Postprint: Influencing Factors of Subendocardial Myocardial Viability Rate in Community Populations

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Abstract

Cardiovascular disease currently still has high morbidity and mortality rates worldwide. Subendocardial Viability Ratio (SEVR) is an index derived from analyzing left ventricular and aortic pressure curves in invasive hemodynamic studies, and is a valuable tool for assessing myocardial perfusion, also possessing potential predictive value for cardiovascular adverse events and mortality in different populations. Non-invasive measurement methods can also estimate SEVR, and although they have certain limitations, they remain valuable tools for evaluating myocardial perfusion and cardiovascular risk and have demonstrated great potential for clinical application. Currently, there is a lack of large-scale epidemiological investigations to explore the practical value of SEVR in primary and secondary prevention of cardiovascular disease.

Objective: To estimate SEVR using non-invasive methods in a large-scale Beijing community population and analyze its related influencing factors.

Methods: This article is based on a cross-sectional follow-up of a cohort study. The study subjects were derived from an atherosclerosis research cohort established by the Department of Cardiology, Peking University First Hospital, in the Shougang Community, Shijingshan District, Beijing, from December 2011 to April 2012, recruiting community residents aged $ $40 years. During the 2018 follow-up, pulse wave analysis examination was performed using non-invasive methods, and SEVR results were obtained. Linear regression analysis was used to explore the influencing factors related to SEVR.

Results: Among the 6,568 study subjects who participated in the follow-up in 2018, those who failed to complete the pulse wave analysis examination to obtain SEVR due to arrhythmia, etc., were excluded, and 6,382 cases were finally included, with 97.2% of study subjects having SEVR results. In

the 6,382 community population, there were 2,130 males and 4,252 females, with a mean SEVR of $(144\$\pm22) = -11.00), age(= -0.53), smoking(= 2.36), hypertension(= -4.12), dyslipidemia(= -1.45), diabetesmellitus(= -4.36), antihypertensivemedication(= 3.72), andglucose-loweringtherapy(= -3.71) wereindependentinfluencingfactorsofSEVR(P < 0.05). Inmales, age(= -0.67), hypertension(= -3.20), dyslipidemia(= -2.73), diabetesmellitus(= -3.42), andglucose-loweringtherapy(= -5.07) wereindependentinfluencingfactorsofSEVR(P < 0.05). Infemales, age(= -0.48), smoking(= 9.44), hypertension(= -4.98), diabetesmellitus(= -4.95), antihypertensivetherapy(= 5.26), andglucose - loweringtherapy(\$=-2.82) were independent influencing factors of SEVR (P<0.05).

Conclusion: Non-invasive SEVR measurement is feasible for application in large-scale community population cohort studies. SEVR is associated with traditional coronary heart disease risk factors such as gender, age, smoking, hypertension, dyslipidemia, and diabetes mellitus, and its relationship with drug therapy requires further research and discussion.

Full Text

Influencing Factors for Subendocardial Viability Ratio in a Community-Based Population

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Abstract

Background: Cardiovascular diseases remain a leading cause of morbidity and mortality worldwide. The subendocardial viability ratio (SEVR) is an index derived from invasive hemodynamic analysis of left ventricular and aortic pressure curves, serving as a valuable tool for assessing myocardial perfusion with potential predictive value for adverse cardiovascular events and mortality across diverse populations. Although non-invasive measurement methods for SEVR have limitations, they represent valuable tools for evaluating myocardial perfusion and cardiovascular risk, demonstrating substantial clinical potential. However, large-scale epidemiological studies investigating the practical value of SEVR in primary and secondary cardiovascular disease prevention are lacking.

Objective: To non-invasively estimate SEVR in a large-scale Beijing community population and analyze its associated influencing factors.

Methods: This cross-sectional follow-up study utilized an atherosclerosis cohort established by the Department of Cardiology at Peking University First Hospital in the Shougang Community, Shijingshan District, Beijing, between December 2011 and April 2012. Participants were community residents aged $ $40 years. During follow-up in 2018, non-invasive pulse wave analysis was performed to obtain SEVR measurements. Linear regression analysis was employed to explore factors associated with SEVR.

Results: Among 6,568 participants who attended follow-up in 2018, 6,382 were ultimately included after excluding those unable to complete pulse wave analysis due to arrhythmia (97.2% had valid SEVR results). The cohort comprised 2,130 males and 4,252 females, with a mean SEVR of $(144\$\pm22) = -11.00), age(= -0.53), smoking(= 2.36), hypertension(= -4.12), dyslipidemia(= -1.45), diabetes(= -4.36), antihypertensivemedicationuse(= 3.72), andhypoglycemictreatment(= -3.71)wereindependentdeterminantsofSEVR(P < 0.05).Inmales, age(= -0.67), hypertension(= -3.20), dyslipidemia(= -2.73), diabetes(= -3.42), andhypoglycemictreatment(= -5.07)wereindependentpredictors(P < 0.05).Infemales, age(= -0.48), smoking(= 9.44), hypertension(= -4.98), diabetes(= -4.95), antihypertensivemedication(= 5.26), andhypoglycemictreatment($=-2.82) were independent predictors (P<0.05).

Conclusion: Non-invasive SEVR measurement is feasible in large-scale community-based cohort studies. SEVR correlates with traditional cardiovascular risk factors including sex, age, smoking, hypertension, dyslipidemia, and diabetes, though its relationship with pharmacological treatment requires further investigation.

Keywords: Subendocardial viability ratio; Atherosclerosis; Community-based population; Cohort study; Influencing factors

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Introduction

The subendocardial viability ratio (SEVR) is an index originally derived by Buckberg et al. and Hoffman et al. in the early 1970s through invasive hemodynamic studies analyzing left ventricular and aortic pressure curves in large animals and humans. Also known as the Buckberg index or diastolic pressure-time index to systolic pressure-time index ratio (DPTI:SPTI), SEVR enables morphological analysis of central arterial pressure waveforms through pulse wave analysis. SEVR and other central hemodynamic parameters can be obtained via pulse wave analysis, providing valuable information beyond traditional cardiovascular risk factors for cardiovascular risk assessment. However, research on non-invasive measurement of SEVR in large-scale populations remains scarce.

SEVR is calculated as the ratio of diastolic pressure-time index (DPTI) to systolic pressure-time index (SPTI). It serves as a reliable indicator of subendocardial myocardial oxygen supply-demand balance, defined through analysis of left

ventricular and aortic pressure curves. The systolic pressure-time index represents the area under the systolic left ventricular (or aortic) pressure curve from the onset of ventricular contraction to the dicrotic notch where ventricular and aortic pressure curves intersect, reflecting cardiac work. SPTI directly correlates with myocardial oxygen consumption, primarily dependent on left ventricular ejection time, ejection pressure, and myocardial contractility. The diastolic pressure-time index represents the area between aortic and left ventricular pressure curves during diastole, influencing coronary artery flow and maintaining adequate subendocardial blood supply pressure. Consequently, SEVR is considered an indicator for evaluating myocardial perfusion and may hold important value in assessing coronary microcirculatory function.

Initial SEVR derivation required pressure curves recorded during cardiac catheterization from the left ventricle and ascending aorta. However, this invasive and cumbersome approach severely limited clinical applicability. Subsequent development of non-invasive central blood pressure recording enabled SEVR measurement through arterial waveform analysis. Recent studies have demonstrated SEVR's predictive value for cardiovascular outcomes in chronic kidney disease patients, its association with heart failure readmission rates, and its correlation with all-cause and cardiovascular mortality in men. Despite these findings, large-scale epidemiological investigations exploring SEVR's practical value in primary and secondary cardiovascular disease prevention are lacking. This study aims to explore the feasibility of non-invasive SEVR measurement and analyze its values and potential influencing factors in a large community-based cohort.

Methods

Study Population Participants were recruited from an atherosclerosis cohort established by the Department of Cardiology at Peking University First Hospital in the Shougang Community, Shijingshan District, Beijing, between December 2011 and April 2012. The cohort comprised community residents aged $ $40 years. Among 6,568 participants who attended on-site follow-up between September and December 2018 and underwent pulse wave analysis, SEVR results were obtained. The study protocol was approved by the Peking University First Hospital Ethics Committee (approval number: IRB00001052-11086; [2018] Research No. 174), and all participants provided written informed consent.

Inclusion Criteria: (1) Registered residents of the Shougang Community in Shijingshan District, Beijing, who previously participated in the atherosclerosis risk factor survey; (2) Both sexes eligible; (3) Good compliance, willingness to participate, and provision of written informed consent.

Exclusion Criteria: (1) Communication barriers, severe physical functional deficits such as aphasia or visual/hearing impairment preventing protocol assessment; (2) Severe psychiatric illness precluding cooperation; (3) Mobility

limitations; (4) Poor compliance; (5) Pregnancy or other conditions deemed unsuitable by investigators.

Data Collection SEVR Measurement: This study employed the Pulsepen pressure sensor (DiaTecne srl, San Donato Milanese, Italy) to obtain pulse waves from the right common carotid and femoral arteries. During pulse wave testing, participants rested in supine position for at least 15 minutes before measurement. SEVR was calculated from pulse wave analysis data using the formula: SEVR = (DPTI ÷ SPTI) × 100%.

Questionnaire and Physical Measurements: Trained research personnel administered standardized questionnaires following uniform protocols. Questionnaire content included demographic characteristics (sex, age, education, occupation), lifestyle factors (smoking, alcohol consumption, dietary habits), medical history (hypertension, coronary heart disease, stroke), and medication use (antihypertensive, hypoglycemic, and lipid-lowering drugs). Current smoking was defined as $ $1 cigarette per day for $ $6 months; current alcohol consumption as $ $1 occasion per week for $ $6 months. Hypertension was defined as self-reported history, current antihypertensive medication use, or elevated blood pressure on examination day (average of 3 measurements at least 1 minute apart: systolic blood pressure [SBP] $ $140 mmHg and/or diastolic blood pressure [DBP] $ $90 mmHg). Diabetes was defined as self-reported history, current hypoglycemic treatment (oral agents or insulin), fasting blood glucose $ $7.0 mmol/L, or 2-hour post-75g oral glucose tolerance test $ $11.1 mmol/L. Dyslipidemia was defined as self-reported hyperlipidemia, current lipid-lowering therapy, or abnormal lipid parameters on examination day: total cholesterol (TC) $ $5.18 mmol/L, triglycerides (TG) $ $1.70 mmol/L, low-density lipoprotein cholesterol (LDL-C) $ $3.37 mmol/L, or high-density lipoprotein cholesterol (HDL-C) < 1.04 mmol/L. Physical measurements included body mass index (BMI), calculated as weight (kg) divided by height

Blood pressure and pulse rate were measured in the right brachial artery using an Omron HEM-7117 electronic sphygmomanometer with a standardized calibrated method and appropriately sized cuff. Three consecutive measurements were taken with at least 1-minute intervals, and averages were calculated for mean SBP, mean DBP, and mean pulse rate.

Laboratory Tests: Following a 12-hour fast, venous blood samples were collected from the forearm. Serum or plasma was separated within 30 minutes and stored at -80°C for determination of fasting blood glucose (FBG), 75g oral glucose tolerance test postprandial glucose, TC, LDL-C, HDL-C, and TG. All laboratory tests were performed using a Roche C8000 automatic analyzer.

Statistical Analysis All statistical analyses were conducted using Empower(R) (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA) and R (http://www.R-project.org). Continuous variables with normal distribution were expressed as mean ± standard deviation, and categorical

data as frequencies (percentages). Comparisons of continuous variables were performed using independent t-tests and one-way ANOVA, while categorical data were compared using Pearson's ^{2} test or Fisher's exact test for variables with counts <10. In analyzing relationships between various factors and SEVR, univariate linear regression was initially performed to screen potential influencing variables for all participants, followed by multivariate linear regression using stepwise selection (forward-backward method). Gender-stratified univariate and multivariate regression analyses were subsequently performed. Two-sided tests were used with P<0.05 considered statistically significant.

Results

Baseline Characteristics Among 6,568 participants attending follow-up in 2018, 6,382 were ultimately included after excluding those unable to complete pulse wave analysis due to arrhythmia, yielding valid SEVR results for 97.2% of participants. The cohort included 2,130 males and 4,252 females, with a mean SEVR of (144$±$22)%. Gender-stratified analysis revealed that males had higher SEVR, BMI, mean SBP, mean DBP, TG, and FBG, and were older (all P<0.05). Females exhibited higher mean pulse rate and TC, HDL-C, and LDL-C levels (all P<0.05). Males had higher proportions of current smoking, alcohol consumption, hypertension, diabetes, coronary heart disease, myocardial infarction history, and stroke, as well as higher rates of antihypertensive and hypoglycemic medication use (all P<0.05). Females showed higher prevalence of dyslipidemia and lipid-lowering medication use (all P<0.05) .

SEVR Influencing Factors in the Overall Population Multivariate linear regression analysis with SEVR as the dependent variable (continuous) and baseline characteristics as independent variables demonstrated that in univariate analysis, sex, age, blood pressure levels, mean pulse rate, TC, HDL-C, FBG, smoking status, alcohol consumption, hypertension, dyslipidemia, diabetes, antihypertensive medication use, hypoglycemic treatment, and lipid-lowering medication use were associated with SEVR (P<0.05). Multivariate analysis identified sex (β=-11.00), age (β=-0.53), smoking (β=2.36), hypertension (β=-4.12), dyslipidemia (β=-1.45), diabetes (β=-4.36), antihypertensive medication (β=3.72), and hypoglycemic treatment (β=-3.71) as independent determinants of SEVR (P<0.05) .

Gender-Stratified Analysis of SEVR Influencing Factors Gender-stratified multivariate linear regression analysis revealed that in males, age (β=-0.67), hypertension (β=-3.20), dyslipidemia (β=-2.73), diabetes (β=-3.42), and hypoglycemic treatment (β=-5.07) were independent predictors of SEVR (P<0.05). In females, age (β=-0.48), smoking (β=9.44), hypertension (β=-4.98), diabetes (β=-4.95), antihypertensive medication (β=5.26), and hypoglycemic treatment (β=-2.82) were independent predictors (P<0.05) .

SEVR Comparison Across Subgroups Significant differences in SEVR were observed across subgroups defined by age, BMI, smoking status, alcohol consumption, hypertension, dyslipidemia, diabetes, coronary heart disease, antihypertensive medication use, lipid-lowering medication use, and hypoglycemic treatment ($P<0.05$). No significant differences were found between subgroups with versus without stroke or myocardial infarction history ($P>0.05$) .

Discussion

This study successfully obtained SEVR measurements via pulse wave analysis in 97.2% (6,382/6,568) of participants, demonstrating the feasibility of non-invasive SEVR assessment in large-scale epidemiological investigations. Previous SEVR research has primarily focused on special populations such as hypertensive patients, chronic kidney disease patients, and heart failure patients, with few studies conducted in large community cohorts. The largest published studies have included approximately 1,400 participants, making this investigation substantially more comprehensive.

Our findings indicate that male SEVR values were higher than female values in the community population, consistent with published literature. A Canadian study of healthy Caucasians using non-invasive SEVR measurement (SphygmoCor, AtCor Medical, Sydney, Australia) reported female SEVR of $(157\$\pm3) and male SEVR of (173\pm4). Similarly, a Spanish population study using the same device found male SEV$ years) studies. Additionally, our population had higher cardiovascular risk burden, with 55% having hypertension compared to 26% in the Spanish study, along with higher prevalence of diabetes, coronary heart disease, and cerebrovascular disease, potentially contributing to lower SEVR values. Device-related differences cannot be excluded, as our study used Pulsepen (DiaTecne srl) while previous studies used SphygmoCor; however, no comparative studies between these devices for SEVR measurement are available.

As a traditional atherosclerotic risk factor, dyslipidemia's relationship with SEVR has yielded inconsistent results across studies. Our multivariate regression analysis demonstrated a significant negative association between dyslipidemia and SEVR, suggesting that lipid metabolism disorders impair coronary perfusion and microcirculation.

The positive association between smoking and SEVR observed in our study is difficult to explain mechanistically. This counterintuitive finding may reflect methodological limitations, as our epidemiological survey defined "non-smoking" as current non-smoking status, potentially including former smokers who quit after developing cardiovascular disease. This misclassification could have biased the smoking-SEVR relationship.

Limited research has examined SEVR's relationship with pharmacological treatment. An Italian study of 75 hospitalized elderly patients (mean age 82.95$\pm$6.45 years) identified sex, creatinine clearance, and orthostatic hypotension as significant SEVR determinants using logistic regression. The

Spanish study found hypertension, diabetes, and obesity associated with SEVR after adjusting for age, sex, and antihypertensive medication use. In rheumatoid arthritis patients, multivariate analysis identified sex, blood pressure, heart rate, TC level, cardiac index, and left ventricular ejection time as independent SEVR predictors. Our results align partially with these findings, demonstrating that hypertension, dyslipidemia, and diabetes were associated with lower SEVR, while smoking was associated with higher SEVR. The inverse relationship between antihypertensive medication and SEVR may reflect confounding by indication, as treated hypertensives likely had more severe disease. Antihypertensive therapy may increase SEVR through heart rate reduction and SBP lowering, while hypoglycemic treatment may identify patients with more advanced microvascular dysfunction, resulting in lower SEVR.

Gender-stratified analysis revealed distinct patterns: in males, age, hypertension, dyslipidemia, diabetes, and hypoglycemic treatment were independent predictors; in females, age, smoking, hypertension, diabetes, antihypertensive therapy, and hypoglycemic treatment were independent predictors. Notably, smoking was not an independent predictor in males, while dyslipidemia was not independent in females, and antihypertensive therapy was associated with higher SEVR only in females. These findings suggest potential gender-specific differences in how age, smoking, and pharmacological treatments influence SEVR.

This study has several limitations. First, its cross-sectional design precludes causal inference. Medical histories of hypertension, coronary heart disease, and stroke were obtained via questionnaire without objective verification, potentially obscuring true associations between SEVR and coronary disease. Second, we employed traditional SEVR calculation methods with inherent limitations: the area-under-the-curve estimation does not account for left ventricular diastolic pressure (LVDP), isovolumic contraction period, or isovolumic relaxation period, resulting in relatively simple and imprecise measurements. Recent research has proposed updated SEVR formulas incorporating aortic pressure waveform analysis with consideration of left ventricular isovolumic phases, demonstrating better agreement with invasive catheterization measurements. Future work should explore these refined non-invasive algorithms in community populations to assess whether SEVR values and influencing factors differ from traditional methods and to further elucidate relationships with cardiovascular events and risk factors.

Conclusion

Non-invasive SEVR measurement is feasible in large-scale community-based cohort studies and correlates with traditional cardiovascular risk factors, suggesting its potential as a comprehensive indicator of cardiovascular status. While SEVR may predict future cardiovascular events and mortality, larger studies are needed to validate its predictive capacity in general populations. Ongoing follow-up of this cohort will further clarify SEVR's prognostic value for incident

cardiovascular events and death in community populations.

Author Contributions

GAO Lan: Conceptualization, data collection and curation, manuscript writing. ZHANG Xiangning: Data curation, manuscript writing. XIE Haotai: Data curation. FAN Fangfang, JIA Jia: Statistical design, data analysis. LI Jianping, MA Wei: Project administration, conceptual guidance. ZHANG Yan: Project administration, conceptual guidance, supervision, and manuscript review.

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Note: Figure translations are in progress. See original paper for figures.