

A NEW METHOD FOR DETERMINING SUBENDOCARDIAL VIABILITY RATIO FROM RADIAL ARTERY PRESSURE WAVES

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Aortic subendocardial viability ratio (SEVR), an index of myocardial oxygen demand relative to supply, has been used for the early detection of hemodynamic changes. We aimed to validate a new method for determining SEVR directly from radial pressures. Hemodynamic parameters were measured in 231 outpatients (108 males and 123 females) for physical examination, aged from 20–77 years (45.9 ± 17.3 years), including 210 healthy and 21 hypertensive subjects. Aortic SEVR was obtained using a validated device (SphygmoCor; AtCor Medical, Sydney, Australia), and radial SEVR was obtained using a portable vascular testing device (IIM-2010A; Institute and Intelligent of Machines, Hefei, China). Radial SEVR was strongly related to aortic SEVR ($r = 0.824$, $p < 0.01$), with approximately 15.7% lower value. Aortic and radial SEVR had similar independent predictors, including diastolic time fraction (DTF), systolic blood pressure, diastolic blood pressure, age, and height. DTF exerted the most influence on both of them. In healthy subjects, there were significant changes in aortic and radial SEVR between age groups in both males and females ($p < 0.05$ for both). Changes in aortic and radial

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SEVR with aging were parallel though the differences between them increased. These results suggested that the simple and easily obtainable radial SEVR could provide equivalent information to aortic SEVR, and has potential for the primary prevention of cardiovascular disease in health screening.

Keywords: Subendocardial viability ratio; radial artery; hemodynamic changes; primary prevention.

1. Introduction

Subendocardial viability ratio (SEVR), derived from aortic pressures, is proposed as an index of myocardial perfusion relative to cardiac afterload.^{1–3} Decreased aortic SEVR indicates an imbalance between myocardial oxygen demand and supply. It has been used not only in elderly patients with cardiovascular disease for the prediction of myocardial ischemia,^{4,5} but also increasingly in young and middle-aged subjects for the early detection of hemodynamic changes.^{6,7} Generally, aortic pressures are non-invasively derived from radial pressures using a transfer function with SphygmoCor (AtCor Medical, Sydney, Australia),^{8,9} which has now been used as a standard device in studies on pulse wave analysis (PWA) of aortic pressures and new instrument validation.^{10–13} In a recent study, Gaon (Hanbyul Meditech, Jeonju, South Korea) was validated for central blood pressure estimates by comparing with SphygmoCor.¹⁰ Though determining hemodynamic parameters from aortic pressures is useful in research and clinic, attempts have been made to obtain them directly from radial pressures for simplifying the measurement procedure.^{14–16} It has been proven that augmentation index (AI), derived from radial pressures, could provide equivalent information to aortic AI.^{14,15} Recently, we have also suggested pulse transit time determined from radial pressures as an index of arterial stiffness.¹⁶ However, to the best of our knowledge, whether SEVR obtained directly from radial pressure waveforms can provide comparable information with SEVR obtained from aortic pressures has not been investigated.

This study aimed to evaluate a new approach for determining SEVR from radial pressures by comparing it with SEVR obtained from aortic pressures. In order to address this comprehensively, we conducted the following assessments. First, we determined the correlation between radial and aortic SEVR in a population of outpatients for physical examination. Second, the independent determinants of radial and aortic SEVR were investigated. Previous studies have demonstrated that diastolic time fraction (DTF) was the most important determinant of aortic SEVR.^{17,18} Third, we compared the changes in radial and aortic SEVR with aging in healthy subjects.

2. Methods

2.1. Study subjects

The study population consisted of 263 outpatients (124 males and 139 females), who went for physical examination in a community hospital between November

2010 and July 2011. Among them, subjects with significant valvular heart disease, fasting glucose >125 mg/dL, familial dyslipidemia, or renal insufficiency were excluded. Subjects with insufficient quality of the recorded pressure waveforms were also eliminated. Finally, a total of 231 individuals (108 males and 123 females) aged from 20–77 years (45.9 ± 17.3 years) were accepted into the study, including 210 healthy subjects and 21 hypertensives. All subjects gave written informed consent. This study was reviewed and approved by the local Institutional Review Board.

2.2. Study protocol

All measurements were performed in a temperature-controlled environment in accordance with consensus recommendations.¹⁹ Each subject rested for a minimum of 10 min before measurements. All measurements were obtained after fasting for 12 h. No consumption of alcohol was allowed for 24 h, and of tea, coffee, chili, or smoking for 8 h before examination. All measurements were performed by the same experienced operator and conducted in a seated position.

2.3. Measurements

Blood pressure was measured twice using a mercury sphygmomanometer at the brachial level. The mean of the two readings of systolic blood pressure (SBP) and diastolic blood pressure (DBP) was used in the study. This was followed by measurements of aortic and radial hemodynamic parameters.

2.4. Measurement of aortic hemodynamics

Aortic hemodynamic parameters were assessed by PWA of aortic pressure waveforms using applanation tonometry (SphygmoCor; AtCor Medical, Sydney, Australia). Radial pressure waveforms were recorded at the wrist with a high-fidelity micromanometer (Millar Instruments, Houston, Texas, USA). A validated generalized transfer function was used to generate the corresponding aortic pressures,^{8,9} from which aortic SBP, DBP, pulse pressure (PP), DTF, AI, and SEVR were derived. Only measurements with high-quality recordings, defined as a quality index >85 , were included in this study.

2.5. Measurement of radial hemodynamics

Radial hemodynamic parameters were determined by PWA of radial pressures using a portable vascular testing device (IIM-2010A; Institute and Intelligent of Machines, Hefei, China). The tonometric signals collected at the radial artery were digitized using a 12-bit analog-to-digital converter with a sampling frequency of 200 Hz. Consistent arterial waveforms were recorded for 12 s to obtain an ensemble averaged radial waveform, which was then calibrated according to brachial SBP and DBP.^{2,21} Feather points of the averaged pressure waveform, including pressure

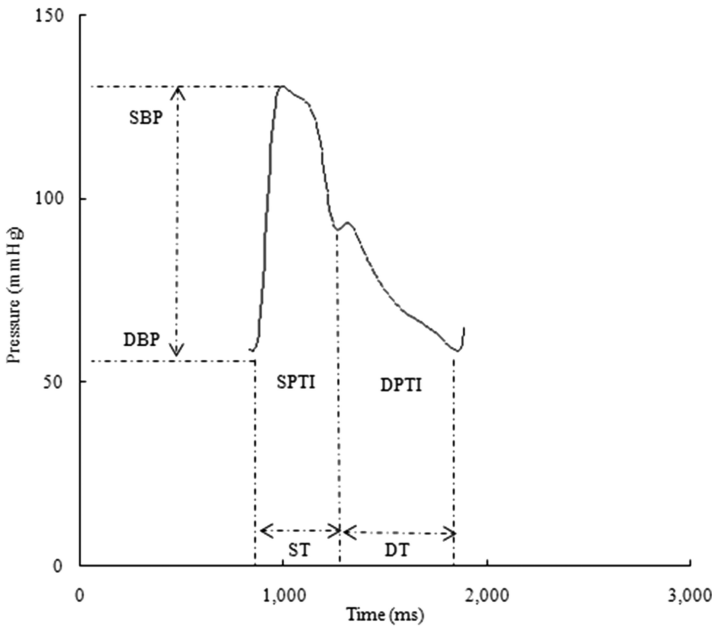


Fig. 1. Calculation of the subendocardial viability ratio (SEVR) from radial pressure waveform: $SEVR = DPTI/SPTI$. SPTI, systolic pressure — time integral; DPTI, diastolic pressure — time interval; ST, systolic time; DT, diastolic time; SBP, systolic blood pressure; DBP, diastolic blood pressure.

upstroke, incisura, and the first and second systolic peaks, were detected automatically using algorithms based on multidimensional derivatives. The validity and reliability of detecting these feature points with the algorithms have been previously established.^{11,22}

As shown in Fig. 1, the following indices are calculated. The systolic time (ST) was measured from the foot of the pressure upstroke to the trough of the incisura, while the diastolic time (DT) was calculated as ST subtracted from a cardiac cycle. DTF was determined as the ratio of DT to ST, expressed as a percentage. The area under the radial systolic pressure curve and diastolic pressure curve were computed as radial systolic pressure—time integral (SPTI) and diastolic pressure—time integral (DPTI) separately. Radial SEVR was calculated as the ratio of DPTI to SPTI, expressed as a percentage. Radial AI was calculated as follows: $[(\text{second peak radial systolic pressure} - \text{diastolic pressure}) / (\text{first peak radial systolic pressure} - \text{diastolic pressure}) \times 100]$.¹⁴

2.6. Statistical analysis

All of the data were reported as mean \pm SD. Student's *t*-test was used to compare anthropometric and hemodynamic parameters between genders. Univariate analyses and the regression model were used to determine the association between aortic and radial SEVR. Agreement between the measured aortic SEVR and the

predicted aortic SEVR from radial SEVR by the regression equation was evaluated by Bland–Altman plots. To determine the independent predictors of aortic and radial SEVR, stepwise regression analysis was performed with independent variables of age, sex, height, body mass, DTF, SBP, DBP, and AI. One-way ANOVA (analysis of variance) was undertaken to examine the effect of aging on both aortic and radial SEVR in healthy subjects. A post-hoc test using the LSD method identified significant differences among mean values. Statistical significance was set *a priori* at $p < 0.05$.

3. Results

The anthropometric and hemodynamic characteristics of the subjects taken into the study are presented in Table 1, grouped by gender. On average, the females in this cohort were older, shorter, lighter, and with a lower body mass index. Females had significantly lower DTF and SEVR but higher AI in both aortic and radial arteries. There were no significant gender differences in SBP, DBP, and HR. Females had significantly higher aortic PP but slightly lower radial PP.

Table 1. Anthropometric and hemodynamic characteristics for gender ($n = 231$).

Variables	Males ($n = 108$)	Females ($n = 123$)
Anthropometric characteristics		
Age (years)	43.2 ± 17.5	48.2 ± 16.8*
Height (cm)	170.9 ± 6.2	158.9 ± 4.7***
Body mass (kg)	68.1 ± 12.0	56.2 ± 7.9***
BMI (kg/m ²)	23.2 ± 3.6	22.1 ± 3.9*
Hemodynamic characteristics		
HR (beats/min)	66.8 ± 9.1	68.7 ± 7.6
Radial		
SBP (mmHg)	119.6 ± 12.4	117.5 ± 15.3
DBP (mmHg)	72.2 ± 7.3	70.7 ± 8.7
PP (mmHg)	47.4 ± 10.6	46.8 ± 9.8
DTF (%)	61.0 ± 4.6	57.8 ± 3.9***
SEVR (%)	126.6 ± 26.1	108.9 ± 19.2***
AI (%)	68.4 ± 13.8	77.3 ± 13.8***
Aortic		
SBP (mmHg)	104.5 ± 14.7	107.2 ± 19.4
DBP (mmHg)	73.8 ± 7.5	71.9 ± 7.4
PP (mmHg)	31.4 ± 11.4	35.3 ± 13.3*
DTF (%)	62.7 ± 4.4	60.3 ± 3.7**
SEVR (%)	140.4 ± 23.8	126.3 ± 18.6***
AI (%)	3.3 ± 17.1	19.9 ± 17.5***

Note: Values are mean ± SD. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, versus male. BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; DTF, diastolic time fraction; SEVR, subendocardial viability ratio; AI, augmentation index.

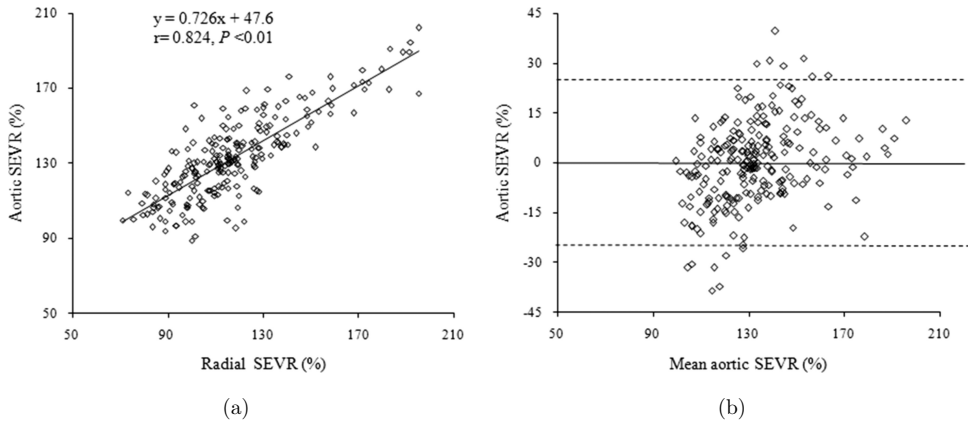


Fig. 2. Correlation between aortic and radial subendocardial viability ratio (SEVR): scatter plots (a) and Bland-Altman plot for the difference between aortic SEVR predicted from radial SEVR via the regression line relating aortic to radial SEVR and derived from synthetic aortic pressures (b) with mean difference ± 2 SD.

3.1. Relation between radial and aortic SEVR

Figure 2 illustrates the correlation between aortic and radial SEVR. Radial SEVR was strongly correlated to aortic SEVR ($r = 0.824$, $P < 0.01$), although radial SEVR was approximately 15.7% lower than aortic SEVR. The regression model was $y = 0.727x + 47.6$ (y : aortic SEVR; x : radial SEVR). When aortic SEVR was estimated from the regression line relating aortic to radial SEVR, the SD of the difference between two measurements was 12.5% in the study population.

Table 2. Stepwise regression analyses for aortic and radial subendocardial viability ratio ($n = 231$).

Variables	β -coefficient	t -value	p -value
Aortic SEVR ($R^2 = 0.953$)			
DTF	0.944	62.156	<0.001
SBP	-0.527	-18.584	<0.001
DBP	0.346	14.888	<0.001
Height	0.077	4.335	<0.001
Age	-0.085	-4.131	<0.001
AI	-0.085	-3.830	<0.001
Radial SEVR ($R^2 = 0.946$)			
DTF	0.901	54.141	<0.001
SBP	-0.289	-11.474	<0.001
DBP	0.260	11.781	<0.001
Age	-0.096	-4.774	<0.001
Height	0.043	2.492	0.013

Note: DTF, diastolic time fraction; SBP, systolic blood pressure; DBP, diastolic blood pressure; AI, augmentation index; SEVR, subendocardial viability ratio.

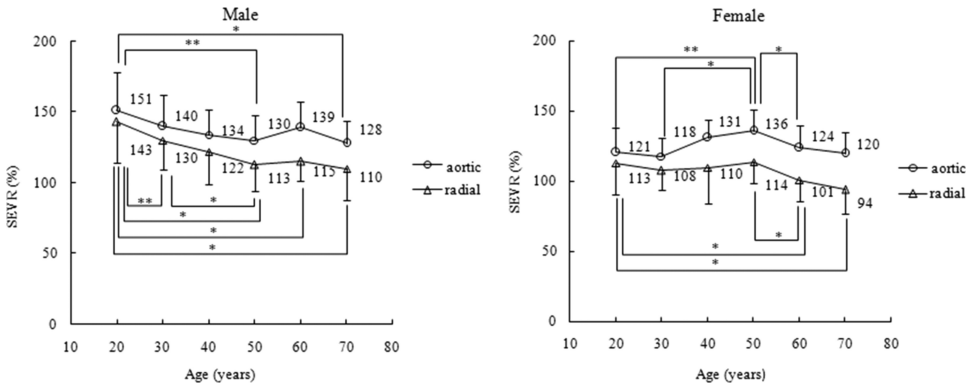


Fig. 3. Changes in aortic and radial subendocardial viability ratio (SEVR) in males and females of healthy subjects for each decade. Values are mean \pm SD. * $p < 0.01$, ** $P < 0.01$ between age groups.

Stepwise regression analyses revealed that DTF, SBP, DBP, age, and height were entered into the model as independent predictors of both aortic and radial SEVR ($R^2 = 0.953$ and $R^2 = 0.946$, respectively; $p < 0.001$ for both; Table 2).

3.2. Aortic and radial SEVR with aging

In healthy subjects of the study population, significant changes were found between age groups in aortic and radial SEVR in both males and females ($P < 0.05$ for both; Fig. 3). Changes in radial SEVR were similar with changes in aortic SEVR though the differences between them increased with age. In males, values of them decreased with aging from the third decade to fifth decade, whereas they increased to the sixth decade. In females, however, they peaked at the fifth decade and then significantly decreased.

4. Discussion

Major findings of this study are as follows. First, SEVR obtained directly from radial pressure waveforms showed a highly significant correlation with SEVR obtained from aortic pressure waveforms in a large population with a wide age range. Second, the independent determinants of radial SEVR were mostly similar to that of aortic SEVR, including DTF, SBP, DBP, age, and height. Third, changes in radial SEVR with aging corresponded to changes in aortic SEVR. These results suggest that the easily obtainable radial SEVR provides information comparable to SEVR determined from aortic pressures.

The first and main part of the present study was to evaluate the association between aortic and radial SEVR. As the invasive nature of cardiac catheterization restricts its use in health screening, arterial tonometry has gained popularity in research and the clinic. Aortic SEVR is generally calculated from synthesized aortic pressure waveform using radial tonometry, the clinical value of which has been

proven in several studies.^{3,10–13} With regards to the issue, aortic SEVR determined by the method was suggested as a reliable predictor for assessing coronary microcirculation in essential hypertensives.³ With the method, SphygmoCor has been used as a common device for PWA of aortic pressure in studies on new instrument validation.^{10,11} In the present study, therefore, we compared SEVR obtained from radial pressure with that calculated from SphygmoCor rather than cardiac catheterization.

As shown in Fig. 2, radial SEVR is strongly related to aortic SEVR ($r = 0.824$, $p < 0.01$) in the study population widely varying in age, though the SD of the difference between two measures was rather large (12.5%). One possible explanation for the lack of a higher correlation may be owing to the methods used by the two devices to acquire radial pulses. In the SphygmoCor device, a micromanometer is handheld, with which the operator can make adjustments during measurement. In contrast, the probe is fixed on the wrist in IIM-2010A. Even a slight change in pulse waves may result in a large difference in the estimated SEVR. However, the correlation between the devices still remains significant.

Multiple regression analysis revealed that DTF, SBP, DBP, age, and height were entered into the model as independent predictors of both aortic and radial SEVR. They were strongly positively correlated with DTF and DBP, while negative correlated with SBP. It could be easily understood from their definition and calculation method. DTF played the most important role on aortic and radial SEVR, which was consistent with the results of previous studies.^{4,17} In a recent study, the ratio of DT to ST was suggested as the main determinant of aortic SEVR.²³ It was also in accordance with our observations. In addition, both aortic and radial SEVR were negatively correlated with age. It corresponded to the results of several studies that, with aging, arterial stiffness increased, leading to decreased SEVR.^{5,18,24}

The age-related changes in radial and aortic SEVR were further investigated in the study. To exclude the influence of hypertension on SEVR, only healthy subjects were taken into account. With aging, radial and aortic SEVR showed parallel changes in both genders, though the differences between them increased (Fig. 3). In males, both of them decreased from the third decade to fifth decade, whereas they increased to the sixth decade. The possible explanation is the complicated vascular–ventricular interaction in elderly,^{5,18,24} which is an important area for future evaluation. By contrast, SEVR in females increased up to the maximum at the fifth decade, and then significantly decreased. The postmenopausal effect on arterial compliance may contribute to this phenomenon,^{6,25} which also needs further investigation.

Possible limitations in the methodology should be emphasized. First, the study lacked the direct data of aortic SEVR determined from invasive aortic measurements. Instead, radial SEVR was compared with an indirect measurement of aortic SEVR determined by SphygmoCor, which has been fully validated and used as a standard device in studies on new instrument validation.^{3,5,10,11} Compared with it, radial SEVR determined by a portable vascular testing device IIM-2010A is simple

and easily obtainable. Second, the population accepted into the study was obtained from outpatients for a physical examination, containing mainly healthy subjects. Further investigation in subjects with various clinical settings is needed for its wide implication.

In summary, SEVR obtained directly from radial pressures was significantly related to aortic SEVR in healthy and hypertensive subjects, with similar independent predictors and age-related changes. The new method could give equivalent information to aortic SEVR, and has potential for early detection of hemodynamic changes in health screening.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

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