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Original article

Usefulness of peripheral arterial signs in the evaluation of aortic regurgitation

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ABSTRACT

Background: Early diagnosis and optimal timing of surgical repair for chronic aortic regurgitation (AR) are topics of interest, because left ventricular compensation delays the clinical signs of the early stages of left ventricular dysfunction. Various physical signs have been described as indicators of chronic AR, but AR screening can be difficult depending on the proficiency of primary care providers. The recent use of the cardio-ankle vascular index (CAVI) measurement to assess peripheral atherosclerosis may detect AR objectively and simply because its arterial pulse wave configuration is closely related to the physical signs of AR.

Methods: CAVI measurements include pulse pressure (PP), the difference in blood pressures between upper and lower limbs (ABD), ankle-brachial index (ABI), ejection time (ET), and upstroke time (UT). We evaluated the differences in CAVI parameters between AR group and age-matched control group, the relationships between CAVI parameters and the echocardiographic semi-quantitative measurements of AR severity such as left ventricular dimensions (Dd, Ds) and vena contracta (VC), and between the changes in CAVI parameters before and after aortic valve replacement.

Results: ABD, PP, ET, ankle systolic pressure and ABI in the AR group were significantly higher than that in the control group. Brachial diastolic pressure and CAVI in the AR group were significantly lower than that in the control group. UT was lower than that in the control group ($p = 0.05$). PP did not correlate with the semi-quantitative AR severity, but ABD was correlated with Dd, Ds, and VC and was negatively correlated with UT. The exaggerated ABD, PP, ET, and ABI were moderated after surgery.

Conclusions: CAVI parameters could be useful in the screening and serial follow-up of AR patients.

Introduction

Aortic regurgitation (AR) is an abnormality of the aortic valve leaflets and/or of the aortic root, and can be caused by rheumatic fever, calcific degeneration, infectious endocarditis, a congenital bicuspid valve, prolapse from a ventricular septal defect, aortic root dilatation due to aging, Marfan syndrome, rheumatoid arthritis, or syphilis [1]. The number of patients with rheumatic fever has decreased because of improved hygiene and the universal use of antibiotics. On the other hand, aortic root dilatation due to hypertension has emerged as a main cause in the aging population.

The patients with AR do not complain of symptoms over a long period because left ventricular (LV) compensation delays the clinical signs of LV dysfunction [2]. Severity of AR, patient's symptoms, LV dimension, and systolic function are the determinants of the need for aortic valve replacement (AVR) in chronic AR. Serial echocardiograms have been recommended for follow-ups and to plan AVR at an appropriate time when there is no apparent

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LV dysfunction [2,3]. A previous study proved that a large LV dimension and decreased systolic function [i.e. LV systolic dimension (Ds) >55 mm and %SF (shortening fraction) <25%] indicates poor prognosis during peri- or post-surgery in patients with symptomatic chronic AR [4]. However, the screening of patients with AR can be difficult when it depends on the proficiency of primary caregivers. The auscultation of a high-pitched diastolic heart murmur is the first step for an AR diagnosis, but it may be overlooked in clinical situations. Therefore, a simple and reliable method for the screening of asymptomatic patients with AR is necessary.

Pulse wave velocity [5] and cardio-ankle vascular index (CAVI) [6] have been established in recent years as noninvasive evaluations of atherosclerosis, or a promising tool to predict major cardiac events after coronary intervention [7]. Both of them are obtained by the analysis of the arterial pulse waves of upper and lower limbs; they also provide various cardiovascular parameters, such as pulse pressure (PP), ankle-brachial difference of blood pressure (ABD), ankle-brachial index (ABI), ejection time (ET), and upstroke time (UT). These parameters are quantitative measures that can be useful for the diagnosis of AR.

The peripheral vascular signs of AR, such as high PP, and a large difference in the systolic blood pressure (SBP) between upper and lower limbs (Hill's sign) are well known [8]. A high PP was defined as higher than 50 mmHg and/or a PP/SBP ratio of >0.5 in a previous paper [9], and Hill's sign was defined as a popliteal arterial pressure that was >20 mmHg higher than the brachial arterial pressure [10]. However, the relationship between these signs and the severity of AR stage has remained unclear.

The purpose of this study was to evaluate the correlation between pulse wave measurements from CAVI report and the severity of AR, which was estimated with echocardiographic semi-quantitative measurements. The results can be applied to assist bedside detection of AR that may require surgical intervention.

Methods

Subjects

Our study subjects consisted of 83 consecutive patients (24 females; average age 59.9 years) with advanced AR who were admitted to our hospital for aortic valve surgery from March 2008 to November 2015. Patients who had other valvular diseases that were more than moderate in severity and/or had peripheral arterial disease were excluded. An age-matched control group consisted of 32 consecutive patients (11 females; average age 60 ± 7.3 years) who underwent CAVI examination from January 2012 to December 2012 due to non-cardiovascular disease. Atrial fibrillation, hemodialysis, and peripheral arterial disease (PAD) were excluded from control group. The institutional ethical committee of Kyoto Prefectural University of Medicine approved this study protocol.

CAVI and echocardiogram

CAVI was recorded approximately 1 week before surgery using VaSera screening system (Fukuda Denshi, Co., Ltd., Tokyo, Japan). The following parameters from CAVI reports were used for the analysis: heart rate, ABI, pre-ejection period (PEP), UT, ET, PEP/ET, %mean arterial pressure, right augmentation index, brachial SBP, brachial diastolic BP (DBP), ankle SBP, PP, ABD, and CAVI. PP was defined as the difference between systolic and diastolic pressures in the right brachial artery, and ABD was defined as the differences in SBP between the right brachial and the right ankle arteries. The time-dependent parameters (PEP, ET, UT, and PEP/ET) were corrected using $\sqrt{RR}$ (square of the preceding R–R interval). At first, these parameters were compared with those of age-matched controls, and also compared before and after surgery.

The echocardiogram was recorded by cardiologists before the operation. The following parameters were examined: LV diastolic dimension (Dd), LVDs, ejection fraction (EF), vena contracta (VC), and aortic pressure half-time. VC was obtained using the average of measurements of two experienced cardiologists who were blinded to CAVI parameters. Semi-quantitative AR severity was evaluated by regurgitation jet penetration into the LV cavity on Doppler color imaging as follows: up to the anterior mitral leaflet (Grade 1), up to the papillary muscle (Grade 2), up to 2/3rds of the LV cavity (Grade 3), and up to the LV apex (Grade 4). We examined the correlation between the PP, ABD, and UCG parameters.

Statistical analysis

All data are expressed as mean ± standard deviation. ABD among the semi-quantitative AR severity groups were compared with one-way analysis of variance (ANOVA). The correlations of two variables (ABD and following parameters: Dd, Ds, VC, UT) were examined with Pearson correlation test. The differences in CAVI parameters between AR group and age-matched controls were compared by unpaired *t*-test. The changes in CAVI parameters before and after surgery were compared by paired *t*-test. Values of $p < 0.05$ were regarded as statistically significant. All statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) Version 21 (Chicago, IL, USA).

Results

Patient characteristics

Table 1 shows the characteristics of patients in this study. Comorbid diseases were as follows: 42 patients (50%) had hypertension, 9 patients (10%) had diabetes mellitus, and 29 patients (35%) had dyslipidemia. According to the echocardiographic measurements and operative records, the etiology of AR was classified as follows: 8 had annulo-aortic ectasia (AAE), 20 had prolapse, 9 had bicuspid valve, 9 needed re-do AVR, 11 had degenerative valve, 12 had sclerotic valve, 1 had infectious endocarditis, 2 had bicuspid valve + prolapse, 4 had bicuspid valve + AAE, 2 had prolapse + AAE, 2 had dissection of the aorta, 1 had quadricuspid valve, 1 had aortitis, and 1 had rheumatic fever. The numbers of patients among the semi-quantitative AR severity groups were 8 (Grade 2), 25 (Grade 3), and 50 (Grade 4).

Table 1
Basic clinical characteristics.

• Patient number	83
• Age	60 ± 18 (22–82) y.o.
• Female	24 (29%)
• Height	161.6 ± 18.8 cm
• Body weight	59.9 ± 11.1 kg
• HT	42 (50%)
• DM	9 (10%)
• HL	29 (35%)
• NYHA (1/2/3/4)	26/44/13/0
• BNP (preopretative)	225 ± 337 (6–1865, *n* = 78) pg/dl
• Creatinine	0.97 ± 0.92 (0.54–7.46, *n* = 83) mg/dl
• EF	53.9 ± 11.5%
• LVDd/Ds	60.8 ± 8.3/43.4 ± 9.1 mm
• PHT of AR	399 ± 153 ms
• VC (*n* = 59)	6.95 ± 1.71
• Semi-quantitative AR severity	Grade 1/2/3/4 = 0/8/25/50

HT: hypertension, DM: diabetes mellitus, HL: hyperlipidemia, NYHA: New York Heart Association Class, EF: ejection fraction, LVDd/Ds: left ventricular diastolic dimension/systolic dimension, PHT of AR: pressure half time of AR, VC: vena contracta.

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