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Original article

Combination of pulse wave velocity with clinical factors as a promising tool to predict major adverse cardiac events after percutaneous coronary intervention

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ABSTRACT

Background: The relationship between aortic stiffness and coronary artery disease has been proven. Logistic Clinical SYNTAX score (LogCSS), which combined the anatomical evaluation of coronary artery disease and three clinical factors (age, left ventricular ejection fraction, and creatinine clearance), showed improved predictive value for cardiovascular events in patients after percutaneous coronary intervention (PCI). The combination of pulse wave velocity (PWV) and clinical factors may show equivalent predictive value.

Methods: Three hundred and seventy-six patients who were diagnosed with non-ST-segment elevation coronary syndrome (ACS) and showed at least one ≥50% angiographic stenosis in a major coronary artery were enrolled. The Clinical PWV score was calculated by assigning points to different levels of age, creatinine clearance, left ventricular ejection fraction, and carotid–femoral PWV (cfPWV). The points for cfPWV were determined based on the cutoff values of quintiles (model 1) or the relationship between cfPWV and SYNTAX scores (model 2). The predictive values of LogCSS and Clinical PWV score for 3-year major adverse cardiac events (MACE), which were defined as all-cause death, nonfatal myocardial infarction, and nonfatal target vessel revascularization, were analyzed in 298 patients undergoing PCI.

Results: The Clinical PWV score based on model 2 demonstrated a similar predictive ability for 3-year MACE compared with LogCSS (AUC 0.72 vs. 0.75; $p = 0.11$). The AUC of LogCSS was significantly higher than the AUC of Clinical PWV score based on model 1 (AUC = 0.70, $p = 0.03$). Compared with cfPWV in isolation (AUC = 0.61), Clinical PWV score from model 2 showed significantly better predictive power ($p = 0.03$).

Conclusion: Combination of PWV with age, creatinine clearance, and left ventricular ejection fraction appears to be a promising tool to predict MACE after PCI in patients with ACS.

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Introduction

The relationship between aortic stiffness and coronary artery disease (CAD) has been proven in previous studies [1–3]. Several pathophysiological phenomena during the development of coronary atherosclerosis, including accumulation of collagen, fibrosis, inflammation, medial smooth muscle necrosis, and calcifications, are known to occur in parallel at the site of aorta accompanying age and cardiovascular risk factors, which may induce aortic stiffening [4,5]. As the gold-standard measurement of aortic stiffness, carotid–femoral pulse wave velocity (cfPWV) shows independent predictive value for cardiovascular events [6,7].

SYNTAX score is an anatomically based tool to quantitatively assess and grade the angiographic characteristics of coronary lesions [8], which has been shown as a predictor of long-term prognoses in patients after coronary revascularization [9,10]. However, one important limitation of SYNTAX score is the lacking of clinical variables in its algorithm. Recently, several SYNTAX score-derived risk scores which combine clinical-based scores with SYNTAX score have been proposed [11], such as Clinical SYNTAX score (CSS) that multiplies the modified ACEF [Age, Creatinine clearance (CrCl) and left ventricular Ejection Fraction

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(LVEF)] score with SYNTAX score [12], and Logistic Clinical SYNTAX score (LogCSS) that grades the SYNTAX score and the 3 clinical variables in ACEF score and then assigns different points [13]. In consideration with the relationship between CAD and aortic stiffness, we hypothesized that the combination of PWV and the ACEF score may show equivalent predicting value with LogCSS.

In this study, we first assessed the relationship between cfPWV and SYNTAX score, and attempted to develop models to combine the results of cfPWV and 3 clinical factors (age, creatinine clearance, and ejection fraction). The predictive value of these models was assessed and compared in a cohort prospectively.

Methods

Study population

We enrolled 376 consecutive patients who were diagnosed as having non-ST-segment elevation acute coronary syndrome (ACS) and showed at least one significant angiographic coronary lesion at the Fuwai Hospital in 2010. A coronary lesion with ≥50% reduction of the luminal diameter in vessel ≥1.5 mm was defined as a significant lesion [8]. Non-ST-segment elevation ACS was defined according to the American College of Cardiology Foundation/American Heart Association guideline for the management of patients with unstable angina/non-ST-elevation myocardial infarction [14]. Exclusion criteria included a history of percutaneous coronary intervention (PCI) or coronary arterial bypass grafting (CABG), and a diagnosis of acute ST-segment elevation myocardial infarction, valvular heart disease, or congenital heart disease. The study was approved by the Ethics Committee of the Fuwai Hospital.

Logistic Clinical SYNTAX score (LogCSS)

The results of angiography were reviewed by two experienced interventional cardiologists, and the SYNTAX scores were assessed. Each coronary lesion with ≥50% reduction of the luminal diameter in vessel ≥1.5 mm was scored separately. The SYNTAX algorithm which is available on the SYNTAX website (www.syntaxscore.com) was used to calculate the overall score. The Logistic Clinical SYNTAX score system has been detailed previously, and the core model was used in this study [13]. In brief, points were assigned according to the values of four variables including age, LVEF, CrCl, and SYNTAX score, and the sum of these points was the result of LogCSS. The CrCl was calculated using the Cockcroft and Gault formula [15]. LVEF was calculated by echocardiographic assessment using Simpson's method.

Clinical cfPWV and Clinical PWV score

Carotid–femoral PWV was measured using the SphygmoCor system (AtCor Medical, Sydney, Australia). Electrocardiogram-gated carotid and femoral waveforms were recorded by applanation tonometry. The distance between the sampling sites (carotid and femoral sites, Dcf) was measured manually above the body surface with a tape. PWV was calculated by dividing this distance by the carotid–femoral transit time which was estimated as the average time difference between the onset of the femoral and carotid waveforms of 10 consecutive cardiac cycles.

We used the formula age/LVEF + 1 point for every 10 mL/min reduction in CrCl below 60 mL/min per 1.73 m^2 (up to a maximum of 6 points) to calculate the modified ACEF score, which has been detailed previously [10]. The Clinical cfPWV was calculated using the formula cfPWV × modified ACEF score.

We used 2 models to assign points to different values of cfPWV. In model 1, the results of cfPWV were divided into quintiles, and points of 0–4 were assigned to each quintile. The lowest quintile got 0 point, and the highest quintile got 4 points. To develop model 2, we first investigated the mean SYNTAX scores in categories with different cfPWV levels. Based on the characteristics of distribution of SYNTAX score, we fixed the cutoff values of cfPWV for different points. We used these points to replace the points from SYNTAX score in the LogCSS model and constructed the model of Clinical PWV score. We gave 1 point for every 5 years increase up to a maximum of 7 points in age above 50 years old to calculate the scores for age, 2 points for every 5 mL/min per 1.73 m^2 reduction up to a maximum of 10 points in CrCl below 90 mL/min per 1.73 m^2, and 2 points for every 5% reduction in LVEF below 50% up to a maximum of 10 points. The sum of these scores plus the scores of PWV was the result of Clinical PWV score.

Follow-up of patients after PCI

The patients who underwent PCI were monitored every 6 months via formal telephone interviews or during their visits to the clinic. Major adverse cardiac events (MACE) were recorded which were defined as all-cause death, nonfatal myocardial infarction (MI), and nonfatal target vessel revascularization (TVR) [16]. MI was defined as chest pain with new ST-segment changes and elevation of cardiac markers which reflected myocardial necrosis to at least twice the upper limit of normal. PCI-related MI was not included as clinical events in this study. TVR was defined as clinically driven percutaneous revascularization or bypass of the target lesion or any segment of the epicardial coronary artery that contained the target lesion.

Statistic analysis

Spearman's correlation test was used to assess the association between continuous variables. The discriminating power to predict MACE was assessed by the area under the receiver operating charactering curve (AUC), which is equal to the *c*-statistic [17]. The *c*-statistic estimates the ability to distinguish a patient with and without a clinical outcome, and ranges from 0.5 (no discrimination) to 1 (theoretical maximum). AUCs were compared using the method described by DeLong [18]. All the data analyses were conducted using SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at a two-side $p < 0.05$.

Results

Characteristics of patients

The mean age of these 376 patients was 56.4 ± 10.2 years, 320 (85.1%) of them were male. PCI was performed in 316 patients, and CABG was performed in 34 patients. The details of the clinical characteristics are presented in Table 1.

Clinical cfPWV

A significant correlation between cfPWV and SS was observed ($r = 0.27$, $p < 0.001$; Fig. 1). A significant correlation was presented between Clinical cfPWV and LogCSS ($r = 0.78$, $p < 0.001$).

Models of Clinical PWV score

In the model 1 of Clinical PWV score, we categorized the results of cfPWV into quintiles with cutoff values as ≤7.2, 7.3–7.9, 8.0–9.0, 9.1–10.1, ≥10.2. Each quintile was assigned the points of 0–4. The mean SYNTAX scores in different categories with different cfPWV are presented in Fig. 2. The cutoff values for points of 0–4 in model 2 were fixed as ≤8.0, 8.1–9.0, 9.1–10.0, 10.1–12, ≥12.1. The

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