velocity (cm/s)	73.3 ± 15.9	66.4 ± 16.4	0.006
A velocity (cm/s)	67.8 ± 17.3	70.1 ± 16.2	0.248
DT (ms)	185.3 ± 41.1	220.6 ± 44.8	< 0.001
E/A	1.3 ± 1.1	1.0 ± 0.4	0.005
E' velocity (cm/s)	5.9 ± 1.7	6.3 ± 1.7	0.006
E/E'	13.4 ± 4.5	11.4 ± 4.4	< 0.001
BNP, pg/mL	271.4 ± 282.5	104.1 ± 129.6	< 0.001
Systolic blood pressure, mmHg	122 ± 22	125 ± 16	0.002
Diastolic blood pressure, mmHg	74 ± 11	77 ± 10	0.030
Heart rate, beats/minute	77 ± 9	64 ± 10	< 0.001
Left ABI	1.14 ± 0.09	1.14 ± 0.08	0.535
baPWV	1558 ± 329	1504 ± 333	0.015
PEP	103.0 ± 18.5	102.9 ± 15.3	0.540
ET	254.1 ± 31.1	292.5 ± 29.3	< 0.001
PEP/ET	0.413 ± 0.097	0.358 ± 0.079	< 0.001

ABI indicates ankle brachial index; A velocity, late diastolic mitral inflow velocity; baPWV, brachial-ankle pulse wave velocity; BNP, b-type natriuretic peptide; DT, deceleration time; E/E', ratio of early diastolic mitral inflow velocity (E) and early diastolic medial mitral annular velocity (E'); ET, ejection time; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end-diastolic diameter; LVESd, left ventricular end-systolic diameter; LVMI, left ventricular mass index; and PEP, pre-ejection period.

Table III. Correlation between LVEF and Variables of PEP/ET and BNP

	<i>r</i>	<i>P</i>	Steiger's <i>Z</i>
Initial			
LVEF and PEP/ET	-0.316	0.001	<i>Z</i> = 2.471
LVEF and BNP	-0.598	< 0.001	<i>P</i> = 0.013
Six-month follow-up			
LVEF and PEP/ET	-0.307	0.003	<i>Z</i> = 3.575
LVEF and BNP	-0.701	< 0.001	<i>P</i> < 0.001

All *r* values are from Spearman's correlation. BNP indicates b-type natriuretic peptide; ET, ejection time; LVEF, left ventricular ejection fraction; and PEP, pre-ejection period.

increase.¹⁴⁾ The duration of ET reflects both the velocity and extent of fiber shortening of the left ventricle. In left ventricular decompensation, the extent of fiber shortening is decreased and the ET will be shortened.¹⁵⁾ Because heart function impairment usually prolongs PEP and shortens ET, the PEP/ET value may reflect the diagnostic value of the identification of left ventricular systolic dysfunction. Until now, studies have reported that the ratio of PEP/ET is well correlated with left ventricular systolic dysfunction in patients with and without various forms of cardiovascular disease.¹⁴⁻¹⁶⁾ This also implies that patients with increased PEP/ET might be in a high risk group for increased CV events in the presence of chronic kidney disease.¹⁷⁾ Both PEP and ET correlated significantly with LVEF, which was consistent with the findings in our study.¹⁵⁾ However, the correlation relating ΔPEP and ΔET with changes in LVEF was less than that for ΔPEP/ET and changes in LVEF in this study. Hence, compared with ΔPEP and ΔET, ΔPEP/ET might be a useful predictor of

ΔLVEF in patients with left ventricular systolic dysfunction. Similarly, the initial and 6-month values of PEP/ET were weakly correlated with LVEF compared with ΔPEP/ET and ΔLVEF. In other words, serial changes in PEP/ET are more valuable for predicting left ventricular systolic function than one point values of PEP/ET. This is similar to the relationship between BNP and C-reactive protein.^{18,19)} More clinical information can generally be obtained when serial changes of measured data are available, compared with one point values.

The value of assessment of BNP levels for the diagnosis of heart failure or left ventricular dysfunction has been widely accepted, and BNP has been recommend for ruling out heart failure.^{6,20)} However, not only single moment BNP values but also changes in BNP over time have clinical significance.^{18,21)} Therefore, several studies have evaluated the correlations between ΔBNP, ΔLVEF, and cardiovascular outcomes, and a significant correlation between ΔBNP and recovery of LV systolic function after coronary bypass surgery has been reported.¹²⁾ In patients with mitral regurgitation, there was a significant negative association between changes in LVEF and ΔBNP after mitral annuloplasty.²²⁾ In the J-CHF study, ΔBNP was a predictor of long-term cardiovascular outcomes after carvedilol treatment.²³⁾ The Valsartan Heart Failure Therapy Trial showed that the relative change in BNP strongly predicted outcomes and superseded the prognostic value of a single BNP measurement.²⁴⁾ In the present study, both the initial and 6-month values of BNP had a stronger correlation with LVEF compared with those between ET/PEP and LVEF. However, the value of ΔPEP/ET had a strong correlation with ΔLVEF, and there was no difference between ΔPEP/ET with ΔLVEF versus ΔBNP with ΔLVEF

Figure 1. Interrelationships between change in left ventricular ejection fraction and change in PEP/ET (A), and between change in left ventricular ejection fraction and change in BNP (B). All values are from Spearman's correlation. ΔBNP , change in B-type natriuretic peptide; $\Delta PEP/ET$, change in pre-ejection period/ change in ejection time; $\Delta LVEF$, change in left ventricular ejection fraction

($r = -0.515$ versus $r = -0.581$; Steiger's $Z = 0.600, P = 0.545$). In addition, the combined parameter of $\Delta PEP/ET \& BNP$ was not more strongly correlated with $\Delta LVEF$ versus ΔBNP alone ($r = -0.630$ versus $r = -0.581$; Steiger's $Z = 0.496, P = 0.620$). This indicates that there was no additive value of $\Delta PEP/ET \& BNP$ over ΔBNP in predicting $\Delta LVEF$; however, considered differently, this also means that there was no difference between $\Delta PEP/ET$ and ΔBNP in predicting changes in left ventricular systolic function.

This study included 82 (79%) patients with ischemic and 22 (21%) patients with non-ischemic left ventricular dysfunction. In patients with non-ischemic heart failure, $\Delta PEP/ET \& BNP$ was more strongly correlated with $\Delta LVEF$ than in the patients with ischemic heart failure ($r = -0.765$ versus $r = -0.524$). The 6-month follow-up BNP measurement showed a strong correlation with LVEF

Figure 2. Correlation between change in LVEF and change in PEP/ET & BNP. The value is from Spearman's correlation. $\Delta PEP/ET \& BNP$, change in pre-ejection period/ change in ejection time*1000 plus change in B-type natriuretic peptide; $\Delta LVEF$, change in left ventricular ejection fraction

compared with that between initial BNP and LVEF ($r = -0.701$ versus $r = -0.598$). This may be because, in patients with acute myocardial infarction, BNP is less effective in predicting left ventricular systolic function than in patients with non-ischemic heart failure. Generally, the measurement of $\Delta PEP/ET$ from ABI device is more simple and less expensive than get $\Delta LVEF$ from echocardiography. This leaves not only ΔBNP but also $\Delta PEP/ET$ as another simple method of predicting changes of left ventricular systolic function after treating patients with decreased LVEF.

Limitations: This study had several potential limitations. First, the subjects were enrolled from only one regional hospital and the number of patients was relatively small. Second, we excluded patients with atrial fibrillation and left bundle branch block because measurements of PEP and ET can be affected by beat-to-beat variation or delayed closure of aortic valve. Third, most of the patients (82%) had decreased LVEF due to ischemic heart failure. Fourth, it remains unclear whether the results could be confirmed in a larger patient sample over a longer period. Therefore, further studies with larger numbers of patients and long-term follow up are needed to generalize this observation.

Conclusion

Our study demonstrated that in patients with left ventricular systolic dysfunction, the serial measurement of $\Delta PEP/ET$ is a useful indicator of changes in LVEF and this is similar to the relationship between ΔBNP and $\Delta LVEF$.

Table IV. Results of the Multivariable Linear Regression to Assess the Independent Correlates of the Delta Left Ventricular Ejection Fraction

	Unstandardized coefficient β	95% CI for β	Standardized coefficient β	P	VIF
Δ HR	0.068	-0.057, 0.193	0.085	0.279	1.204
Δ SBP	-0.031	-0.125, 0.063	-0.073	0.512	2.455
Δ DBP	0.058	-0.110, 0.225	0.079	0.496	2.667
Δ BNP	-0.018	-0.023, -0.012	-0.506	< 0.001	1.248
Δ PEP/ET	-53.862	-74.678, -33.047	-0.416	< 0.001	1.307

BNP indicates b-type natriuretic peptide; CI, confidence interval; DBP, diastolic blood pressure; ET, ejection time; HR, heart rate; LVEF, left ventricular ejection fraction; PEP, pre-ejection period; SBP, systolic blood pressure; VIF, variance inflation factor; and Δ , delta value of Model F ratio = 22.048, $P < 0.001$.

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Disclosures

Conflicts of interest: The Authors declare that there is no conflict of interest.

References

- Cintron G, Johnson G, Francis G, Cobb F, Cohn JN. Prognostic significance of serial changes in left ventricular ejection fraction in patients with congestive heart failure. The V-HeFT VA Cooperative Studies Group. *Circulation* 1993; 87: VII7-23.
- Quinones MA, Greenberg BH, Kopelen HA, *et al.* Echocardiographic predictors of clinical outcome in patients with left ventricular dysfunction enrolled in the SOLVD registry and trials: significance of left ventricular hypertrophy. *Studies of Left Ventricular Dysfunction*. *J Am Coll Cardiol* 2000; 35: 1237-44.
- Nielsen OW, McDonagh TA, Robb SD, Dargie HJ. Retrospective analysis of the cost-effectiveness of using plasma brain natriuretic peptide in screening for left ventricular systolic dysfunction in the general population. *J Am Coll Cardiol* 2003; 41: 113-20.
- Sim V, Hampton D, Phillips C, *et al.* The use of brain natriuretic peptide as a screening test for left ventricular systolic dysfunction- cost-effectiveness in relation to open access echocardiography. *Fam Pract* 2003; 20: 570-4.
- Latour-Perez J, Coves-Orts FJ, Abad-Terrado C, Abaira V, Zamora J. Accuracy of B-type natriuretic peptide levels in the diagnosis of left ventricular dysfunction and heart failure: a systematic review. *Eur J Heart Fail* 2006; 8: 390-9.
- Doust JA, Glasziou PP, Pietrzak E, Dobson AJ. A systematic review of the diagnostic accuracy of natriuretic peptides for heart failure. *Arch Intern Med* 2004; 164: 1978-84.
- Yamashina A, Tomiyama H, Takeda K, *et al.* Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertens Res* 2002; 25: 359-64.
- Su HM, Lin TH, Lee CS, *et al.* Myocardial performance index derived from brachial-ankle pulse wave velocity: a novel and feasible parameter in evaluation of cardiac performance. *Am J Hypertens* 2009; 22: 871-6.
- Munakata M, Ito N, Nunokawa T, Yoshinaga K. Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. *Am J Hypertens* 2003; 16: 653-7.

- Lang RM, Bierig M, Devereux RB, *et al.* Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; 18: 1440-63.
- Cokkinos DV, Heimonas ET, Demopoulos JN, Harralambakis A, Tsatsalis G, Gardikas CD. Influence of heart rate increase on uncorrected pre-ejection period/left ventricular ejection time (PEP/LVET) ratio in normal individuals. *Br Heart J* 1976; 38: 683-8.
- Chello M, Mastroberro P, Perticone F, *et al.* Plasma levels of atrial and brain natriuretic peptides as indicators of recovery of left ventricular systolic function after coronary artery bypass. *Eur J Cardiothorac Surg* 2001; 20: 140-6.
- Lewis RP, Rittogers SE, Froester WF, Boudoulas H. A critical review of the systolic time intervals. *Circulation* 1977; 56: 146-58.
- Veyrat C, Larrazet F, Pellerin D. Renewed interest in preejectional isovolumic phase: new applications of tissue Doppler indexes: implications to ventricular dyssynchrony. *Am J Cardiol* 2005; 96: 1022-30.
- Garrard CL Jr, Weissler AM, Dodge HT. The relationship of alterations in systolic time intervals to ejection fraction in patients with cardiac disease. *Circulation* 1970; 42: 455-62.
- Pellerin D, Cohen L, Larrazet F, Pajany F, Witchitz S, Veyrat C. Preejectional left ventricular wall motion in normal subjects using Doppler tissue imaging and correlation with ejection fraction. *Am J Cardiol* 1997; 80: 601-7.
- Chen SC, Chang JM, Tsai JC, *et al.* A systolic parameter defined as the ratio of brachial pre-ejection period to brachial ejection time predicts cardiovascular events in patients with chronic kidney disease. *Circ J* 2010; 74: 2206-10.
- Januzzi JL, Troughton R. Are serial BNP measurements useful in heart failure management? Serial natriuretic peptide measurements are useful in heart failure management. *Circulation* 2013; 127: 500-7; discussion 8.
- Manian FA. A prospective study of daily measurement of C-reactive protein in serum of adults with neutropenia. *Clin Infect Dis* 1995; 21: 114-21.
- Remme WJ, Swedberg K. Comprehensive guidelines for the diagnosis and treatment of chronic heart failure. Task force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology. *Eur J Heart Fail* 2002; 4: 11-22.
- Nitta D, Kinugawa K, Imamura T, Kato NP, Komuro I. High dose beta-blocker therapy triggers additional reverse remodeling in patients with idiopathic non-ischemic cardiomyopathy. *Int Heart J* 2016; 57: 717-24.
- Kainuma S, Taniguchi K, Toda K, *et al.* B-type natriuretic peptide response and reverse left ventricular remodeling after surgical correction of functional mitral regurgitation in patients with advanced cardiomyopathy. *J Cardiol* 2015; 66: 279-85.

23. Okamoto H, Hori M, Matsuzaki M, *et al.* Minimal dose for effective clinical outcome and predictive factors for responsiveness to carvedilol: Japanese chronic heart failure (J-CHF) study. *Int J Cardiol* 2013; 164: 238-44.
24. Masson S, Latini R, Anand IS, *et al.* Prognostic value of changes in N-terminal pro-brain natriuretic peptide in Val-HeFT (Valsartan Heart Failure Trial). *J Am Coll Cardiol* 2008; 52: 997-1003.