Risk of Post-Percutaneous Coronary Intervention Adverse Cardiac Events: What does the Autonomic Nervous Systems have to do with it?

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Abstract

Post percutaneous intervention (PCI) outcomes have improved in the last 10 years due to advancements in equipment, techniques and follow-up. However, whether there is a reduction in fatal and nonfatal MI following PCI is still under discussion. ST-segment resolution (STR) is a current measure to assess PCI outcome but results are variable. Heart rate variability (HRV) has been shown to be an indicator of risk of nonfatal or fatal MI. The current study therefore investigated the changes in HRV following elective PCI. Patients were selected at the Mediclinic Middle East Cardiology Department. Pre-PCI and post-PCI (up to 4 hours) HRV was determined from 5-minute heart rate recordings and analyzed using Kubios software. Mean values for rMSSD, TINN, and SD1, , showed significant decreases associated with primarily parasympathetic regulation (p<0.05, whereas DFAα1 and Stress Indexincreased significantly (p<0.05). Patients were divided into two groups based on a Euclidean paradigm indicating primarily increased stress in the majority of patients. Our results indicate that PCI outcomes are variable and HRV may be a suitable clnical feature to assess short and long term outcomes.

1. Introduction

In the United Arab Emirates (UAE), cardiovascular diseases (CVD) are the leading cause of mortality, with the incidence of premature coronary artery diseases (CAD) being about 10-15 years earlier compared to developed nations including ST-elevation myocardial infarct (Figure 1) [1]. Outcomes of PCI have improved because of advancements in equipment and techniques. Never-the-less whether there is an increased risk of fatal or nonfatal MI, in CAD presentations following PCI is currently still under discussion. Following fibrinolysis for STEMI for instance, time for ST-segment elevation resolution (STR) is highly variable leading to lower accuracy for predicting future morbidity or mortality [2, 3]. These STR findings suggest that additional post-intervention assessment to traditional the ECG usually recorded at 60-90 minutes post-PCI may be warranted to determine increased risk of morbidity and mortality. In addition, the optimal time for assessing STR is unknown. Heart rate variability (HRV) has been shown to be a strong indicator of CAD and risk of nonfatal or fatal myocardial infarct. Although HRV associated with post-PCI has been assessed for long-term follow-up, HRV following PCI up to 4 hours has not been investigated [4, 5]. The current study therefore investigated the changes in HRV as a factor in assessment of PCI outcomes and possible factors in post-PCI recovery within 4 hours of post-PCI.

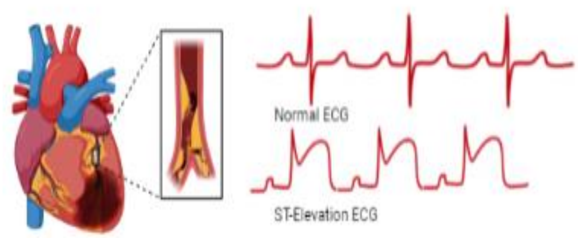

Figure 1. Blocked vessel with ST-elevation ECG.

2. Methods

2.1. Experimental Data Acquisition

Suitable patients were selected at the MCME Cardiology Department for elective PCI between January and December 2022. The research was approved by the MCME Research Committee and ethics approval obtained from the Department of Health, Abu Dhabi, UAE (DOH/CVDC/2021/1423). All protocols followed the ethical standards of the World Medical Association's Declaration of Helsinki [6].

2.2. Heart Rate Variability Features

Fifteen patients that underwent PCI were recruited for the study. Five-minute heart rate recordings Pre-PCI and post-PCI (up to 4 hours) were obtained using a Nexus-10 device (Mindmedia) and analyzed for HRV features using Kubios software [7]. In order to analyze only normal-to-normal beat intervals, abnormal beat intervals (including ectopic beats) were corrected using an automated beat correction algorithm [8]. Furthermore, since sympathetic and parasympathetic nervous activities affect only the low and high frequency HRV components (frequencies above 0.04 Hz), the very low frequency (frequencies below 0.04 Hz) component was removed by using a smoothness priors detrending method [9].

HRV features included: *RMSSD* Square root of the mean squared differences between successive RR intervals; *TINN* Baseline width of the RR interval histogram, *PNS Index* **(**Parasympathetic Nervous System Index) is computed from the mean RR intervals, rMSSD and the Poincaré plot index SD1 in normalized units. A positive PNS index value indicates how many standard deviations (SDs) above the normal population average the parameter values are, whereas a negative value indicates how many SDs below the normal population average the parameter values are [7]. *SD1 & SD2* a graphical representation of the correlation between successive RR intervals. SD1 describes short-term variability which is mainly caused by respiratory sinus arrhythmia and SD2, which describes long-term variability. *TINN* is the baseline width of the distribution measured as a base of a triangle approximating the normal-to-normal interval distribution using the minimum square difference to find such a triangle [10]. *DFA* (Detrended fluctuation analysis) measures the correlation within the signal. DFA the correlations are divided into short-term and long-term fluctuations which are reflected by the α1 and α2 coefficients.

2.3. Statistical Analysis

Statistical analysis was undertaken with EXCEL and SPSS V22(IBM Inc). Significance was set at $p<0.05$ for a repeated measures design t-test.

3. Results

The current results reflect expected outcomes following invasive procedures that indicate the stress experienced by the patient as highlighted by the autonomic nervous system derived cardiac autonomic indices (Table 1).

Table 1. HRV pre and post PCI

HRV features	prePCI	postPCI	P value
RMSSD	0.49±0.2	0.354±0.1	0.02
TINN	28.08±9.3	18.1±6.9	0.001
SNS Index	88.73±15.6	93.92±18.7	0.04
SD1	0.363±0.2	0.254±0.1	0.02
SD2	4.63±2	3.18±1.1	0.01
DFAα1	1.76±0.1	1.84±0.03	0.05

This is reflected by the PNS Index (although not significant (p=0.09) that decreased from -6.142±0.06 to -6.175±0.04 (p=0.046), which is about 6 standard deviations below the normal range. In terms of cardiac function and ANS modulation, rMSSD decreased from 0.49±0.2 to 0.354±0.1(p = 0.02). Similarly, the indices reflecting vagal activity, SD1, TINN decreased. Of the vagal indices DFAα1showed improvement and SD2, a sympathetic marker also decreased and SD2 however, increased post-PCI. However, The SNS Index increased (p=0.04) indicating overall physiological stress across the post-PCI findings. A closer analysis using aa Pareto chart visualization, which separates the distribution into bins of how often a certain value occurs indicates a bimodal distribution for post-PCI patients (Figure 2) and suggests that a portion of the patients had improved HRV post-PCI.

Figure 2. Pareto chart for Post PCI HRV distribution.

4. Discussion

Percutaneous coronary intervention (PCI) refers to minimally invasive procedures that unblock coronary arteries. Various clinical trials and meta-analyses have shown that PCIs are associated with improved outcomes, especially among patients with acute coronary syndromes.

However, the clinical benefit of PCIs among patients with stable ischemic heart disease (SIHD) other than improvement in anginal symptoms is less well established [11]. In large-scale clinical trials, PCI has not shown to reduce myocardial infarction (MI) or mortality compared to medical therapy when it is performed for SIHD or ST-elevation MI [2, 3]. The main benefit of PCI procedures was the reduction in anginal symptoms and improvement in the quality of life, though, this has been contradicted by the Objective Randomized Blinded Investigation with Optimal Medical therapy of Angioplasty in Stable angina (ORBITA) trial [12]. A recent study has shown similar results and concluded that there is significant improvement in resting cardiovascular parameters, resting autonomic tone as measured by HRV, which shows increase in both parasympathetic as well as sympathetic reactivity following revascularization by PCI in chronic stable angina patients. However, the time following PCI was not indicated [13]. Acute PCI outcomes are based on age and time to hospital amongst other factors leading to a number of subgroups in terms of risk of morbidity and mortality following PCI [14]. Previous work by one of us has shown long-term improvement following PCI and cardiac rehabilitation [15]. The current research extends these findings and suggests that non-acute/elective PCI may also lead to disparate outcomes in terms of in-hospital recovery and long-term outcomes. Our results agree with previous work that recorded ECGs within 24 hours and analyzed HRV. Results showed that after PCI, Poincaré plot derived features decreased significantly [16]. Division of the cohort by Pareto visualization, indicates that outcomes are strongly influenced by pre-PCI HRV. HRV and specifically vagal influence may be associated with level of stress experienced during hospital stay and should be taken into consideration by ameliorating stress in patients prior to PCI for improved outcomes in increased risk of adverse outcomes group. Establishing appropriate risk markers such as combining HRV with current practice for elective PCI patients may improve effectiveness of risk stratification in post-PCI recovery.

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