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Original Article

Effects of coronary revascularization by elective percutaneous coronary intervention on cardiac autonomic modulation assessed by heart rate variability: a single-center prospective cohort study

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Abstract: Objective: To study the effects of coronary revascularization using elective percutaneous coronary intervention (PCI) on autonomic modulation assessed by heart rate variability measurement (HRV) in coronary artery disease (CAD) patients. Methods: A single-center prospective cohort study included 100 patients were included undergoing elective PCI excluding those with contraindication to contrast or dual antiplatelet therapy, atrial fibrillation or multiple premature beats, receiving anti-arrhythmic drugs and those who underwent previous PCI or coronary artery bypass graft (CABG). Short-term measurement of time domain parameters (mean, SDNN, RMSSD) and frequency domain parameters (LF component, HF component, LF/HF ratio) of HRV was performed at the same time of the day, pre-PCI, 24 hours and 6 months post-PCI by CheckMyheart™ handheld HRV device. 5-min HRV analysis software was used to interpret the data using standard methods of HRV measurement of the Task Force of The European Society of Cardiology (ESC) and The North American Society of Pacing and Electrophysiology. SYNTAX (SX) score was calculated before PCI and residual SYNTAX (rSS) score was calculated after PCI using SYNTAX score calculator software. Results: The mean age of the studied population was 56.89±10.75 years with 85% males. HRV time and frequency domain parameters showed a statistically significant improvement at different time intervals (before PCI, 24 hours and 6 months after PCI) (*p*-value <0.001). HRV time and frequency domain measures showed a statistically significant difference between time and frequency domain HRV parameters 24 hours and 6 months after PCI in patients who had complete revascularization (CR) with those who had incomplete revascularization (IR). (*p*-value <0.001). Conclusion: Autonomic modulation in CAD patients was improved by coronary revascularization using PCI assessed by serial HRV measurement. Patients with CR had better autonomic modulation than those with IR assessed by HRV 24 and 6 months after PCI.

Keywords: Coronary artery disease, coronary revascularization, percutaneous coronary intervention, autonomic modulation, heart rate variability, syntax score, residual syntax score, complete revascularization, major adverse cardiovascular and cerebrovascular events

Introduction

Cardiac autonomic dysfunction is commonly associated with increased risk of cardiovascular morbidity and mortality [1]. It is now well established that decreased heart rate variability (HRV) is an independent risk factor for sudden cardiac death (SCD) in patients with CAD or previous myocardial infarction [2]. It is also an independent predictor of increased cardiovascular risk in patients with diabetes mellitus (DM) [3].

CAD patients and exercise-induced angina pectoris have a state of sympathetic overactivity [4]. Myocardial ischemia is the trigger of this sympathetic hyperactivity. So, theoretically coronary revascularization using

PCI can result in restoration of normal cardiac autonomic function assessed by the standard methods for HRV measurement of the Task Force of the European Society of Cardiology (ESC) and The North American Society of Pacing and Electrophysiology [5]. Objective: The study aimed to assess coronary revascularization effects by elective PCI in CAD patients on cardiac autonomic modulation assessed by HRV.

Patients and methods

Study population: The study was designed as a single-center prospective cohort study included 100 patients.

Inclusion criteria:

• Patients undergoing elective PCI when clinically indicated by patient's symptoms or if there was evidence of ischemia either by a stress test, a viability study or post-acute coronary syndrome (ACS).

Exclusion criteria:

• Patients with contraindication to contrast or dual antiplatelet therapy.

• Patients with atrial fibrillation or multiple premature beats, receiving anti-arrhythmic drugs.

• Patients with previous PCI or Coronary Artery Bypass Graft (CABG).

Informed consent was acquired from all participants. The ethical committee of the hospital approved the study protocol.

Clinical evaluation: Full history taking, thoughtful clinical examination, routine laboratory investigations including (hemoglobin %, creatinine level) a standard 12 lead electrocardiogram (ECG) and a 2D transthoracic echocardiography (TTE) were obtained from all patients.

Coronary angiographic data: SYNTAX (SX) score before PCI and residual SYNTAX (rSS) score after PCI was done were calculated using SYNTAX score calculator software. Complete revascularization (CR) was defined as rSS <8 while Incomplete revascularization was defined as rSS ≥ 8.

Heart rate variability measurement: 5-minute (short-term) HRV measurement was performed pre-PCI, 24 hours and 6 months post-PCI at the same time of the day by CheckMyheart™ handheld HRV device manufactured by DailyCare BioMedical Inc, Taiwan. Data were interpreted by CheckMyheart™ 5-min HRV analysis software using the standard methods for HRV measurement as analyzed in the Task Force of the ESC and the NASPE with emphasis on HRV time domain measures including the mean-time, SDNN and RMSSD (**Table 1**) and HRV frequency domain measures including low frequency (LF), high frequency (HF) and LF/HF ratio (**Table 2**).

Table 1. Summary of used time-domain measures of HRV

Variable	Unit	Description
Mean time	ms	Time average of RR interval
SDNN	ms	Standard deviation of all normal to normal (NN) intervals
RMSSD	ms	Square root of the mean of the sum of the square of differences between adjacent NN interval

ms = milliseconds.

Table 2. Summary of used frequency-domain measures of HRV

Variable	Units	Description	Frequency range
LF	ms^2	Low frequency power	0.04-0.15 Hz
HF	ms^2	High frequency power	0.15-0.4 Hz
LF/HF		Ratio between low to high frequency power	

ms^2 = millisecond square.

Follow-up: Our studied cases were followed-up post-PCI for major adverse cardiovascular and cerebrovascular events (MACCE) occurrence. Follow-up time intervals were during hospital stay, 1-month and 6-month post-PCI.

Statistical analysis of the data: Statistical analysis was done using IBM SPSS software package version 20.0. (Armonk, NY: IBM

Corp). Number and percent were used to describe qualitative data. Range (minimum, maximum), mean, standard deviation (SD) and median were used to describe quantitative data. Significant level was set at 5%.

Statistical tests used:

1. Chi-square test for categorical variables comparing different groups.

2. Fisher's Exact correction for chi-square if >20% of the cells have expected count <5.

3. Mann Whitney test for abnormally distributed quantitative variables comparing two groups.

4. Kruskal Wallis test for abnormally distributed quantitative variables comparing between more than two groups.

5. Wilcoxon signed ranks test for abnormally distributed quantitative variables, to comparing two periods.

6. Friedman test for abnormally distributed quantitative variables, to compare between more than two periods or stages.

7. Spearman coefficient to correlate between two distributed abnormally quantitative variables.

Results

Baseline demographic and clinical data

The mean age of the studied population was 56.89±10.75 years, with 85% males. (The demographic and clinical data of the studied population illustrated in **Table 3**).

Coronary angiographic and PCI data

Multi-vessel CAD was found in 42 patients while single-vessel CAD was found in 58 patients.

The mean SX was 13.11±8.52.90 patients (90%) had CR, while 10 patients (10%) had IR with a mean rSS of 2.0±5.77 (**Table 3**).

Table 3. Baseline demographic, clinical and angiographic data of the studied population (n=100)

Table (1)	
1. Demographic data	
Age (years)	56.89±10.75
Male Sex	85 (85%)
2. Risk factors	
Diabetes Mellitus	41 (41%)
Hypertension	47 (47%)
Smoking	79 (79%)
Family history of CAD	11 (11%)
Dyslipidemia	8 (8%)
Others	4 (4%)
3. Indication for intervention	
Typical ischemic symptoms	6 (6%)
Positive stress test	8 (8%)
Post-ACS	86 (86%)
4. Clinical data	
Mean heart rate (beats/minute)	77.95±11.79
Mean LVEF (%)	54.03±11.08
5. Coronary angiographic and PCI data	
Single-vessel CAD	58 (58%)
Mean SX score	13.11±8.52
TIMI III distal flow	65 (65%)
Complete revascularization (CR)	90 (90%)
rSS	2.0±5.77
Results are shown in % and numbers of patients	

ACS = Acute Coronary Syndrome; LVEF = left ventricular ejection fraction; SX = SYNTAX Score; rSS = residual SYNTAX Score.

HRV parameters in relation to different time intervals of PCI

A statistically significant difference was found between HRV parameters at different time intervals (Pre-PCI, 24 hours and 6 months post-PCI). Time domain parameters (mean time, SDNN, RMSSD) and frequency domain measures (LF and HF) showed a significant increase while LF/HF ratio revealed a statistically significant reduction at different time intervals (pre-PCI, 24 hours and 6 months post-PCI) (*P*-value <0.001) (**Table 4**; **Figure 1**).

Table 4. HRV parameters before PCI, 24 hours and 6 months after PCI

	HRV Parameters	Before PCI (n=100)	After PCI		FrX^2	P
			24 hours (n=100)	6 months (n=92)#		
Time domain	Mean (ms)					
	Mean ± SD.	685.11±46.82	775.40±57.57	864.02±37.78	184.0*	<0.001*
	% of change		↑13.2	↑11.4		
	Sig. bet. Periods	p_1<0.001*, p_2<0.001*, p_3<0.001*				
	SDNN (ms)					
	Mean ± SD.	11.90±3.36	19.55±4.56	29.72±4.61	184.0*	<0.001*
	% of change		↑64.3	↑52.0		
	Sig. bet. Periods	p_1<0.001*, p_2<0.001*, p_3<0.001*				
	RMSSD (ms)					
	Mean ± SD.	7.17±2.05	12.52±2.98	20.47±3.68	184.0*	<0.001*
	% of change		↑74.6	↑63.5		
	Sig. bet. Periods	p_1<0.001*, p_2<0.001*, p_3<0.001*				
Frequency domain	LF (ms^2)					
	Mean ± SD.	42.23±6.81	56.21±8.72	71.68±8.83	200.0*	<0.001*
	% of change		↑33.1	↑27.5		
	Sig. bet. Periods	p_1<0.001*, p_2<0.001*, p_3<0.001*				
	HF (ms^2)					
	Mean ± SD.	11.65±3.49	22.28±6.07	39.72±8.26	184.000*	<0.001*
	% of change		↑91.25	↑78.28		
	Sig. bet. Periods	p_1<0.001*, p_2<0.001*, p_3<0.001*				
	LF/HF (ms^2)					
	Mean ± SD.	3.80±0.72	2.65±0.54	1.85±0.29	184.0*	<0.001*
	% of change		↓30.3	↓30.2		
	Sig. bet. Periods	p_1<0.001*, p_2<0.001*, p_3<0.001*				

#: 8 cases (3 cases were lost to follow up, 1 case had non-cardiac death, 4 cases had MACCE), % of change: between each successive interval. X^2: Chi-square for Friedman test. Sig between periods was done using Wilcoxon signed ranks test. p: *p*-value for comparison between the different intervals. p_1: *p*-value for comparison between before and after 24 hours after PCI. p_2: *p*-value for comparison between before and after 6 months after PCI. p_3: *p*-value for comparison between 24 hours and after 6 months after PCI. *: Statistically significant at P ≤ 0.05.

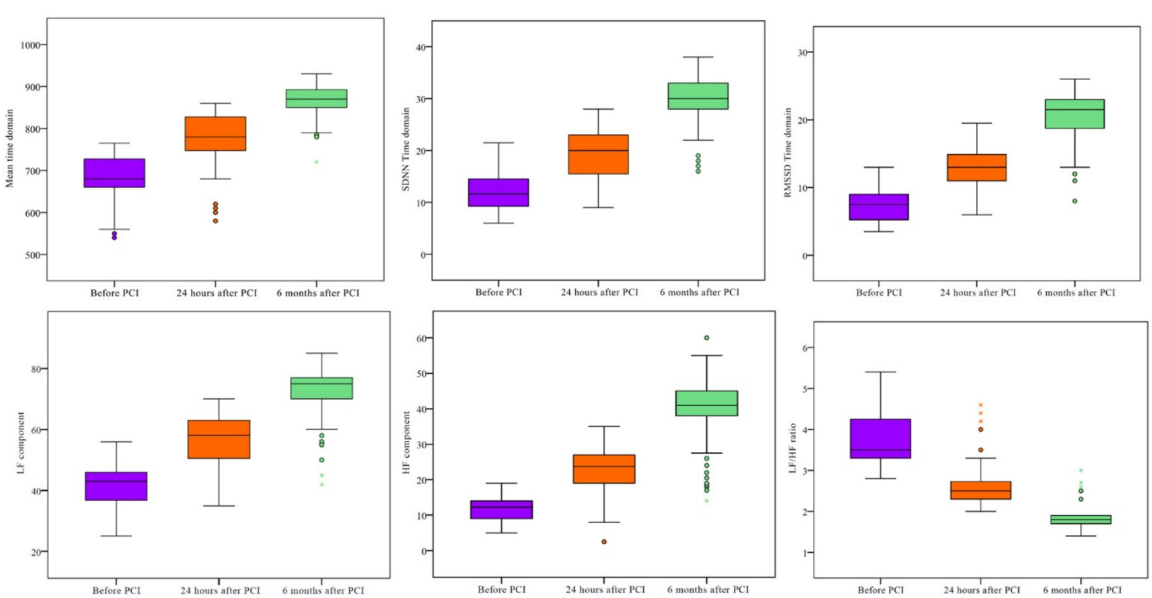

Figure 1. Correlation between HRV parameters at different time intervals before, showing a significant improvement 24 hours and 6 months after PCI.

HRV parameters in relation to type of revascularization at different time intervals

A statistically significant difference was found between HRV time and frequency domain parameters 24 hours post-PCI in patients who had CR with those who had IR. Time domain parameters included mean time, SDNN, RMSSD which was lower in patients with RSS ≥ 8 and statistically higher in patients with rSS <8 (*P*-value <0.001). Frequency domain parameters included LF, HF was lower in patients with rSS ≥ 8 and higher in patients with rSS <8 while LF/HF ratio was higher in patients with rSS ≥ 8 and higher in patients with rSS <8 (*P*-value <0.001) (**Table 5**; **Figure 2**).

Table 5. Relation between RSS and different HRV parameters 24 hours after PCI (n=100)

	HRV parameters 24 hours after PCI	RSS		U	P
		<8 (n=90)	≥ 8 (n=10)		
Time domain	Mean (ms)				
	Mean ± SD.	787.94±40.79	622.5±65.37	4.766*	<0.001*
	SDNN (ms)				
	Mean ± SD.	20.46±3.82	11.45±1.92	4.986*	<0.001*
	RMSSD (ms)				
	Mean ± SD.	13.13±2.43	7.05±0.83	5.047*	<0.001*
Frequency domain	LF (ms^2)				
	Mean ± SD.	58.11±6.85	39.10±3.28	5.029*	<0.001*
	HF (ms^2)				
	Mean ± SD.	23.62±4.64	10.18±2.35	5.500*	<0.001*
	LF/HF (ms^2)				
	Mean ± SD.	2.50±0.27	3.95±0.58	5.117*	<0.001*

U, p: U and *p* values for Mann Whitney test for comparing between the two groups. *: Statistically significant at P ≤ 0.05.

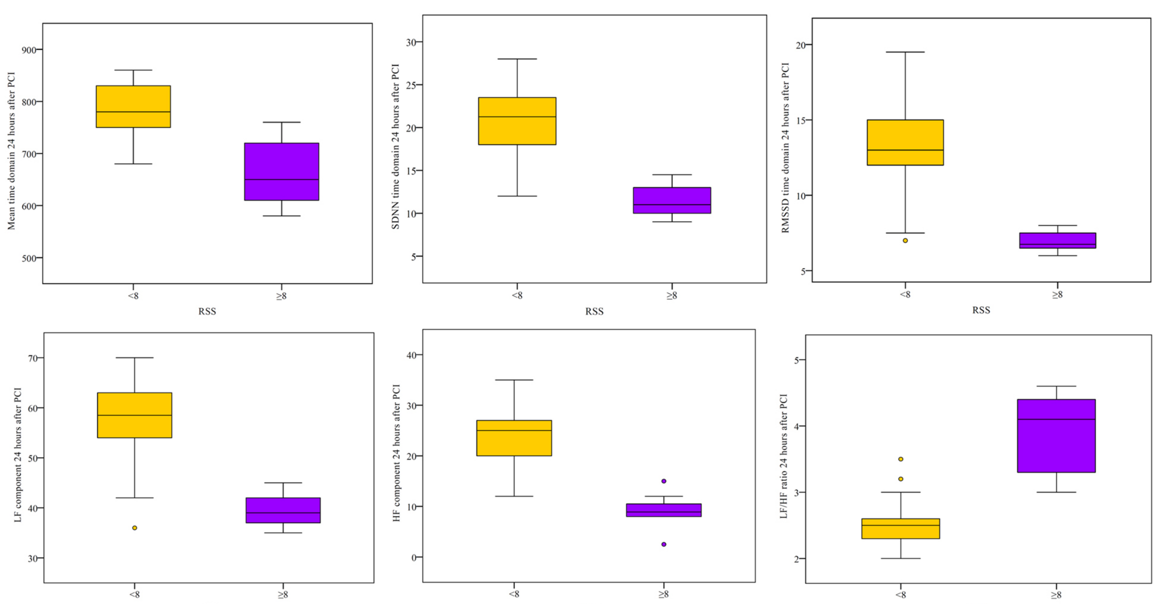

Figure 2. Relation between different HRV parameters and rSS 24 hours after PCI.

Also, there was a significant difference between HRV parameters 6 months post-PCI in patients who had CR with those who had IR. Mean time, SDNN, RMSSD of time domain which was lower in patients with RSS ≥ 8 and higher in patients with rSS <8 (*P*-value <0.001). Frequency domain parameters included LF, HF which was significantly lower in patients with rSS ≥ 8 and higher in patients with rSS <8 while LF/HF ratio was higher in patients with rSS ≥ 8 and higher in patients with rSS <8 (*P*-value <0.001) (**Table 6**; **Figure 3**).

Table 6. Relation between revascularization and different HRV parameters after 6 months of PCI (n=92)

	HRV parameters after 6 months	Revascularization		U	P
		Complete (n=87)	Incomplete (n=5)		
Time domain	Mean				
	Mean ± SD.	868.91±31.54	779.0±39.12	14.000*	<0.001*
	SDNN				
	Mean ± SD.	30.33±3.92	19.20±2.77	8.500*	<0.001*
	RMSSD				
	Mean ± SD.	20.98±3.04	11.60±2.30	8.500*	<0.001*
Frequency domain	LF				
	Mean ± SD.	72.90±7.28	50.50±6.48	8.500*	<0.001*
	HF				
	Mean ± SD.	40.95±6.62	18.40±3.11	5.000*	<0.001*
	LF/HF				
	Mean ± SD.	1.80±0.19	2.76±0.23	2.500*	<0.001*

U, p: U and *p* values for Mann Whitney test for comparing between the two groups. *: Statistically significant at P ≤ 0.05. #: 8 cases were excluded (3 cases lost to follow-up, 1 case had non-cardiac death, 4 cases had MACCE).

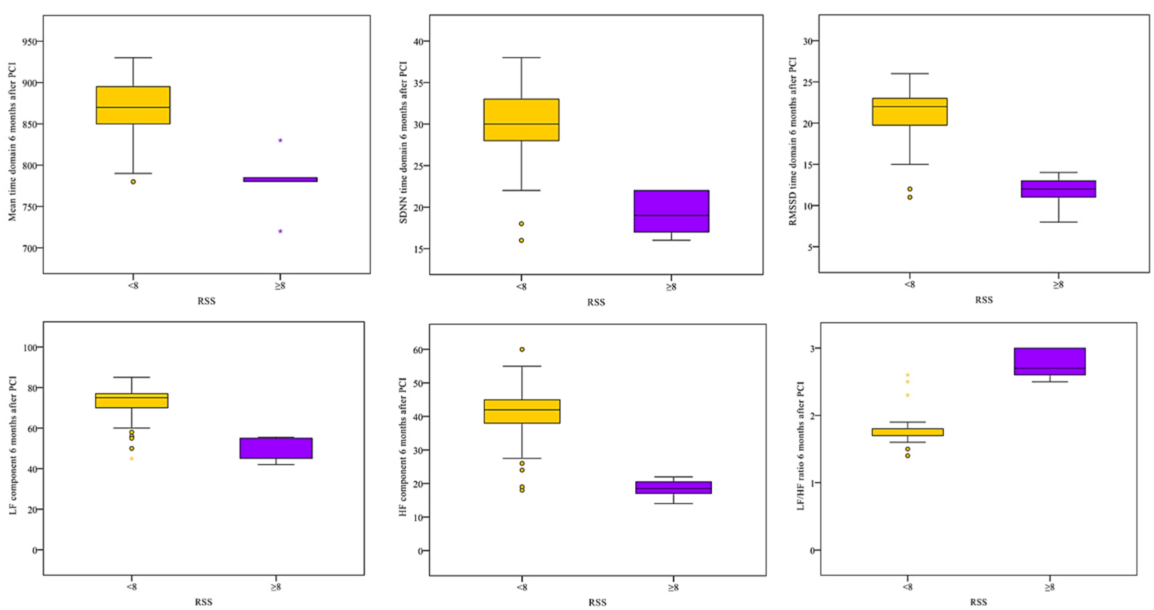

Figure 3. Relation between different HRV parameters and rSS 6 months after PCI.

Follow-up

Our cases were followed-up during hospital stay, 1- and 6-month post-PCI MACCE occurrence. During follow-up, three patients were lost to follow-up and four patients experienced MACCE, sudden cardiac death occurred in three patients, reinfarction at the territory of the target vessel of revascularization occurred in one patient while non-cardiac death occurred in one patient (hepatocellular carcinoma).

All four patients who had MACCE had a multi-vessel CAD with a mean SYNTAX score of 31.50±11.71. All patients had IR with a mean rSS of 22.75±7.96. No statistically significant difference was found between HRV parameters before and 24 hours after PCI in all patient who had MACCE (**Table 7**; **Figure 4**).

Table 7. Comparison between different HRV parameters before and 24 hours after PCI in patients who had MACCE (n=4)

	HRV parameters	Before PCI	24 hours after PCI	Wx	P
Time domain	Mean (ms)				
	Mean ± SD.	560.0±18.26	602.50±17.08	1.841	0.066
	% of change		↑7.59%		
	SDNN (ms)				
	Mean ± SD.	6.25±0.50	9.75±0.50	1.857	0.063
	% of change		↑56.0%		
	RMSSD (ms)				
	Mean ± SD.	4.25±0.87	6.50±0.41	1.890	0.060
	% of change		↑52.9%		
Frequency domain	LF (ms^2)				
	Mean ± SD.	32.50±2.52	37.75±2.99	1.890	0.059
	% of change		↑16.15%		
	HF (ms^2)				
	Mean ± SD.	6.18±0.72	8.50±1.0	1.841	0.066
	% of change		↑37.5%		
	LF/HF (ms^2)				
	Mean ± SD.	5.25±0.17	4.45±0.19	1.841	0.066
	% of change		↓15.24%		

Sig between periods was done using Wilcoxon signed ranks test. *: Statistically significant at $P \leq 0.05$.

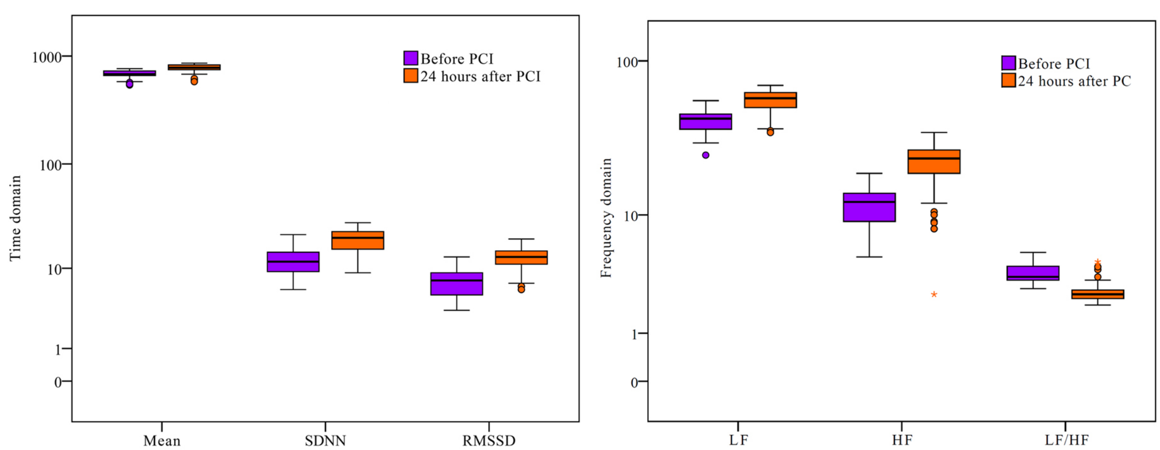

Figure 4. Comparison between HRV time and Frequency domain before and 24 hours after PCI in patients who had MACCE.

Discussion

Our study included 100 patients undergoing elective PCI with a broad spectrum of patient selection including patients with all different indications for intervention such as patients with typical anginal symptoms or positive stress testing also, post-ACS patients either unstable angina or post-MI angina patients with or without a viability study. Unlike all previous studies [1], in our study we calculated SX score and rSS to quantify the CAD complexity pre- and post-PCI and its correlation to HRV parameters.

Our study revealed a significant increase in HRV parameters 24 hours as well as 6 months post-PCI in comparison to HRV parameters pre-PCI. Similar results were obtained by Bonnemeier et al. [6] who conducted a study to assess the impact of successful reperfusion induced by primary PCI in 123 acute myocardial infarction (AMI) patients on HRV time and frequency domain parameters which were analyzed from 2-lead 24-hours Holter monitoring. The study concluded that AMI early reperfusion induced a significant improvement of HRV parameters indicating the regain of balance between parasympathetic and sympathetic activities. HRV parameters were significantly lesser in patients with late perfusion compared to those with early reperfusion so, early reperfusion has a beneficial effect by normalization of HRV parameters, reflecting attenuation of cardiac autonomic impairment that results in better outcome in AMI patients. Also, Sedziwy et al. [2] conducted a study to evaluate HRV parameters pre- and during a one-year follow-up post-PCI in 65 patients with or without MI history who underwent successful and uncomplicated PCI. Time domain parameters of HRV were measured from serial 24-hour Holter monitoring (before PCI, 14 days, 3-, 6- and 12-month post-PCI). A significant improvement of time domain HRV parameters mainly noted during the first 3-month follow-up with no additional significant changes in HRV valves in 6- and 12-month post-PCI. The main conclusions of the study that myocardial revascularization with successful PCI resulted in an enhancement of HRV parameters which reflect improvement in the autonomic modulation of heart rate, the increase in parasympathetic control of the heart rate was already being observed 2 weeks after successful PCI and beneficial increased influence of both parts of the autonomic nervous system on heart rate persisted for 12 months after PCI.

Other studies were conducted aiming to assess the effect of elective PCI on HRV parameters in patients with CAD. Aydinlar et al. [7] aimed to analyze parameters reflecting the sympathovagal control of ventricular depolarization and repolarization (HRV parameters and QT interval dispersion (QTd)) in patients undergoing elective PCI, and to determine whether HRV parameters correlated with corrected QT interval dispersion (QTcd) parameters in 26 consecutive patients undergoing elective PCI. The main conclusions of the study were that successful PCI caused an improvement in the autonomic control of the heart immediately after PCI and an improvement in HRV parameters, indicating parasympathetic nervous activation was negatively correlated with QTcd after PCI and successful PCI may improve ventricular repolarization abnormalities, and therefore it may reduce the incidence of ventricular arrhythmias.

Abrootan et al. [8] in 2015 conducted a study aiming to study the impact of PCI on HRV parameters. 64 patients admitted for elective PCI who were enrolled. Short-term HRV measurement of time domains were done before PCI and 24 hours post-PCI at the same daytime with a noted significant improvement of SDNN time domain of HRV parameters 24 hours after successful PCI. The study concluded that revascularization eliminate the state of sympathetic hyperactivity associated with myocardial ischemia and restore the balance between sympathetic and parasympathetic autonomic control of the heart which can be proven by noninvasive techniques such as HRV measurement.

Our current study was the 1st to score the CAD complexity using SX score before PCI and rSS after PCI to identify patients who had complete revascularization (rSS <8) and those who had incomplete revascularization (rSS ≥ 8) and to correlate it to HRV parameters as quantitative assessment of cardiac autonomic modulation. It showed a statistically significant difference between HRV parameters 24 hours and 6 months after PCI in patients who had complete revascularization with those who had incomplete revascularization.

Several studies were concerned with the issue of type of revascularization to be adopted in patients with multi-vessel CAD. Nikolsky et al. [9] compared CR to IR in multi-vessel CAD diabetic patients who underwent PCI and demonstrated that CR patients had a significantly higher 5-year survival rate and significantly higher MI-free survival. Chung et al. [10] studied the benefit of CR patients with multi-vessel CAD in the DES era. He concluded that in multi-vessel CAD patients treated with DES, CR was associated with the long-term benefit in reducing any or cardiac death and MI. The main beneficiaries of CR were those with diabetes, reduced LVEF and low eGFR. Song et al. [11] proved that CR strategy using DES in patients with multi-vessel CAD was associated with lower incidence of MACCE compared to IR strategy. Généreux et al. [12] quantified the extent and complexity of residual coronary stenoses following PCI using a novel approach of calculating the rSS and evaluated its impact on adverse ischemic outcomes. He concluded that the rSS is useful to quantify and risk-stratify the degree and complexity of residual stenosis after PCI. Specifically, RSS >8.0 after PCI in patients with moderate- and high-risk ACS is associated with a poor 30-day and 1-year prognosis. Witberg et al. [13] studied the incremental impact of rSS on long-term clinical outcomes in patients with multi-vessel CAD treated by PCI and concluded RSS ≤ 8 was associated with a significant reduction in 3-year MACCE Loutfi et al. [14] studied the impact of rSS on the outcome of revascularization in Patients with STEMI and Multi-vessel CAD and concluded that CR (RSS <8) improved mid-term survival and reduced the incidence of repeat PCI in patients with STEMI and Multi-vessel CAD. Zhang et al. [15] examined the clinical outcomes of CR and IR at five-year follow-up after PCI of an unprotected left main CAD with DES and concluded that IR was associated with worse long-term clinical outcomes than CR. Bravo et al. [16] conducted a database review using 9 RCTs comparing CR versus culprit-only revascularization in STEMI with multi-vessel CAD. Concluded that compared to culprit-only intervention, CR strategy may be superior due to lower proportions of long-term MACCE. Song et al. [17] this study assessed the prognostic capacity of rSS in a large single centre cohort of patients undergoing PCI in clinical practice and he concluded that After multivariate analysis, rSS was an independent predictor of 2-year cardiac death, myocardial infarction, revascularization, and MACCE. Jang et al. [18] evaluated the clinical impact of the rSS after PCI in patients with chronic total occlusion (CTO) and multi-vessel CAD and concluded that an RSS ≤ 12 after PCI may reduce the risk of cardiac mortality and could be a measure of reasonable IR in patients with CTO and multi-vessel CAD. Braga et al. [19] to assess the prognostic impact of rSS in patients with STEMI and multi-vessel CAD undergoing primary-PCI. He concluded that rSS was an independent predictor of MACCE and all-cause mortality during follow-up.

In our study during the follow-up intervals, 4 patients had MACCE, 3 of them had sudden cardiac death and one patient had reinfarction at the territory of the target vessel of revascularization. All MACCE patients had multi-vessel CAD with a with mean SYNTAX score of 31.50±11.71. All patients had incomplete revascularization with a mean RSS of 22.75± 7.96. All MACCE patients had reduced HRV parameters before PCI with no statistically significant improvement of HRV parameters 24 hours after PCI.

Janszky et al. [20] conduced The Stockholm Female Coronary Risk Study to assess the role of HRV parameters in the long-term prognosis of middle-aged women with established CAD concluding that low HRV was a predictor of longterm mortality amongst middle-aged women with CAD when measured 3-6 months after hospitalization for an ACS, even after controlling for established clinical prognostic markers.

Lanza et al. [21] assessed the prognostic value of ventricular arrhythmias (VA) and HRV in patients with unstable angina through a multicentered prospective study that enrolled 543 consecutive patients with unstable angina and preserved left ventricular function. Patients underwent 24-hours ECG Holter monitoring within 24-hour of hospital admission. The study concluded that unstable angina patients with preserved myocardial function, both VA and HRV are independent predictors of in-hospital and medium-term mortality, suggesting that these factors should be taken into account in the risk stratification of these patients.

Hillebrand et al. [22] performed a meta-analysis of studies assessing the association between HRV and CAD to study the association between HRV and incident cardiovascular events in populations without known CAD. He concluded that depressed HRV was associated with a 32-45% increase in the risk of the first cardiovascular event in patients without known CAD. 1% increase in SDNN was associated with 1% reduction of fatal or non-fatal CAD.

Harris et al. [23] examined the prognostic effects of HRV measurement for ACS patients presented to Emergency Department. 193 patients were enrolled with 24-hour Holter recordings were initiated within 45 minutes of emergency department arrival. Recordings with ≥ 18 hours of sinus rhythm were selected for HRV analysis. Time domain, frequency domain, and nonlinear HRV were examined. Survival analysis was performed with primary outcomes were all-cause rehospitalization or death between ED discharge and end of follow-up. The study concluded that HRV measured close to the ACS onset may assist in risk stratification. HRV cutpoints may provide additional, incremental prognostic information to established assessment guidelines, and may be worthy of additional study.

Heldeweg et al. [24] in 2016 investigated a novel cardiovascular risk stratification model incorporating vital signs, ECG variables and HRV parameters for patients presenting with chest pain conducting a single-center, observational cohort study on 763 patients presenting with chest pain. Eligible patients were >21 years of age and had a sinus rhythm. The primary endpoint of the study was 1-month MACCE in comparing a non-invasive method using ECG and HRV to thrombolysis in myocardial infarct (TIMI) score using receiver operating characteristic (ROC) analysis concluding that a non-invasive risk stratification method based on ECG and HRV was beneficial in comparison to TIMI score. Further research was required to externally validate the results.

Study limitations

Several limitations were encountered in our study. First, the study was a single-center cohort prospective study that involved a relatively small number of patients. Second, lack of randomization, as PCI with either complete or incomplete revascularization, was done only if clinically indicated by patient's symptoms or if there was an evidence of ischemia either by a stress test or a viability study. Third, Regarding the MACCE group of patients, a low number of patients was involved with a short time to follow-up.

Study recommendations

A large-scale randomized study is recommended to define the patient factors linked to reduced HRV in CAD patients before PCI, Multicentric large scale randomized trials are required for further validation of usefulness of HRV as one of the prognostic assessor for CAD, A large-scale randomized prospective study is recommended to confirm the positive correlation between revascularization by PCI by PCI and improvement of HRV parameters after PCI in CAD patients and to define the effect of completeness of revascularization on cardiac autonomic modulation assessed by HRV measurement.

Based on the results and conclusions of the current study, we do recommend performing total revascularization whenever feasible in patients with CAD for an improved autonomic modulation and overall survival.

Conclusion

Coronary revascularization was associated with improved HRV parameters 24 hours and 6 months post-PCI. Complete revascularization whenever feasible is recommended in patients with CAD for an improved autonomic modulation and overall survival.

Disclosure of conflict of interest

None.

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