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Original Article

Relationship between R-R interval and left ventricular systolic synchrony in subjects with coronary artery disease determined using angiography

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Abstract: The aim of this study was to assess the relationship between R-R interval and left ventricular systolic synchrony in subjects with coronary artery disease determined using angiography. A total of 277 subjects who underwent coronary angiography for suspected CAD were recruited in this study. For all subjects, the R-R interval was quantified using simultaneous ECG, and the times to peak systolic longitudinal strain (Tssl) on 17 LV segments were quantified using four-dimensional (4D) speckle tracking echocardiography (STE) and manually measured. The independent predictors of *R-R* interval using multiple linear regression analyses were the time to peak systolic longitudinal strain in the apical-septal segment (Tssl-Apical-S) (β=0.325, *P*=0.000), smoking status (β=0.141, *P*=0.013), and the time to peak systolic longitudinal strain in the basal-anterolateral segment (Tssl-Basal-AL) (β=0.151, *P*=0.014), which were significantly independently associated with the R-R interval. In multiple regression analyses, smoking status (*OR*, 1.943; 95% *CI*, 1.119-3.375, *P*=0.018), Tssl-Basal-AL (*OR*, 1.002; 95% *CI*, 1.000-1.004, *P*=0.043), the time to peak systolic longitudinal strain in the mid-inferoseptal segment (Tssl-Mid-IS) (*OR*, 1.008; 95% *CI*, 1.003-1.013, *P*=0.004), and Tssl-Apical-S (*OR*, 1.010; 95% *CI*, 1.004-1.016, *P*=0.002) remained independently associated with the risk of a longer *R-R* interval (the median 849.49 ms was set as the cutoff value) in the population. Our findings may provide the basis for future investigations of LV systolic synchrony and cardiac resynchronization therapy.

Keywords: Coronary artery disease, speckle-tracking echocardiography, time to peak, systolic longitudinal strain, *R-R* interval

Introduction

Left ventricular (LV) systolic synchrony is defined as the simultaneous and coordinated activation of certain ventricular segments. Dyssynchrony is defined as impairment of LV systolic synchrony or reduced systolic function and myocardial perfusion, which may lead to reduced exercise capacity, prognosis, and quality of life [1, 2]. Coronary artery disease is the primary cause of morbidity and mortality worldwide [3]. LV mechanical dyssynchrony is less prevalent than dyssynchrony with depressed ejection fraction (EF), but LV mechanical dyssynchrony is evident in coronary artery disease (CAD) patients with preserved EF [4]. Recently, real-time three dimensional echocardiography (RT3DE) was shown to provide an accurate and reproducible quantification of LV systolic synchrony, and as a RT3DE-derived parameter, the time to peak systolic longitudinal strain (Tssl) is a powerful predictor for LV systolic dyssynchrony [5, 6]. To the best of our knowledge, the impact of the *R-R* interval on LV systolic synchrony has not been elucidated. And, a rare report was found that indicated a relationship between the *R-R* interval and left ventricular systolic synchrony in subjects with coronary artery disease, as estimated using angiography. Therefore, the objective of the current study was to investigate the impact of the *R-R* interval on LV systolic synchrony using simultaneous ECG and 4D STE in a carefully defined population with CAD.

Subjects and methods

Study population

A total of 277 subjects who underwent coronary angiography for suspected CAD (mean age, 57.86±9.95 years; range, 38-78 years; 184 male subjects and 93 female subjects) at the

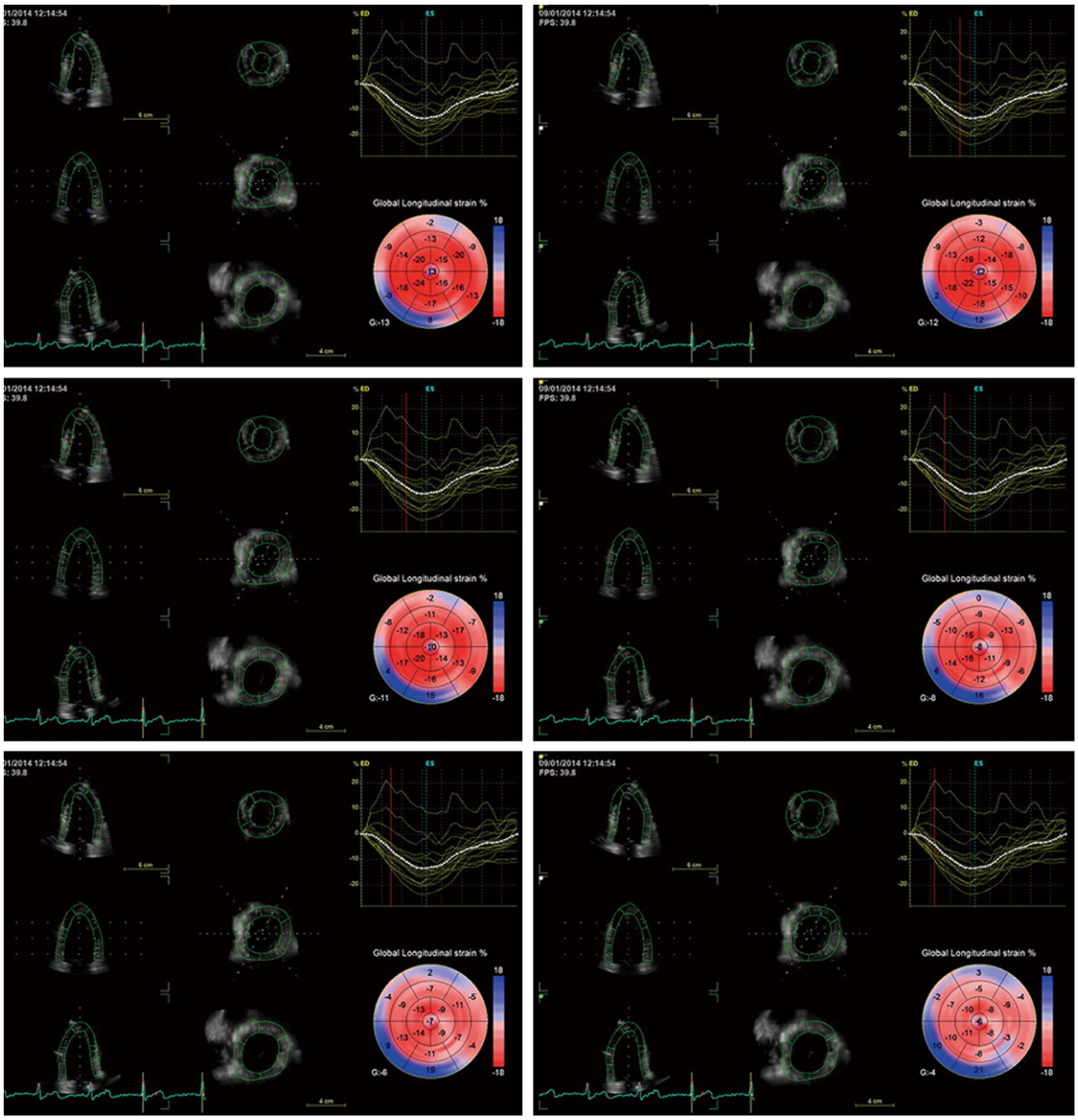

Figure 1. The curve picture of time to peak systolic longitudinal strain (Tssl) which contain 17 segment and 17 segment null eye picture of longitudinal strain. In the curve picture of time to peak systolic longitudinal strain, Yellow curves mean LS-time of 17 segment, white curve means GLS-time. Red line means time to the peak systolic longitudinal strain (Tssl) from ES to ED, we received the strain frame frequency of 17 segment through moving Redline from ES to ED.

First Affiliated Hospital of Xinjiang Medical University (Urmuqi, China) and were recruited from December 20, 2013, to July 31, 2014. All subjects underwent conventional 2D, simultaneous ECG and RT3DE examinations. The exclusion criteria were as follows: (1) unstable clinical conditions, (2) cardiomyopathy, (3) severe valvular heart disease, (4) congenital heart disease or (5) arrhythmias such as atrial fibrillation, atrial flutter, or frequent ventricular ectopy. The study was approved by the ethics committee of the First Affiliated Hospital of Xinjiang Medical University (Urmuqi, China), and written informed consent was obtained from all patients.

Echocardiography

Experienced sonographers using a Vivid E9 ultrasound scanner (GE Vingmed Ultrasound AS, Horten, Norway) with a transthoracic matrix phased-array transducer scanned patients in the left lateral recumbent position while we

conducted simultaneous ECG. RT3DE data were acquired in the LV apical four-chamber, two-chamber, and long-axis views. Grayscale images were obtained with frame rates of 50 to 70 frames/second. Images were acquired during four cardiac cycles to ensure optimal temporal and spatial resolution at a frame rate set to ≥40% of the heart rate [7], which can be manually adjusted from the machine settings to ensure the correct frame rate. Multibeat image acquisition was performed while the patients held their breath to eliminate breathing-related motion artifacts. The sector width and depth were carefully adjusted in order to include the entire LV myocardium, including the epicardial surface, within the pyramidal scan volume.

All data were stored on a hard disk, and the images with source formatting were copied to the workstation for off-line analysis.

LV systolic synchrony

We used EchoPAC BT112 software (GE Vingmed Ultrasound AS). First, R-R interval was calculated using simultaneous ECG. Then the operator selected the RT3DE picture, which was used to obtain the volume frame of the picture by clicking the 4D speckle-tracking software. Curve pictures of the time to peak systolic longitudinal strain (Tssl) for 17 segments and 17 segments of null eye pictures of longitudinal strain were automatically obtained [8, 9]. We obtained the strain frame frequency by moving the Redline from ES to ED (**Figure 1**). The computer automatically calculated the Tssl of 17 LV segments using the formula: Tssl =1000 ÷ volume frame of picture × strain frame frequency.

We calculated Tssl from 17 standard LV segments (six basal, six middle, and five apical segments) according to the American Heart Association and American Society of Echocardiography segmentation schema [10]. Tssl was identified in each segment. Therefore, the following RT3DE of LV systolic synchrony parameters in the present study were used: 1. Tssl in the basal-anterior segment (Tssl-Basal-A); 2. Tssl in the basal-anteroseptal segment (Tssl-Basal-AS); 3. Tssl in the basal-inferoseptal segment (Tssl-Basal-IS); 4. Tssl in the basal-inferior segment (Tssl-Basal-I); 5. Tssl in the basal-inferolateral segment (Tssl-Basal-IL); 6. Tssl in the basal-anterolateral segment (Tssl-Basal-AL); 7. Tssl in the mid-anterior segment (Tssl-Mid-A); 8. Tssl in the mid-anteroseptal segment (Tssl-Mid-AS); 9. Tssl in the mid-inferoseptal segment (Tssl-Mid-IS); 10. Tssl in the mid-inferior segment (Tssl-Mid-I); 11. Tssl in the mid-inferolateral segment (Tssl-Mid-IL); 12. Tssl in the mid-anterolateral segment (Tssl-Mid-AL); 13. Tssl in the apical-anterior segment (Tssl-Apical-A); 14. Tssl in the apical-septal segment (Tssl-Apical-S); 15. Tssl in the apical-inferior segment (Tssl-Apical-I); 16. Tssl in the apical-lateral segment (Tssl-Apical-L); and 17. Tssl in the apical segment (Tssl-Apical).

Independent, blinded observers assessed the observer reliability of our study using 4D STE. The Tssl values could not be calculated if more than 3 strain segments were suboptimal.

Coronary angiography

Coronary angiography was conducted using the Judkins technique [11], and coronary angiography was performed from several projections one minute after the direct intracoronary injection of isosorbide dinitrate (ISDN; 2.5 mg/5 ml solution over 20 s). Significant CAD was diagnosed if there was a 50% diameter stenosis in at least one major epicardial coronary artery or main tributary [12, 13]. Coronary atherosclerosis severity was defined using the Gensini scoring system. The Gensini score was computed by assigning a severity score to each area of coronary stenosis, according to the degree of luminal narrowing and the lesion's geographic importance [14].

Laboratory measurements

Levels of total cholesterol (TCH, mmol/L), triglyceride (TG, mmol/L), fasting blood glucose (FBG, mmol/L), fasting high-density lipoprotein cholesterol (HDL-c, mmol/L), and fasting low-density lipoprotein cholesterol (LDL-c, mmol/L) were determined using enzymatic procedures on an automated autoanalyzer (AU 2700 Olympus, 1st Chemical Ltd, Japan).

Cigarette smoking

Cigarette smoking status was determined using a standardized questionnaire. Status was classified as either "not smoking" or "smoking", and the latter group included both former and current smokers.

Statistical analysis

Data were statistically analyzed using Statistics Package for Social Sciences (ver. 16.0; SPSS

Table 1. The characteristics of the subjects as quartiles of the *R-R* interval

Variable	*R-R* interval (ms)				*Statistical parameter*	*P*
	-763.99 (n=66)	764.00-849.48 (n=72)	849.49-961.31 (n=70)	961.32- (n=69)		
Age (years)	56.61±9.16	57.49±10.59	58.96±9.34	58.32±10.63	0.713	0.545
Sex (male/female)	38/28	49/23	48/22	49/20	3.200	0.362
Smoking status (yes/no)	21/45	27/45	33/37	34/35	5.659	0.129
Total cholesterol (mmol/L)	4.28±1.20	4.10±0.98	4.07±1.20	4.00±0.90	0.813	0.488
Triglycerides (mmol/L)	1.77 (1.20-2.78)	1.63 (1.22-2.41)	1.49 (1.11-2.33)	1.46 (0.88-1.99)	0.479	0.697
Glucose (mmol/L)	5.20 (4.63-7.14)	5.19 (4.65-6.50)	5.22 (4.67-7.21)	5.07 (4.54-6.09)	0.976	0.404
HDL-C (mmol/L)	1.04±0.28	1.05±0.30	1.04±0.25	1.06±0.28	0.123	0.947
LDL-C (mmol/L)	2.49 (1.88-3.25)	2.42 (1.92-3.04)	2.30 (1.82-3.11)	2.35 (1.82-3.09)	0.337	0.799
SBP (mmHg)	139.50 (120.00-180.00)	131.00 (120.00-160.00)	150.00 (120.00-180.00)	150.00 (120.00-170.00)	1.160	0.325
DBP (mmHg)	90 (79.25-108.75)	80 (75.00-109.75)	90 (80.00-110.00)	85 (70.00-110.00)	0.967	0.409
Gensini scores	7.50 (0.00-41.50)	6.50 (0.00-54.25)	20.00 (0.00-40.00)	7.00 (0.00-36.50)	0.196	0.899
Tssl-Basal-A (ms)	250.26±122.35	273.68±100.01	298.92±125.02	331.67±145.03	5.394	0.001
Tssl-Basal-AS (ms)	300.79 (198.83-344.82)	292.13 (233.26-352.99)	326.63 (226.13-403.21)	348.10 (264.43-421.82)	13.496	0.004
Tssl-Basal-IS (ms)	314.01 (259.42-354.74)	289.86 (216.52-356.93)	331.83 (240.60-395.63)	351.97 (237.77-417.15)	12.746	0.005
Tssl-Basal-I (ms)	318.44 (250.28-349.94)	303.42 (238.64366.44-)	318.95 (241.07-379.35)	369.52 (203.56-426.85)	11.974	0.007
Tssl-Basal-IL (ms)	256.78 (149.08-329.09)	292.29 (165.61-330.69)	286.60 (174.59-361.46)	373.83 (156.49-423.12)	14.122	0.003
Tssl-Basal-AL (ms)	251.26 (91.85-327.03)	287.66 (185.54-334.38)	331.80 (194.72-399.62)	375.34 (247.17-418.60)	27.065	0.000
Tssl-Mid-A (ms)	285.69 (245.90-329.01)	308.79 (269.91-350.98)	328.66 (301.27-368.61)	355.19 (296.21-391.59)	26.426	0.000
Tssl-Mid-AS (ms)	291.91 (262.04-318.69)	307.57 (261.37-335.48)	325.56 (293.35-356.43)	337.08 (300.03-385.54)	22.909	0.000
Tssl-Mid-IS (ms)	295.08 (267.56-317.26)	308.72 (270.27-329.39)	328.43 (304.54-356.68)	348.53 (313.60-378.35)	43.008	0.000
Tssl-Mid-I (ms)	290.01 (265.61-330.35)	304.57 (273.88-338.40)	326.92 (301.27-360.50)	329.46 (304.89-375.38)	24.881	0.000
Tssl-Mid-IL (ms)	281.91 (203.31-328.48)	293.61 (234.27-353.89)	321.00 (272.73-355.23)	346.82 (298.30-388.87)	20.290	0.000
Tssl-Mid-AL (ms)	292.53 (212.08-337.89)	309.16 (233.29-358.70)	333.70 (293.91-382.61)	33.33 (262.65-379.38)	16.296	0.001
Tssl-Apical-A (ms)	295.03 (251.29-331.19)	290.80 (216.78-343.44)	327.25 (295.80-352.65)	349.08 (303.31-382.66)	28.374	0.000
Tssl-Apical-S (ms)	296.25 (267.81-327.66)	309.32 (266.74-337.65)	331.49 (309.96-353.83)	344.26 (313.27-375.64)	43.775	0.000
Tssl-Apical-I (ms)	304.97 (268.64-329.70)	306.78 (289.02-336.31)	327.53 (301.27-349.89)	341.30 (314.80-373.37)	32.762	0.000
Tssl-Apical-L (ms)	295.47 (271.48-328.27)	297.12 (263.53-329.63)	334.01 (305.71-354.28)	346.42 (314.56-374.77)	37.715	0.000
Tssl-Apical (ms)	309.67 (263.23-346.83)	299.70 (261.28-339.31)	341.09 (275.99-380.14)	375.00 (329.75-419.66)	31.394	0.000

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; Tssl-Basal-A, the time to peak systolic longitudinal strain in the basal-anterior segment; Tssl-Basal-AS, the time to peak systolic longitudinal strain in the basal-anteroseptal segment; Tssl-Basal-IS, the time to peak systolic longitudinal strain in the basal-inferoseptal segment; Tssl-Basal-I, the time to peak systolic longitudinal strain in the basal-inferior segment; Tssl-Basal-IL, the time to peak systolic longitudinal strain in the basal-inferolateral segment; Tssl-Basal-AL, the time to peak systolic longitudinal strain in the basal-anterolateral segment; Tssl-Mid-A, the time to peak systolic longitudinal strain in the mid-anterior segment; Tssl-Mid-AS, the time to peak systolic longitudinal strain in the mid-anteroseptal segment; Tssl-Mid-IS, the time to peak systolic longitudinal strain in the mid-inferoseptal segment; Tssl-Mid-I, the time to peak systolic longitudinal strain in the mid-inferior segment; Tssl-Mid-IL, the time to peak systolic longitudinal strain in the mid-inferolateral segment; Tssl-Mid-AL, the time to peak systolic longitudinal strain in the mid-anterolateral segment; Tssl-Apical-A, the time to peak systolic longitudinal strain in the apical-anterior segment; Tssl-Apical-S, the time to peak systolic longitudinal strain in the apical-septal segment; Tssl-Apical-I, the time to peak systolic longitudinal strain in the apical-inferior segment; Tssl-Apical-L, the time to peak systolic longitudinal strain in the apical-lateral segment; Tssl-Apical, the time to peak systolic longitudinal strain in the apical segment.

Table 2. The Spearman correlation between subjects' characteristics and *R-R* interval

Variables	Relationship coefficient	*P* value
Age (years)	0.081	0.177
Total cholesterol (mmol/L)	-0.068	0.264
Triglycerides (mmol/L)	-0.117	0.053
Glucose (mmol/L)	-0.070	0.247
HDL-C (mmol/L)	0.039	0.519
LDL-C (mmol/L)	-0.045	0.455
SBP (mmHg)	0.072	0.235
DBP (mmHg)	-0.039	0.521
Gensini scores	0.018	0.772
Tssl-Basal-A (ms)	0.268	0.000
Tssl-Basal-AS (ms)	0.222	0.000
Tssl-Basal-IS (ms)	0.185	0.002
Tssl-Basal-I (ms)	0.197	0.001
Tssl-Basal-IL (ms)	0.222	0.000
Tssl-Basal-AL (ms)	0.348	0.000
Tssl-Mid-A (ms)	0.313	0.000
Tssl-Mid-AS (ms)	0.215	0.000
Tssl-Mid-IS (ms)	0.395	0.000
Tssl-Mid-I (ms)	0.285	0.000
Tssl-Mid-IL (ms)	0.303	0.000
Tssl-Mid-AL (ms)	0.232	0.000
Tssl-Apical-A (ms)	0.345	0.000
Tssl-Apical-S (ms)	0.449	0.000
Tssl-Apical-I (ms)	0.380	0.000
Tssl-Apical-L (ms)	0.379	0.000
Tssl-Apical (ms)	0.339	0.000

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; Tssl-Basal-A, the time to peak systolic longitudinal strain in the basal-anterior segment; Tssl-Basal-AS, the time to peak systolic longitudinal strain in the basal-anteroseptal segment; Tssl-Basal-IS, the time to peak systolic longitudinal strain in the basal-inferoseptal segment; Tssl-Basal-I, the time to peak systolic longitudinal strain in the basal-inferior segment; Tssl-Basal-IL, the time to peak systolic longitudinal strain in the basal-inferolateral segment; Tssl-Basal-AL, the time to peak systolic longitudinal strain in the basal-anterolateral segment; Tssl-Mid-A, the time to peak systolic longitudinal strain in the mid-anterior segment; Tssl-Mid-AS, the time to peak systolic longitudinal strain in the mid-anteroseptal segment; Tssl-Mid-IS, the time to peak systolic longitudinal strain in the mid-inferoseptal segment; Tssl-Mid-I, the time to peak systolic longitudinal strain in the mid-inferior segment; Tssl-Mid-IL, the time to peak systolic longitudinal strain in the mid-inferolateral segment; Tssl-Mid-AL, the time to peak systolic longitudinal strain in the mid-anterolateral segment; Tssl-Apical-A, the time to peak systolic longitudinal strain in the apical-anterior segment; Tssl-Apical-S, the time to peak systolic longitudinal strain in the apical-septal segment; Tssl-Apical-I, the time to peak systolic longitudinal strain in the apical-inferior segment; Tssl-Apical-L, the time to peak systolic longitudinal strain in the apical-lateral segment; Tssl-Apical, the time to peak systolic longitudinal strain in the apical segment.

Incorporated, Chicago, IL, USA). Subjects were classified into 4 groups according to R-R interval quartiles. Data for age, TCH, HDL-C, LDL-c and Tssl-Basal-A were normally distributed parameters and presented as the means ± SD. Comparisons of these parameters were analyzed using one-way ANOVA. Skewed data, including TG, FBG, SBP, DBP, Tssl-Basal-AS, Tssl-Basal-IS, Tssl-Basal-I, Tssl-Basal-IL, Tssl-Basal-AL, Tssl-Mid-A, Tssl-Mid-AS, Tssl-Mid-IS, Tssl-Mid-I, Tssl-Mid-IL, Tssl-Mid-AL, Tssl-Apical-A, Tssl-Apical-S, Tssl-Apical-I, Tssl-Apical-L, Tssl-Apical and Gensini score, are expressed as medians and quartile ranges, and comparisons were analyzed using the Kruskal-Wallis H test. Categorical variables of gender and smoking status were compared using chi-squared analysis. The Spearman two-way test assessed the relationship between subjects' characteristics and *R-R* interval, and we evaluated independent predictors of *R-R* interval using multiple regression analyses. *OR* for the presence of a longer *R-R* interval (the median *R-R* interval was set as the cutoff value) was determined using univariate and multivariate logistic regression. Logistic regressions are presented with 95% *CI*. Significance was identified if the null hypothesis could be rejected with >95% confidence. All *p*-values are two-tailed.

Results

Baseline characteristics of the subjects grouped according to the quartile of R-R interval

Table 1 shows the baseline characteristics of the subjects grouped according to the quartile of *R-R* interval. The *R-R* interval of the subjects in the present study ranged from 363.13 ms to 1425.00 ms, with a median of 849.49 ms (quartile range, 764.00-961.32 ms). Significant differences in the Tssl-Basal-A (*P*=0.001), Tssl-Basal-AS (*P*=0.004), Tssl-Basal-IS (*P*=0.005), Tssl-Basal-I (*P*=0.007), Tssl-Basal-IL (*P*=0.003), Tssl-Basal-AL (*P*=0.000), Tssl-Mid-A (*P*=0.000), Tssl-Mid-AS (*P*=0.000), Tssl-Mid-IS (*P*=0.000), Tssl-Mid-I (*P*=0.000), Tssl-Mid-IL (*P*=0.000), Tssl-Mid-AL (*P*=0.001), Tssl-Apical-A (*P*=0.000), Tssl-Apical-S (*P*=0.000), Tssl-Apical-I (*P*=0.000), Tssl-Apical-L (*P*=0.000), and Tssl-Apical (*P*=0.000) levels were observed between the various groups, but no significant differences were found between the groups in the distribution of age (*P*=0.545), sex

Table 3. Predictors of *R-R* interval from multiple linear regression between subjects

Variable	Non-standardized Coefficient		Standardized Coefficients	t	p
	B	Std. Error	(Beta)		
Constant	570.701	40.995	----	13.921	0.000
Tssl-Apical-S (ms)	0.717	0.134	0.325	5.332	0.000
Smoking status (yes or no)	40.058	16.039	0.141	2.498	0.013
Tssl-Basal-AL (ms)	0.159	0.065	0.151	2.464	0.014

Tssl-Basal-AL, the time to peak systolic longitudinal strain in the basal-anterolateral segment; Tmsv-Apical-S, the time to peak systolic longitudinal strain in the apical-septal segment.

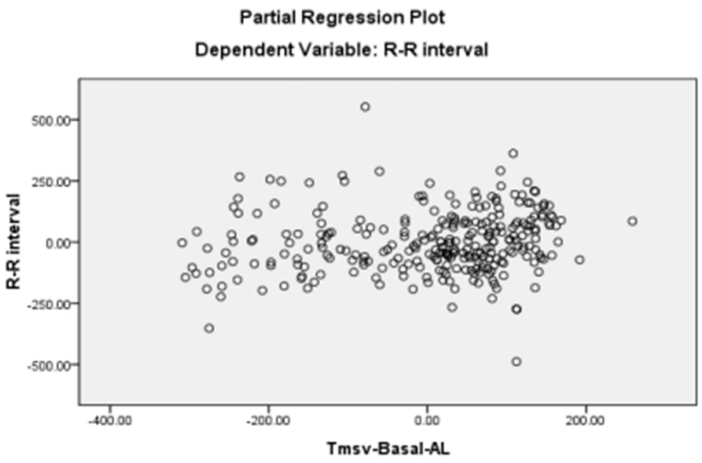

Figure 2. Partial regression plot of Tmsv-Basal-AL (*R-R* interval as dependent variable).

(*P*=0.362), smoking status (*P*=0.129), TCH (*P*=0.488), TG (*P*=0.697), FBG (*P*=0.404), HDL-C (*P*=0.947), LDL-C (*P*=0.799), SBP (*P*=0.325), DBP (*P*=0.409), or Gensini score (*P*=0.899).

Spearman correlations between R-R interval, age and clinical and biochemical characteristics

Table 2 shows the results of the Spearman correlations among the *R-R* interval, age and clinical and biochemical characteristics. Spearman correlation analyses indicated that the *R-R* interval was positively associated with Tssl-Basal-A (*r*=0.268, *P*=0.000), Tssl-Basal-AS (*r*=0.222, *P*=0.000), Tssl-Basal-IS (*r*=0.185, *P*=0.002), Tssl-Basal-I (*r*=0.197, *P*=0.001), Tssl-Basal-IL (*r*=0.222, *P*=0.000), Tssl-Basal-AL (*r*=0.348, *P*=0.000), Tssl-Mid-A (*r*=0.313, *P*=0.000), Tssl-Mid-AS (*r*=0.215, *P*=0.000), Tssl-Mid-IS (*r*=0.395, *P*=0.000), Tssl-Mid-I (*r*=0.285, *P*=0.000), Tssl-Mid-IL (*r*=0.303, *P*=0.000), Tssl-Mid-AL (*r*=0.232, *P*=0.000), TsslApicalA (*r*=0.345, *P*=0.000), Tssl-Apical-S (*r*=0.449, *P*=0.000), Tssl-Apical-I (*r*=0.380, *P*=0.000), Tssl-Apical-L (*r*=0.379, *P*=0.000), and Tssl-Apical (*r*=0.339, *P*=0.000).

Multiple linear regression analysis with the R-R interval as a dependent variable

Multiple linear regression analysis was performed to examine the independent associations between R-R interval and LV systolic synchrony. In this model, the *R-R* interval was used as the dependent variables and the independent variables included age, sex, smoking status, TCH, TG, FBG, HDL-C, LDL-C, SBP, DBP, Gensini score, and all 17 LV systolic synchrony parameters in the present study. Tssl-Apical-S (β=0.325, *P*=0.000), smoking status (β=0.141, *P*=0.013), and Tssl-Basal-AL (β=0.151, *P*=0.014) were significantly independently associated with the *R-R* interval in the final model (**Table 3**; **Figures 2**, **3**).

Univariate logistic regression analysis of characteristics between the shorter-and longer-R-R-interval groups

Table 4 shows the results of univariate logistic regression for the presence of a longer R-R interval (the median (849.49 ms) was set as the cutoff value). The results indicated that the risk for the presence of a longer R-R interval increased 0.9% with a 1-ms increase in Tssl-Mid-IS (odds ratio [*OR*], 1.009; 95% confidence interval [*CI*], 1.002-1.017, *P*=0.009) in the present population.

Multivariate logistic regression analysis of characteristics between the shorter- and longer-R-R-interval groups

Multivariate logistic regression (Forward: Conditional method) was used to identify the independent risk factors for a longer *R-R* interval (the median 849.49 ms was set as the cutoff value) in the present population. We included age, sex, smoking status, TCH, TG, FBG, HDL-C,

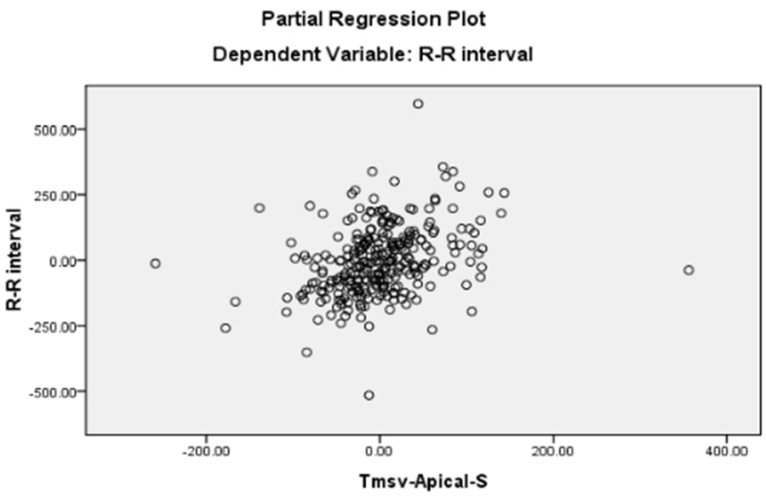

Figure 3. Partial regression plot of Tmsv-Apical-S *(R-R* interval as dependent variable).

LDL-C, SBP, DBP, Gensini score, and all 17 LV systolic synchrony parameters in the multivariate model in the study. The results are reported in **Table 5** as adjusted *OR*s and the respective confidence intervals at 95%. Smoking status (*OR*, 1.943; 95% *CI*, 1.119-3.375, *P*=0.018), Tssl-Basal-AL (*OR*, 1.002; 95% *CI*, 1.000-1.004, *P*=0.043), Tssl-Mid-lS (*OR*, 1.008; 95% *CI*, 1.003-1.013, *P*=0.004), and Tssl-Apical-S (*OR*, 1.010; 95% *CI*, 1.004-1.016, *P*=0.002) remained independently associated with the risk of a longer *R-R* interval in the population.

Discussion

This hospital-based cross-sectional study of adult Chinese patients with CAD demonstrated the following main findings. The Tssl of 17 LV segments were significantly and positively associated with R-R interval. The Tssl in the apical-septal segment, smoking status, and the Tssl in the basal-anterolateral segment were significantly independently associated with the *R-R* interval. Smoking status, Tssl in basal-anterolateral segment, Tssl in mid-inferoseptal segment, and Tssl in apical-septal segment remained independently associated with the risk of a longer R-R interval in the population. To the best of our knowledge, this is the first study to focus on the relationship between the R-R interval and left ventricular systolic synchrony.

The cardiac cycle is a complete heartbeat from its generation to the beginning of the next beat, comprising diastole, systole, and the intervening pause. The frequency of the cardiac cycle is described as the heart rate, and the time of the cardiac cycle is described as the *R-R* interval. Each beat of the heart involves five major stages: early diastole, atrial systole, isovolumic contraction, ventricular ejection, and isovolumic relaxation time [15]. Each cycle takes 0.8 seconds under normal circumstances; the systole phase takes 0.3 seconds, and the diastole phase takes 0.5 seconds [16]. The heart is a four-chambered organ that consists of right and left halves. The role of the left ventricle is to pump newly oxygenated blood to the body through the aorta. According to American Heart Association Scientific Statement, the heart should be divided into 17 segments for assessment of the myocardium and the left ventricular cavity [10]. The time to peak systolic longitudinal strain in (Tssl) of 17 LV segments has recently received much attention as an LV systolic synchrony parameter [17-19]. Resting heart rate predicts longevity and cardiovascular diseases, and current evidence suggests that it is also an important marker of outcome in cardiovascular disease, including coronary artery disease [20]. Therefore, it is necessary to explore the factors associated with the *R-R* interval as the time indicator of the resting heart rate in subjects with coronary artery disease.

Tobacco smoking is associated with cardiovascular levels [21]. A study from India in 88 18- to 30-year-old healthy male volunteers with CAD risk factors including higher resting heart rate, central obesity, and adverse serum lipid showed that the RR interval was shorter in smokers than in non-smokers, which was highly statistically significant [22]. The results of the present study contradict those of previous studies. The multiple linear regression analysis results indicated that smoking was significantly independently associated with the *R-R* interval, and the results from multivariate logistic regression identified smoking as an independent risk factor for a longer *R-R* interval compared to non-smokers. The risk for smokers to suffer from an *R-R* interval greater than 849.49 ms (resting heart rate fewer than 71 beats per minute) increased 94.3%. The mechanism

Table 4. Univariate logistic regression for the presence of a longer *R-R* interval (the median 849.49 ms was set as the cutoff value)

Variable	All subjects			
	B	OR	*95% CI*	P
Age (years)	0.000	1.000	0.966, 1.036	0.978
Sex (male/female)	-0.722	0.486	0.203, 1.163	0.105
Smoking status (yes/no)	0.388	1.473	0.714, 3.039	0.294
Total cholesterol (mmol/L)	-0.527	0.591	0.189, 1.846	0.365
Triglycerides (mmol/L)	0.083	1.087	0.787, 1.501	0.614
Glucose (mmol/L)	-0.034	0.967	0.866, 1.080	0.548
HDL-C (mmol/L)	0.607	1.834	0.417, 8.068	0.422
LDL-C (mmol/L)	0.393	1.481	0.426, 5.157	0.537
SBP (mmHg)	0.017	1.017	0.999, 1.035	0.070
DBP (mmHg)	-0.022	0.978	0.954, 1.003	0.082
Gensini scores	-0.002	0.998	0.989, 1.006	0.618
Tssl-Basal-A (ms)	0.000	1.000	0.997, 1.004	0.781
Tssl-Basal-AS (ms)	-0.001	0.999	0.996, 1.002	0.412
Tssl-Basal-IS (ms)	0.000	1.000	0.997, 1.003	0.954
Tssl-Basal-I (ms)	-0.002	0.998	0.995, 1.001	0.224
Tssl-Basal-IL (ms)	0.001	1.001	0.998, 1.004	0.377
Tssl-Basal-AL (ms)	0.002	1.002	1.000, 1.005	0.085
Tssl-Mid-A (ms)	0.001	1.001	0.997, 1.005	0.669
Tssl-Mid-AS (ms)	-0.003	0.997	0.992, 1.002	0.189
Tssl-Mid-IS (ms)	0.009	1.009	1.002, 1.017	0.009
Tssl-Mid-I (ms)	0.001	1.001	0.996, 1.006	0.745
Tssl-Mid-IL (ms)	0.000	1.000	0.996, 1.003	0.813
Tssl-Mid-AL (ms)	0.001	1.001	0.998, 1.004	0.510
Tssl-Apical-A (ms)	0.002	1.002	0.999, 1006	0.184
Tssl-Apical-S (ms)	0.007	1.007	0.999, 1.016	0.087
Tssl-Apical-I (ms)	0.000	1.000	0.992, 1.007	0.906
Tssl-Apical-L (ms)	0.002	1.002	0.998, 1.007	0.284
Tssl-Apical (ms)	0.001	1.001	0.998, 1.005	0.380

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; Tssl-Basal-A, the time to peak systolic longitudinal strain in the basal-anterior segment; Tssl-Basal-AS, the time to peak systolic longitudinal strain in the basal-anteroseptal segment; Tssl-Basal-IS, the time to peak systolic longitudinal strain in the basal-inferoseptal segment; Tssl-Basal-I, the time to peak systolic longitudinal strain in the basal-inferior segment; Tssl-Basal-IL, the time to peak systolic longitudinal strain in the basal-inferolateral segment; Tssl-Basal-AL, the time to peak systolic longitudinal strain in the basal-anterolateral segment; Tssl-Mid-A, the time to peak systolic longitudinal strain in the mid-anterior segment; Tssl-Mid-AS, the time to peak systolic longitudinal strain in the mid-anteroseptal segment; Tssl-Mid-IS, the time to peak systolic longitudinal strain in the mid-inferoseptal segment; Tssl-Mid-I, the time to peak systolic longitudinal strain in the mid-inferior segment; Tssl-Mid-IL, the time to peak systolic longitudinal strain in the mid-inferolateral segment; Tssl-Mid-AL, the time to peak systolic longitudinal strain in the mid-anterolateral segment; Tssl-Apical-A, the time to peak systolic longitudinal strain in the apical-anteriorsegment; Tssl-Apical-S, the time to peak systolic longitudinal strain in the apical-septal segment; Tssl-Apical-I, the time to peak systolic longitudinal strain in the apical-inferior segment; Tssl-Apical-L, the time to peak systolic longitudinal strain in the apical-lateral segment; Tssl-Apical, the time to peak systolic longitudinal strain in the apical segment.

underlying this inconsistency is not clear, but the results from the present study are convincing because a multivariate analysis was used. Therefore, physicians and society may use the results of this study in efforts to persuade smokers to stop smoking as soon as possible.

The Tssl of 17 LV segments was significantly positively associated with *R-R* interval, but only the Tssl in the basal-anterolateral segment and the Tssl in the apical-septal segment were significantly independently associated with the *R-R* interval. The Tssl in the basal-anterolateral segment, Tssl in the mid-inferoseptal segment, and Tssl in the apical-septal segment remained independently associated with the risk of a longer *R-R* interval in our population. To the best of our knowledge, this is the first study to focus on the relationship between *R-R* interval and left ventricular systolic synchrony. However, the exact mechanism underlying these associations is not known. A previous study demonstrated that the excitatory waves initially reach the endocardial aspect of the LV at three points simultaneously: (1) an area high on the anterior paraseptal wall just below the mitral valve, (2) a central area in the left side of the interventricular septum, and (3) the posterior paraseptal area at approximately one-third of the distance from the apex to the base [23]. A study in seven isolated normal human hearts by Durrer and colleagues in the mid-1970s may partially explain the results of the present study. Our findings may provide the basis for future investigations of LV systolic synchrony and cardiac resynchronization therapy.

In conclusion, this study demonstrates that strain parameters measured using 3D STE strain analyses are useful for detecting severe multivessel coronary artery stenosis and that GLS and GAS are more valuable indicators that may provide a conve-

Table 5. Multivariate logistic regression for the presence of a longer *R-R* interval (the median, 849.49 ms, was set as the cutoff value)

Characteristic	All subjects			
	B	OR	*95% CI*	P
Smoking status (no/yes)	0.664	1.943	1.119, 3.375	0.018
Tssl-Basal-AL (ms)	0.002	1.002	1.000, 1.004	0.043
Tssl-Mid-IS (ms)	0.008	1.008	1.003, 1.013	0.004
Tssl-Apical-S (ms)	0.010	1.010	1.004, 1.016	0.002
Constant	-6.597	0.001	------	0.000

Tssl-Basal-AL, the time to peak systolic longitudinal strain in the basal-anterolateral segment; Tssl-Mid-IS, the time to peak systolic longitudinal strain in the mid-inferoseptal segment; Tmsv-Apical-S, the time to peak systolic longitudinal strain in the apical-septal segment.

nient and non-invasive method for identifying severe multi-vessel coronary stenosis.

Limitations

The present study must be interpreted within the context of its potential limitations. First, the sample size was relatively small. Second, this study investigated only the relationship between the R-R interval and the time to peak systolic longitudinal strain in 17 LV segments; we did not study the mechanism underlying the association. Third, the present study was a single-center cross-sectional study. Therefore, a prospective multicenter large-sample study is needed. Finally, echocardiographic measurements such as Tssl, are prone to measurement errors due to poor visualization.

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Disclosure of conflict of interest

None.

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