Diagnostic Accuracy Study

Medicine®

OPEN

The value of 3-dimensional longitudinal strain in the evaluation of complex coronary lesions in non-ST-segment elevation acute coronary syndrome patient

Zekun Cai, MD[a,b], Jianwei Dai, PhD[b], Dan Wu, MD[c], Jian Qiu, MD[a], Jun Ma, MD[a], Guoying Li, MD[d], Wei Zhu, MD[a], Hongqiang Lei, MD[a], Wenhua Huang, PhD[e], Heye Zhang, PhD[c,*], Lin Xu, PhD[a,*]

Abstract

The aim of this study is to investigate the value of 3-dimensional global peak longitudinal strain (GPLS) derived from the 3-dimensional speckle-tracking echocardiography (3D-STE) in the diagnosis of the complex non-ST-segment elevation acute coronary syndromes (NSTE-ACS) by comparing GPLS to the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score.

A total of 59 inpatients with NSTE-ACS in our hospital between October 2014 and January 2015 were enrolled into our study. All these subjects underwent the coronary angiography (CAG) and 3D-STE examination. The results of CAG were used to calculate the SYNTAX scores in each subject. The GPLS was assessed with speckle-tracking analysis using the dedicated software developed by GE Healthcare (Horten, Norway).

We grouped all subjects according to the SYNTAX scores. A total of 23 patients (39%) were grouped as complex NSTE-ACS in our experiment. In our analysis, the values of GPLS significantly decreased from low SYNTAX scores to intermediate or high SYNTAX scores ($-14.0\pm2.7\%$ and $-9.5\pm2.8\%$, respectively, $P<0.001$). Multivariate regression analysis showed that GPLS and diabetes mellitus were independent predictors for complex NSTE-ACS. The area under the receiver operator characteristic curve (AUC) for GPLS to evaluate patients with complex NSTE-ACS was 0.882 (95% confidence interval [CI], 0.797–0.967, $P<0.001$) with an optimal cutoff value of −11.76% (sensitivity 82.6% and specificity 83.3%). The evaluative value of the adjusted AUC for evaluating patients with complex NSTE-ACS improved after inclusion of GPLS (C statistics, 0.827–0.948, $P<0.001$).

The value of GPLS is significantly associated with the complexity of coronary artery lesions, according to SYNTAX score. Therefore, our study indicates that GPLS could be reproducible and efficient to evaluate the complex coronary artery disease in NSTE-ACS patients.

Abbreviations: 3D-STE = 3-dimensional speckle-tracking echocardiography, AUC = the area under the receiver operator characteristic curve, BMI = body mass index, CABG = coronary artery bypass graft surgery, CAG = coronary angiography, GPLS = 3-dimensional global peak longitudinal strain, HR = heart rate, LDL-C = low-density lipoprotein cholesterol, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, LVESV = left ventricular end-systolic volume, NSTE-ACS = non-ST-segment elevation acute coronary syndromes, PCI = percutaneous coronary intervention, ROC = receiver operator characteristic.

Keywords: 3-dimensional speckle-tracking echocardiography, coronary lesions, longitudinal strain, non-ST-segment elevation acute coronary syndrome, SYNTAX score

Editor: Imo Hoefer.

ZC and JD have contributed equally to the article.

Funding/support: This work was supported in part by the Science and Technology Planning Project of Guangdong Province (2013A022100036 and 2014A020212257), the Shenzhen Innovation Funding (JCYJ20140901003939025 and CXZZ20140901004122087), Key Lab for Health Informatics of Chinese Academy of Sciences, and Guangdong Image-guided Therapy Innovation Team (2011S013).

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

The authors have no conflicts of interest to disclose.

[a] Department of Cardiology, Guangzhou General Hospital of Guangzhou Military Region, PLA, Guangzhou, [b] The Second Affiliated Hospital of Shantou University Medical College, Shantou, [c] Institute of Biomedical and Health Engineering, Shenzhen Institutes of Advanced Technology, Shenzhen, [d] Department of Ultrasound, Guangzhou General Hospital of Guangzhou Military Region, PLA, [e] Southern Medical University, Guangzhou, China.

[*] Correspondence: Lin Xu, Department of Cardiology, Guangzhou General Hospital of Guangzhou Military Region, PLA, Guangzhou 510010, China (e-mail: xxgnk_xlin@126.com); Heye Zhang, Institute of Biomedical and Health Engineering, Shenzhen Institutes of Advanced Technology, Shenzhen 518055, Guangdong, China (e-mail: hy.zhang@siat.ac.cn)

Medicine (2016) 95:39(e4667)

Received: 5 February 2016 / Received in final form: 18 July 2016 / Accepted: 2 August 2016

http://dx.doi.org/10.1097/MD.0000000000004667

1. Introduction

An early evaluation of patients with severe and complex coronary lesions, such as 3-vessel disease and/or left main lesion, plays an important role in the prognosis and selection of reasonable treatment strategy in non-ST-segment elevation acute coronary syndromes (NSTE-ACS) patients. The recent clinical guidelines for the management of NSTE-ACS recommended the early initiation of dual antiplatelet therapy with clopidogrel and aspirin.[1,2] However, dual antiplatelet therapy can increase the risk of perioperative bleeding events in patients undergoing early coronary artery bypass graft (CABG) surgery. Therefore, clinicians might withhold clopidogrel in patients likely to require CABG. The early initiation of dual antiplatelet therapy would postpone CABG because of concern about operative bleeding events. On the other hand, delayed treatment of clopidogrel can increase the fatal events in NSTE-ACS patients.[2] Therefore, in order to guide our further treatment efficiently, we need 1 early (i.e., before angiography) indicator to cost-effectively evaluate the severe and complex coronary lesions.

The synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score was established in the SYNTAX trial.[3] It was reported as "an angiographic tool grading the complexity of coronary artery disease"[4] in 2005. SYNTAX score is a comprehensive angiographic scoring tool based on lesions complexity in coronary vasculature.[5,6] The SYNTAX score could grade the degree of coronary artery stenosis and also assess calcification, tortuosity, bifurcation-, or trifurcation-type lesions in the coronary arteries. However, it is still an invasive method based on coronary angiography.

The real-time 3-dimensional speckle-tracking echocardiography (3D-STE) can noninvasively and quantitatively assess the global and regional myocardial wall motion. The performance of this technology has been compared to the magnetic resonance imaging tagging technique.[7] Recent studies have shown that strain and strain rate in the assessment of myocardial systolic dysfunction was superior to conventional wall motion analysis and left ventricular ejection fraction (LVEF).[7,8] One previous study reported that 3-dimensional global peak longitudinal strain (GPLS) derived from 3D-STE technology can detect subtle change of left ventricular (LV) longitudinal systolic function.[9] Thus, the strain or strain rate has the potential in early evaluation of the complex coronary artery disease. During clinical practice, it is of great importance to identify the NSTE-ACS patients with high probability of complex lesions in early stage for timely and optimally treatment. However, the performance of GPLS in the evaluation of the complex NSTE-ACS has not been carefully examined.

The aim of our study is to investigate the value of GPLS in the evaluation of the complex NSTE-ACS. In this study, we investigate the performance of GPLS in the evaluation of the complex NSTE-ACS using SYNTAX score as a reference standard. In our study, we found that GPLS level could be an independent risk factor to evaluate the complex NSTE-ACS through the multivariate regression analysis.

2. Materials and methods

2.1. Study population

A total of 64 patients (mean age 59.9±9.9 years, 81.4% men) with established diagnosis of NSTE-ACS[10] in the General Hospital of Guangzhou Military Command of People's Liberation Army (PLA) between October 2014 and January 2015 were enrolled into our study. The inclusion criteria manifested the following: typical symptoms of angina pectoris, lasting at least 5 minutes, occurring within 24 hours before admission, and involving an unstable pattern of pain including pain at rest, new-onset, severe or frequent angina, or accelerating angina[1,2]; no conditions precluding evaluation ST-segment changes on electrocardiogram (ECG) such as left bundle branch block, left ventricular hypertrophy, or ventricular pacing; fully assessable ECG on admission; and detailed angiographic data after admission. We excluded patients with persistent new ST-segment elevation in leads other than lead augmented unipolar limb lead (aVR), recent percutaneous coronary intervention (PCI) within 6 months, or previous CABG.[11] Patients with known ischemic heart disease, heart valvular lesions, intraventricular conduction disturbances, arrhythmias, cardiac shock, and poor echocardiographic conditions to take STE examination were excluded. This study was approved by the institutional ethics committee of the General Hospital of Guangzhou Military Command of PLA. Moreover, the informed consent was obtained from all individual participants included in the study.

2.2. Clinical information and laboratory analyses

The clinical information of the participants was recorded within the first 1 hour, such as age, gender, symptom onset, and cardiovascular risk factors including smoking, hypertension, and diabetes. Then the clinical data, including heart rate (HR), systolic blood pressure, diastolic blood pressure, and body mass index (BMI), were measured. Fasting blood test was carried out in the department of clinical biochemistry, including glycosylated hemoglobin, low-density lipoprotein cholesterol (LDL-C, mmol/L), high-density lipoprotein cholesterol (mmol/L), triglycerides (mmol/L), and creatinine (μmol/L). We used a Germany Lee Pa automatic biochemical analyzer (XL300 [Bade Behring, Schwalbach, Germany]) to perform biochemical measurement in our study.

2.3. Echocardiographic image acquisition and analysis

All the echocardiographic image acquisitions were performed in all the subjects immediately within the first 1 hour after their admission. The examinations were carried out independently by 2 experienced examiners who were blinded to the study protocol and patient characteristics. Echocardiographic data were acquired with an ultrasound Vivid E9 system (GE Vingmed Ultrasound AS, Horten, Norway), which was equipped with 1 2-dimensional 3.5-MHz transducer (M5S-D), 1 3-dimensional 3.5-MHz transducer (4C-D), 1 off-line speckle-tracking analysis software, and 1 background processing workstation (EchPAC BT 11.1.0, GE Medical System, Horten, Norway). During the examination, all subjects were connected to the ECG and maintained in the left lateral decubitus position. Two-dimensional transducer was used to collect images of the parasternal long axis, short axis, and apical 4-chamber view for calculating LVEF. Then the 3-dimensional volumetric transducer was used to obtain a clear image of the LV endocardium with an apical 4-chamber view in the 4-dimensional mode. The imaging allows a sector with a depth of 30° and a width of 100° in real time. Then the larger pyramidal volume which was combined by small real-time subvolumes of 4 to 6 cardiac cycles were collected and stored. The frame rate of the volumetric image was 25 to 35 frames/s. Three-dimensional left ventricular end-diastolic volume, left ventricular end-systolic volume (LVESV), and GPLS

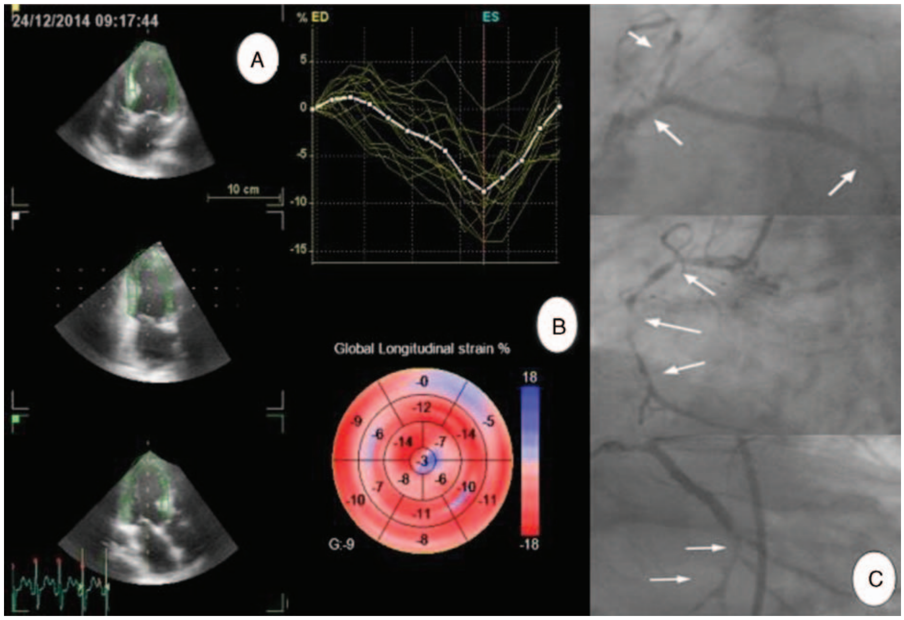

Figure 1. Three-dimensional global peak longitudinal strain (GPLS) and the images of coronary angiography. (A) The software traces the endocardial/epicardial border to include the entire myocardial wall, as shown in the 4-,2-,3-chamber apical views, and the left ventricle is automatically divided into 17 segments. (B) GPLS is therefore automatically provided by the dedicated software and is displayed as the bull's eye plot. (C) The outcomes of coronary angiography. This is a non-ST-segment elevation acute coronary syndromes patient with left main and 3-vessel disease. ED = end-diastolic; ES = end-systolic.

were obtained by the dedicated software (Fig. 1). Patients with poor visualization (more than 2 segments) were excluded from further investigation. Five patients were excluded from our study.

2.4. Angiographic assessment and SYNTAX score

All the patients were required to take coronary angiography examination within the first 12 hours when they were admitted into our hospital. All the coronary angiography (CAG) examinations were performed after the echocardiographic image acquisitions. The radial artery was punctured by the method of Seldinger when the CAG was performed on all patients. Stenosis of more than 50% in the diameter of the left main coronary artery or stenosis of more than 75% in at least 1 major epicardial vessels or their main branches was considered clinically significant. Coronary angiography was performed with a digital subtraction angiography machine (Allura Xper FD20, Philips Medical Systems Nederland B.V. [Veenpluis 4–6, 5684 PC Best, Netherlands]). The SYNTAX scores were calculated after the angiographic procedure using the online calculator version 2.11.[12] The calculations were independently carried out by 2 experienced interventional cardiologists blinded to the study protocol and patient characteristics. When there was disagreement of the scores, the mean of the values was used as the final result. In our study, patient with intermediate or high SYNTAX score (22 and above) was defined as severe and complex NSTE-ACS (high-score group), while low SYNTAX score (0–22) was defined as not severe and complex NSTE-ACS (low-score group).[13]

2.5. Statistical analysis

All continuous variables were presented as mean ± standard deviation or median (25th and 75th percentiles) whether the data were normally distributed or not. The normally distributed was assessed with the Kolmogorov–Smirnov test. Categorical data were presented as frequencies and percentages (%). Comparisons of parametric values among groups (grouping by SYNTAX score: 0–22, 22, and above)[12,13] were performed by Student *t* test and χ^2 test, when appropriate. Correlation between GPLS level and the SYNTAX score was assessed on the basis of 2-tailed Spearman test. Receiver operator characteristic (ROC) curve analysis was performed to discover the optimal cutoff value of GPLS for evaluating patients with intermediate or high SYNTAX scores.

Univariate and multivariate linear regression analyses were used to identify independent variables of high SYNTAX scores. Independent variables in univariate analysis were age, gender, HR, BMI, LDL-C, left ventricular end-systolic volume, left ventricular ejection fraction, diabetes mellitus, hypertension, and GPLS. After performing univariate analysis, significantly obtained variables were selected into the multivariate linear regression analysis with the stepwise method. The incremental value of GPLS over the clinical relevant variables was calculated by the χ^2 test and C statistic in the multivariate logistic regression analysis. ROC curves were constructed for the models 1 and 2. The model 1 combined the clinical relevant variables, while the model 2 is addition of GPLS to the model 1. A 2-tailed *P* value <0.05 was considered to indicate statistical significance. All the statistical analyses were carried out using SPSS software (IBM Company, North Castle, NY).

3. Results

3.1. Patient characteristics

A total of 59 participants met the inclusion criteria, and 5 patients with poor visualization were excluded from our study. Table 1 shows the demographic data, clinical features, laboratory biochemical markers, the CAG results, GPLS, and SYNTAX scores of all patients. The mean SYNTAX score was 19.52 ± 8.09, and 3-vessel disease (including the left main lesion) was

Table 1

Baseline patient characteristics.

Total number	n=59
Age, y	59.9±9.9
Male gender, %	48 (81.4%)
Heart rate	82.8±13.5
BMI, kg/m^2	24.1±2.9
Smoking	37 (62.7)
Hypertension	27 (45.8%)
Systolic blood pressure, mm Hg	126.2±20.1
Diastolic blood pressure, mm Hg	74.5±13.0
Diabetes mellitus	19 (32.2%)
Low-density lipoprotein, mmol/L	3.3±1.2
High-density lipoprotein, mmol/L	1.2±0.3
Triglyceride, mmol/L	2.0±1.9
Creatinine, μmol/L	97.6±44.8
Symptom onset ≤6 h	48 (81%)
Anterior wall MI	41 (69%)
Three-vessel disease	27 (45.8%)
Left ventricular end-diastolic volume, mL	106.0±29.9
Left ventricular end-systolic volume, mL	52.6±22.5
Global 3-dimensional peak longitudinal strain, %	−12.2±3.5
Left ventricular ejection fraction, %	51.7±9.7
SYNTAX score	19.5±8.1
Low (0–22)	36
Intermediate (23–32)	20
High (≥33)	3

Data are presented as number (%) or mean±standard deviation. BMI=body mass index, MI=myocardial infarction, SYNTAX=synergy between percutaneous coronary intervention with taxus and cardiac surgery.

Table 2

Characteristics of patients with low or high synergy between percutaneous coronary intervention with taxus and cardiac surgery score.

	Low score (n=36)	High score (n=23)	P
Age, y	57.7±9.7	63.2±9.4	**0.035**
Male gender, %	32 (89%)	16 (70%)	0.065
Heart rate	81.4±12.7	84.9±14.7	0.336
BMI, kg/m^2	24.2±2.9	24.1±3.0	0.946
Smoking	26 (72%)	11 (48%)	0.061
Hypertension	17 (47%)	10 (43%)	0.780
SBP, mm Hg	130.3±15.5	120.0±24.9	0.085
DBP, mm Hg	76.9±11.2	70.7±15.0	0.070
Diabetes mellitus	7 (19%)	12 (52%)	*0.009*
LDL-C, mmol/L	3.4±1.3	3.2±1.2	0.630
HDL-C, mmol/L	1.2±0.3	1.2±0.3	0.617
Triglyceride, mmol/L	2.3±2.4	1.6±0.8	0.192
Creatinine, μmol/L	93.0±23.3	105.0±65.8	0.315
Symptom onset ≤6 h	30 (83%)	18 (78%)	0.617
Three-vessel disease	11 (31%)	16 (70%)	*0.004*
LV end-diastolic volume, mL	100.8±28.2	114.1±31.2	0.095
LV end-systolic volume, mL	46.03±19.1	62.8±24.1	*0.004*
GPLS, %	−14.0±2.7	−9.5±2.8	*0.000*
LVEF, %	55.3±8.1	46.0±9.3	*0.000*
SYNTAX score	14.7±5.4	26.5±4.7	*0.000*

BMI=body mass index, DBP=diastolic blood pressure, GPLS=global 3-dimensional peak longitudinal strain, HDL-C=high-density lipoprotein cholesterol, LDL-C=low-density lipoprotein cholesterol, LV=left ventricular, LVEF=left ventricular ejection fraction, SBP=systolic blood pressure, SYNTAX=synergy between percutaneous coronary intervention with taxus and cardiac surgery.
Bold and italic values signifies *P* value <0.05 was considered to indicate statistical significance.

present in 27 patients (45.8%). The mean value of GPLS was −12.24±3.50%. Table 2 shows the comparison of patient characteristics divided by SYNTAX score (0–22, 22, and above). Patients with high SYNTAX score had significantly larger age, larger LVESV, higher prevalence of diabetes, and 3-vessel disease ($P<0.05$). The LVEF was significantly lower in the high-score group than in the low-score group ($P<0.001$).

3.2. Univariate and multivariate linear regression analysis

Table 3 shows the results of linear regression analysis for the SYNTAX score. As shown in univariate linear regression analysis, LVESV, LVEF, and GPLS were significantly related to the SYNTAX score ($P<0.001$). As shown in multivariate linear regression analysis, only having diabetes mellitus and GPLS were identified as independent determinants of SYNTAX score (diabetes mellitus: beta 0.253, $P=0.019$; GPLS: beta −0.7, $P<0.001$). However, age, gender, BMI, hypertension, serum lipid, smoking, and HR were not involved into the regression model. In addition, we found the significant correlation between GPLS level and the SYNTAX score ($R=-0.678$, $P<0.001$).

3.3. Prediction of the severity and complexity of NSTE-ACS

A total of 23 patients (39%) were identified as severe and complex NSTE-ACS according to the intermediate or high SYNTAX scores. The absolute value of GPLS decreased from low SYNTAX scores to intermediate or high SYNTAX scores (−14.0±−2.7%, −9.5±−2.8%, respectively, $P<0.001$). The ROC curve analysis (Fig. 1) showed the value of GPLS in the diagnosis of the severe and complex NSTE-ACS by comparing to the SYNTAX score. The area under the ROC curve (AUC) was 0.882 (95% confidence interval [CI], 0.797–0.967, $P<0.001$). The ROC curve analysis revealed that the optimal cutoff value for GPLS in the diagnosis of the severe and complex NSTE-ACS was found to be −11.76%, with a sensitivity of 82.6% and a specificity of 83.3% (Fig. 2). Table 4 shows the results of multivariate logistic regression analysis for evaluating patients with severe and complex NSTE-ACS. The model 2 indicated that

Table 3

Univariate and multivariate linear regression analysis for synergy between percutaneous coronary intervention with taxus and cardiac surgery score.

	Bivariate		Multivariate	
	Beta	P	Beta	P
Dependent variable				
SYNTAX score				
Independent variables				
Age, y	0.161	0.223		
Gender	0.171	0.196	0.001	0.996
BMI	0.107	0.420		
LVESV	0.505	0.000	0.218	0.174
LVEF	−0.514	0.000	0.232	0.213
Heart rate	0.127	0.339		
DM	0.249	0.057	0.253	*0.019*
Hypertension	−0.099	0.454		
Smoking	−0.234	0.074	−0.122	0.267
GPLS	−0.678	0.000	−0.700	*0.000*
LDL-C	0.074	0.578		

BMI=body mass index (kg/m^2), CI=confidence interval, DM=diabetes mellitus, LDL-C=low-density lipoprotein cholesterol, LVEF=left ventricular ejection fraction (%), LVESV=left ventricular end-systolic volume (mL), SYNTAX=synergy between percutaneous coronary intervention with taxus and cardiac surgery.
Italic values signifies *P* value <0.05 was considered to indicate statistical significance.

Table 4

Multivariate logistic regression analysis for evaluating patients with complex acute coronary syndromes.

	Odds ratio	95% CI	χ^2	*P*
Model 1: Clinical relevant variables			41.600	<0.001
DM	6.524	1.527–27.877		0.011
LVEF	0.867	0.793–0.948		0.002
Model 2: Model 1 plus GPLS			45.839	<0.001
GPLS	0.455	0.308–0.673		<0.001
DM	25.600	2.844–130.46		0.004
LVEF	0.189	NS		0.664

Model 1: clinical relevant variables (age, gender, heart rate, smoking, left ventricular end-systolic volume, left ventricular ejection fraction, and diabetes mellitus), model 2: model 1 plus global 3-dimensional peak longitudinal strain. CI = confidence interval, DM = diabetes mellitus, GPLS = 3-dimensional global peak longitudinal strain, LVEF = left ventricular ejection fraction, NS = no significant.

GPLS levels and diabetes mellitus were great predictors to identify the severity and complexity of NSTE-ACS. The evaluative value of GPLS to reflect the complex NSTE-ACS was evaluated by the adjust AUC in models 1 and 2 (Fig. 3). The GPLS provide prominent incremental value over clinical relevant variables in evaluating patients with severe and complex NSTE-ACS, and the C statistics improved from 0.827 (95% CI, 0.719–0.936) to 0.948 (95% CI, 0.896–1.000).

3.4. Reproducibility

A total of 20 patients were randomly chosen for the inter- and intraobserver variability analysis. Inter- and intraobserver agreement for GPLS level and SYNTAX score were calculated. The intraclass correlation coefficient for interobserver comparisons of GPLS levels and SYNTAX scores were 0.91 (95% CI, 0.89–0.96) and 0.93 (95% CI, 0.91–0.97), while the intraobserver comparisons were 0.86 (95% CI, 0.83–0.92) and 0.91 (95% CI, 0.89–0.96), respectively.

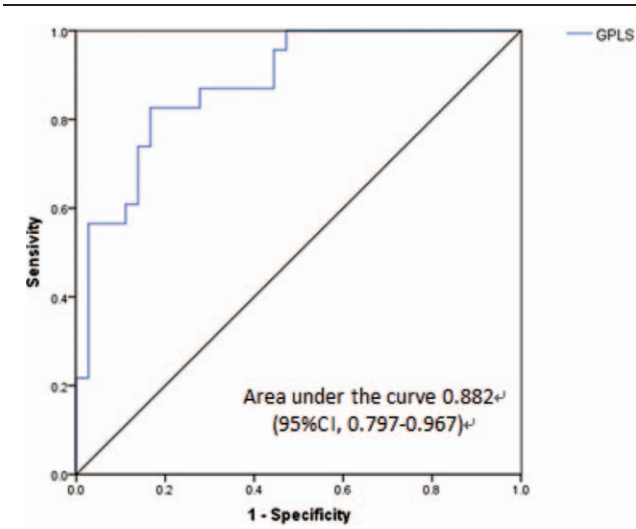

Figure 2. Receiver operating characteristic curve, including the area under the curve for 3-dimensional global peak longitudinal strain to evaluate patients with intermediate or high synergy between percutaneous coronary intervention with taxus and cardiac surgery scores.

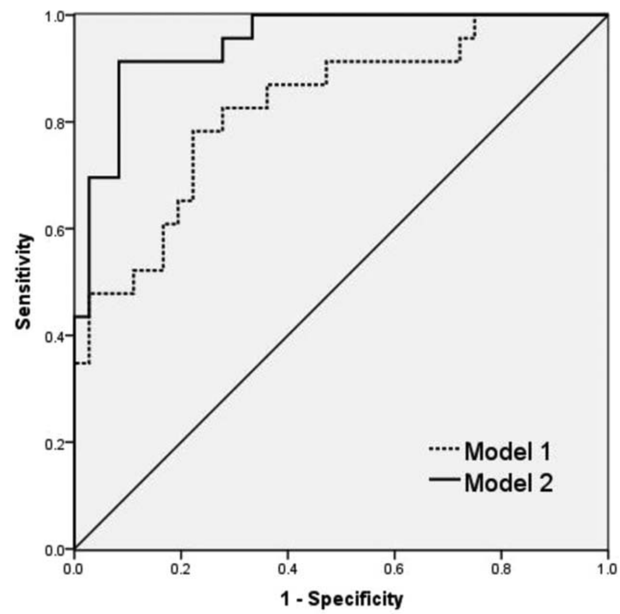

Figure 3. Adjusted receiver operator characteristic curves to predict patients with intermediate or high synergy between percutaneous coronary intervention with taxus and cardiac surgery scores by the models 1 and 2. Model 1: clinically relevant variables (age, gender, heart rate, left ventricular end-systolic volume, left ventricular ejection fraction, and diabetes mellitus), model 2: model 1 plus 3-dimensional global peak longitudinal strain. 95% CI = 95% confidence interval.

4. Discussion

We investigated the diagnostic value of GPLS using 3D-STE technique in the examination of complex coronary disease in NSTE-ACS patients. Our study shows that the GPLS levels were significantly lower in the NSTE-ACS patients with complex coronary artery disease than noncomplex coronary lesion group; GPLS levels could evaluate the complexity of coronary lesions in NSTE-ACS patients after the adjustment for many conventional risk factors for NSTE-ACS.

Patients with suspected NSTE-ACS are a heterogeneous group. Coronary occlusion and/or significant stenosis may or may not be present, which caused different extents of myocardial deformation, and coronary angiography and revascularization therapy might be unnecessary in as many as 1/3 of coronary artery disease (CAD) patients. The 3-year SYNTAX trial showed that CABG remains the better treatment of patients with complex coronary disease, defined by the intermediate or high SYNTAX scores.[3,14] If we could identify the NSTE-ACS patients with complex coronary lesions in early stage, we had the ability to choose the suitable therapeutic strategies and control risk factors at follow-up stage. In our study, the regression analysis showed that diabetes mellitus and low GPLS level were great risk factors in the complexity of NSTE-ACS. While NSTE-ACS patients present with the above factors, they might have the high possibility of complex and severe coronary lesions and deserve to undergo an angiography and withhold clopidogrel therapy to allow early, timely treatment of CABG, not PCI.

4.1. Relationship between SYNTAX score and GPLS

The performance of GPLS in the evaluation of the complex NSTE-ACS has not been carefully studied. In this study, we found that GPLS levels had a strong correlation with the SYNTAX score ($R=-0.678$, $P<0.001$), which was used to calculate the coronary lesions complexity in NSTE-ACS patient. The studies on the use of 3D-STE to assess the extent of coronary artery were rare. However, we found that several previous studies which used 2D-STE to evaluate the myocardial deformation were in agreement with our finding.[15–19] Biering-S⊘rensen et al[16] calculated the GPLS including the 6 basal and 6 middle-ventricular segments ($GPLS_{12}$) to identify the high-risk patients. They reported that $GPLS_{12}$ decreased incrementally with increasing severity of CAD defined by increasing number of coronary lesions. Choi et al[17] had found that the resting GPLS obtained by 2D-STE could identify patients with left main and/or 3-vessel CAD. They showed that the cutoff value of −19.4%, according to the ROC curve analysis, seemed to be helpful for identifying the severe CAD with a sensitivity of 76.3% and a specificity of 74.1%. Our study showed that the optimal cutoff value for identifying patients with intermediate or high SYNTAX scores was −11.76%, with a sensitivity of 82.6% and a specificity of 83.3%. The cause of the discrepancy is the different definition of the complex coronary disease. Choi et al defined complex coronary lesion as patients with left main or 3-vessel disease and not detailed coronary assessment. Furthermore, in the present study, we used SYNTAX score to evaluate the coronary lesion, which has detailed coronary evaluation, including coronary calcification, tortuosity, bifurcation or trifurcation lesions, and so forth. In addition, the study inclusion criteria were not the same. Their study included patients without regional wall motion abnormality, while our research included the type of NSTE-ACS; thus, we hope to refine the further research in the homogeneous population, such as the same LVEF groups comparison and to compare 3D-STE with the 2D-STE technique.

Although 2D-STE was validated for the evaluation of myocardial deformation, 3D-STE has recently been regarded as a more promising technique to accurately and reproducibly evaluate the segmental and global LV function.[20] This was because 3D-STE was not affected by the foreshortened views, avoiding the out of plane motion weakness as the heart moves in and out of the incident imaging plane, making it difficult or impossible to track the same speckle during the heart cycle. Moreover, 3D-STE only needed 1 single apical 4-chamber view to carry out all the analysis. Noteworthy, in our study, 3D-STE demonstrated the ability in detecting the impaired longitudinal deformation caused by NSTE-ACS. This could be explained by the fact that longitudinally orientated myocardial helical fibers are located in the inner myocardium which is most susceptible to myocardial ischemia or transmural infarct.[16] The exact mechanism for the subclinical impairment of myocardial function in patients with NSTE-ACS also has been investigated. Chio et al[17] investigation revealed that repetitive insults to myocardium due to severe coronary stenosis could reduce systolic longitudinal function, while resting regional wall motion remained normal. Edvardsen et al[21] suggested that subclinical myocardial damage could be a marker of coronary atherosclerosis even in the absence of overt myocardial infarction, mainly due to small-vessel microembolization, endothelial dysfunction, and chronic ischemia. In another study, Geer et al[22] described morphological changes in subendocardial myocardium that appeared to be caused by severe and chronic subendocardial ischemia in patients without the evidences of myocardial infarction. These hypotheses could imply that how deformation imaging can recognize the early subclinical myocardial dysfunction and damage. This indicated that the GPLS could provide prominent value compared with conventional echocardiography and stress test in the diagnosis of the coronary disease.

In addition, the risk of exercise stress test was higher in complex coronary disease patients.[23] Therefore, considering GPLS was superior to the LVEF, the ability of GPLS in the assessment of cardiac function has the potential to become clinical use.[24] We believe that 3D-STE can be used as routine examinations for diagnosis and risk stratification of high-risk NSTE-ACS patients and may therefore provide enhanced patient management. We hope to validate the importance of these findings with further large sample studies and then implement this alternative technique into clinical practice.

Results of the logistic regression analysis showed that among the conventional risk factors, only the presence of diabetes mellitus is associated with the higher SYNTAX scores. More importantly, female, hypertension, dyslipidemia, and smoking were not found to be independent risk factors. The previous study had a similar result.[25] Several previous studies had reported that diabetic patients had a greater incidence of triple-vessel or left main coronary artery lesion compared with nondiabetic patients.[26–28]

4.2. Study limitation

The following limitations of this study should be considered: first, this was a retrospective study with a small number of patients at a single center. In spite of this limitation, GPLS derived from 3D-STE technique was found to be an independent predictor in the diagnosis of the complex NSTE-ACS. Second, the patients with or without LV wall motion abnormalities were enrolled in our study. We did not exclude the congestive heart failure patients which was caused by the NSTE-ACS. This may affect the results of the speckle tracking. Because the weakened heartbeat caused by the congestive heart failure would confuse speckle tracking, the pathogenesis of heart failure in our study is definite. The heart failure was all caused by myocardial ischemia or infarction. Third, 3D-STE technique has some limitations, such as the variable algorithms, frequent upgrades of the speckle tracking softwares. The influencing factors for the result of GPLS is the performance of 3D-STE, including spatial resolution, signal noise, temporal resolution, lower optimal frame rate, and the reliability of measurements in patients with tachycardia.[2] 3D-STE was performed on all the patients on the same machine of GE Vivid E9 (Horten, Norway), which had the same frame rate, temporal resolution, and spatial resolution.[20]

5. Conclusion

GPLS assessed by 3D-STE at rest is an independent risk factor of the complex NSTE-ACS patients. The absolute value of GPLS is significantly associated with the complexity of coronary artery lesions in the NSTE-ACS patients, who should promptly take CAG examination and not receive clopidogrel therapy to allow early CABG. The present study indicates that 3D-STE is a noninvasive, reproducible, and efficient tool that has a potential clinical practice to evaluate the coronary lesion in NSTE-ACS patients.

References

[1] Hamm CW, Bassand JP, Agewall S, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2011;32:2999–3054.

[2] Mehta RH, Roe MT, Mulgund J, et al. Acute clopidogrel use and outcomes in patients with non-ST-segment elevation acute coronary syndromes undergoing coronary artery bypass surgery. J Am Coll Cardiol 2006;48:281–6.
[3] Palmerini T, Genereux P, Caixeta A, et al. Prognostic value of the SYNTAX score in patients with acute coronary syndromes undergoing percutaneous coronary intervention: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) trial. J Am Coll Cardiol 2011;57:2389–97.
[4] Sianos G, Morel M, Kappetein A, et al. The SYNTAX Score an angiographic tool grading the complexity of coronary artery disease. Euro Intervion 2005;1:219–27.
[5] Serruys P, Morice M, Kappetein A, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961–72.
[6] Valgimigli M, Serruys PW, Tsuchida K, et al. Cyphering the complexity of coronary artery disease using the syntax score to predict clinical outcome in patients with three-vessel lumen obstruction undergoing percutaneous coronary intervention. Am J Cardiol 2007;99:1072–81.
[7] Brown J, Jenkins C, Marwick TH. Use of myocardial strain to assess global left ventricular function: a comparison with cardiac magnetic resonance and 3-dimensional echocardiography. Am Heart J 2009;157: e101–5.
[8] Hayat D, Kloeckner M, Nahum J, et al. Comparison of real-time three-dimensional speckle tracking to magnetic resonance imaging in patients with coronary heart disease. Am J Cardiol 2012;109:180–6.
[9] Ersboll M, Valeur N, Mogensen UM, et al. Prediction of all-cause mortality and heart failure admissions from global left ventricular longitudinal strain in patients with acute myocardial infarction and preserved left ventricular ejection fraction. J Am Coll Cardiol 2013; 61:2365–73.
[10] Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;64:e139–228.
[11] Kosuge M, Ebina T, Hibi K, et al. Early, accurate, non-invasive predictors of left main or 3-vessel disease in patients with non-ST-segment elevation acute coronary syndrome. Circ J 2009;73:1105–10.
[12] Genereux P, Palmerini T, Caixeta A, et al. SYNTAX score reproducibility and variability between interventional cardiologists, core laboratory technicians, and quantitative coronary measurements. Circ Cardiovasc Intervent 2011;4:553–61.
[13] Yamazaki K, Iijima R, Nakamura M, et al. High-sensitivity cardiac troponin T level is associated with angiographic complexity of coronary artery disease: a cross-sectional study. Heart Vessels 2016;31:890–6.
[14] Kappetein AP, Feldman TE, Mack MJ, et al. Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial. Eur Heart J 2011;32:2125–34.
[15] Alireza R, Maryam S, Yousef R, et al. Diagnostic accuracy of myocardial deformation indices for detecting high risk coronary artery disease in patients without regional wall motion abnormality. Int J Clin Exp Med 2015;8:9412–20.
[16] Biering-S⊘rensen T, Hoffmann S, Mogelvang R, et al. Myocardial strain analysis by 2-dimensional speckle tracking echocardiography improves diagnostics of coronary artery stenosis in stable angina pectoris. Circ Cardiovasc Imaging 2014;7:58–65.
[17] Choi JO, Cho SW, Song YB, et al. Longitudinal 2D strain at rest predicts the presence of left main and three vessel coronary artery disease in patients without regional wall motion abnormality. Eur J Echocardiogr 2009;10:695–701.
[18] Sarvari SI, Haugaa KH, Zahid W, et al. Layer-specific quantification of myocardial deformation by strain echocardiography may reveal significant CAD in patients with non-ST-segment elevation acute coronary syndrome. JACC Cardiovasc Imaging 2013;6:535–44.
[19] Hoshi H, Takagi A, Uematsu S, et al. Risk stratification of patients with non-ST-elevation acute coronary syndromes by assessing global longitudinal strain. Heart Vessels 2014;29:300–7.
[20] Biswas M, Sudhakar S, Nanda NC, et al. Two- and three-dimensional speckle tracking echocardiography: clinical applications and future directions. Echocardiography 2013;30:88–105.
[21] Edvardsen T, Detrano R, Rosen BD, et al. Coronary artery atherosclerosis is related to reduced regional left ventricular function in individuals without history of clinical cardiovascular disease: the Multiethnic Study of Atherosclerosis. Arterioscler Thromb Vasc Biol 2006;26:206–11.
[22] Geer JC, Crago CA, Little WC, et al. Subendocardial ischemic myocardial lesions associated with severe coronary atherosclerosis. Am J Pathol 1980;98:663–80.
[23] Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). J Am Coll Cardiol 2002;40:1531–40.
[24] Krishnasamy R, Isbel NM, Hawley CM, et al. Left ventricular global longitudinal strain (GLS) is a superior predictor of all-cause and cardiovascular mortality when compared to ejection fraction in advanced chronic kidney disease. PLoS One 2015;10:e0127044.
[25] Tanaka T, Seto S, Yamamoto K, et al. An assessment of risk factors for the complexity of coronary artery disease using the SYNTAX score. Cardiovasc Intervent Ther 2013;28:16–21.
[26] Baris N, Akdeniz B, Uyar S, et al. Are complex coronary lesions more frequent in patients with diabetes mellitus. Can J Cardiol 2006;22: 935–7.
[27] Kedhi E, Genereux P, Palmerini T, et al. Impact of coronary lesion complexity on drug-eluting stent outcomes in patients with and without diabetes mellitus: analysis from 18 pooled randomized trials. J Am Coll Cardiol 2014;63:2111–8.
[28] Dortimer A, Shenoy P, Shiroff R, et al. Diffuse coronary artery disease in diabetic patients fact or fiction? Circulation 1978;57:133–6.