

Impact of Elective Percutaneous Transluminal Coronary Angioplasty (PTCA) on Heart Rate Variability in Patients with Coronary Artery Disease

Anahita R. Shenoy Basti¹, Venkatesh D.², V. S. Prakash²

¹Assistant Professor, Department of Physiology, Father Muller Medical College, Mangalore-575002, India,

²Professor, Department of Physiology, M.S. Ramaiah Medical College, Bangalore-560054, India

Abstract

Coronary artery disease (CAD) is a major public health problem in India and is one of the leading causes of mortality and morbidity. Impairment of heart rate variability (HRV) has been observed in patients with CAD. Percutaneous transluminal coronary angioplasty (PTCA) is one of the common modalities of treatment of CAD. In this study we have studied the effect of successful elective PTCA on HRV parameters in patients with CAD.

Material and Method: HRV parameters in both time and frequency domain were studied in 30 male patients before PTCA, one day and three day after PTCA.

Results: - The time and frequency domain parameters between pre PTCA and 1st day post PTCA were not found to be statistically significant. Changes in the time domain parameter rMSSD and SDNN was statistically significant between pre and 3rd day post PTCA but no significant difference was observed in pNN50. A significant decrease in LF n.u and increase in HF n.u was observed between pre and 3rd day post PTCA.

Conclusion: Revascularization with PTCA results in improvement of the autonomic tone. Improved autonomic modulation is seen as early as 3rd day post PTCA. It indicates that restoring the blood flow reverses to some extent the autonomic modulatory effect of coronary artery disease.

Keywords: Coronary artery disease, heart rate variability, PTCA

Introduction

Heart rate variability (HRV) is defined as the physiological variation in the duration of intervals between sinus beats¹. The property of automaticity is intrinsic to the pacemaker tissue of the heart but the rate

and rhythm are influenced by the autonomic nervous system. HRV reflects the activity of the divisions of the autonomic nervous system on the heart rate (HR)².

HRV is a non invasive, affordable and reproducible technique to measure the autonomic function. HRV is altered in conditions such as obesity, diabetes mellitus, asthma and also coronary artery disease(CAD).

Coronary artery disease is a major public health problem in India and is one of the leading causes of mortality and morbidity³. Impairment of HRV in CAD has been extensively studied and has been attributed to arrhythmias and risk of sudden cardiac deaths^{4,5,6}. PTCA is one of the common modalities of treatment of CAD. Successful PTCA results in improved left ventricular

Corresponding Author:

Dr. D. Venkatesh

Professor of Physiology, M.S. Ramaiah Medical College, Bangalore -560054

e-mail: venkatesh40@gmail.com

Mobile: 9845938810

(LV) systolic function, reduced anginal symptoms, increased exercise capacity and an increase in survival^{7,8}.

However, there is limited information on the effect of successful PTCA on the recovery pattern of HRV. The importance of studying the recovery pattern of HRV following PTCA is to understand the mechanisms involved in arrhythmias and reperfusion injuries. Variable alterations in HRV have been documented in patients after undergoing PTCA. Some studies have shown a decrease in the parasympathetic tone associated with or without an increase in the sympathetic tone following revascularisation^{9,10}.

The reason for these variations may be due to incomplete understanding of the manner in which obstruction to coronary artery and its reperfusion affects HRV.

Thus, in this study, influence of successful elective PTCA on the parameters of HRV in patients with uncomplicated CAD was evaluated. In addition, the alteration in HRV based on the artery involved is also studied.

Material and Method

Male patients admitted to the hospital with TMT positive for inducible angina and angiography with a single vessel block of more than 70% were screened. Patients in the age group of 40-65 years and satisfying the exclusion criteria were recruited for the study. The control group consisted of age, sex and anthropometrically matched TMT negative subjects. The patients with diseases or on drugsthat altered the autonomic functions, athletes and obese individuals were excluded from the study.

The sample size of 30 was determined based on the projected availability of patients during the period of study.

Detailed protocol of the study, extent of their involvement, the right to terminate during the study and the possible complications was explained in patient's own language. An informed written consent was obtained from the participants.

Detailed history was taken followed by clinical examination of the subject and the findings were confirmed by the attending physician/cardiologist. Their

height was measured in meters using a stadiometer and weight was measured in kilograms using sensitive balance. BMI was calculated by using the formula weight in Kg/height in meter². Waist circumference was measured at a level midway between the lowest rib and the iliac crest, the hip circumference at the level of the great trochanters and Waist hip ratio was calculated.

The HRV recordings were done between 9.00am to 12.00 noon of the day in a quiet semi-dark room to avoid the bias of changes due to circadian rhythm. HRV recordings were done a day before, 24 hours after and on the third day after PTCA.

The patient scheduled for HRV recording was instructed to abstain from rigorous exercise, consumption of alcohol, stimulants beverages like coffee or tea and smoking. The patient was rested for period of 15 minutes in supine position. 5 min ECG was recorded by placing the electrodes in right infraclavicular, left infraclavicular and left iliac regions. The ECG was analyzed using RMS Vagus HRV software (RMS, India).

The analysis from the HRV software provides information about time domain and frequency domain parameters.

Statistical Analysis: The data was expressed as mean + standard deviation. One way analyses of variance (ANOVA) were used to test the difference between groups.

Results

The mean age of our study population was 53.97±6.42yrs. The mean BMI was 25.69±2.57kg/m² and 0.88±0.87 was the mean waist hip ratio. The resting heart rate was 88.77±4.20 beats/min.

The time and frequency domain parameters between before PTCA and 1st day post PTCA were not found to be statistically significant.

Time domain parameters rMSSDand SDNN was statistically significant between pre and 3rd day post PTCA but no significant change was observed in pNN50. A significant decrease in LF n.u and increase in HF n.u was observed between pre and 3rd day post PTCA.

No statistical significance was found between the involved artery and alteration of HRV.

Table No. 1: Comparison of HRV pre, 1st and 3rd day post PTCA

| HRV parameters (n=30) | Pre PTCA | Post day 1 | Post day 3 |
|-----------------------|-------------|-------------|-------------|
| HR (beats/min) | 88.77±4.20 | 89.60±2.71 | 84.73±3.89 |
| SDNN(ms) | 20.08±7.43 | 19.12±9.04 | 26.30±10.40 |
| rMSSD | 12.62±7.77 | 12.29±7.53 | 19.69±10.08 |
| pNN50 | 1.92±4.19 | 1.78±5.50 | 2.34±6.17 |
| LF ms ² | 51.50±44.95 | 49.50±39.55 | 42.70±33.93 |
| HF ms ² | 21.47±19.00 | 23.00±22.74 | 36.26±34.95 |
| LF (n.u.) | 67.95±14.12 | 65.67±14.89 | 55.06±15.60 |
| HF (n.u.) | 31.98±14.12 | 34.28±14.91 | 44.83±15.77 |
| LF/HF ratio | 2.70±1.26 | 2.38±1.24 | 1.56±1.16 |

Table No. 2: Comparison of HRV parameters pre, 1st and 3rd day post PTCA

| Dependent Variable | Comparison between | Mean Difference | Std. Error | Sig. | |
|--------------------|--------------------|-----------------|------------|------|-------|
| SDNN(ms) | Pre | Post Day 1 | 0.959 | 2.33 | 1.000 |
| | | Post Day 3 | -6.22 | 2.33 | 0.028 |
| rMSSD | Pre | Post Day 1 | 0.33 | 2.20 | 1.000 |
| | | Post Day 3 | -7.07 | 2.20 | 0.006 |
| pNN50 | Pre | Post Day 1 | 0.14 | 1.38 | 1.000 |
| | | Post Day 3 | -0.42 | 1.38 | 1.000 |
| LF (n.u.) | Pre | Post Day 1 | 2.27 | 3.84 | 1.000 |
| | | Post Day 3 | 12.88 | 3.84 | 0.004 |
| HF (n.u.) | Pre | Post Day 1 | -2.30 | 3.86 | 1.000 |
| | | Post Day 3 | -12.84 | 3.86 | 0.004 |
| LF/HF Ratio | Pre | Post Day 1 | 0.32 | 0.31 | 0.925 |
| | | Post Day 3 | 1.14 | 0.31 | 0.002 |

Discussion

Alteration of HRV in CAD has been implicated in various adverse outcomes like arrhythmias and also death. Ischemia and infarction resulting from CAD are known to alter the functioning of the autonomic balance to the heart. However, little information exists on the modulation of autonomic system following PTCA, which is a common modality of treatment of CAD.

We have studied the effect of successful PTCA on the parameters of heart rate variability a day before, one day and three day after the procedure. Both the time domain and frequency domain parameters were assessed. In the time domain, SDNN, rMSSD, pNN50 were assessed and in the frequency domain L.F, H.F, and LF/HF ratios were analysed.

Time domain parameter SDNN assesses overall variation in the heart rate. rMSSD estimates the vagally mediated changes reflected in HRV, pNN50 correlated with parasympathetic nervous system activity. Frequency domain parameter L.F reflects baroreflex activity, H.F reflects parasympathetic activity and LF/HF ratio reflecting the sympathovagal balance^{11,12}.

In our study, there was a significant improvement in rMSSD and SDNN accompanied by decrease in LF nu and increase in HF nu three day post PTCA. This indicates a decrease in sympathetic tone and a shift in the autonomic balance towards parasympathetic system.

In a similar study by Ali Aydinlar et al, found SDNN, rMSSD and HF to be increased and LF to be decreased immediately after PTCA indicating an increase in

parasympathetic tone associated with a decrease in sympathetic tone¹³.

A study by Agnieszka Janowska-Kulińska et al analysed the effect of PTCA before and 24 hours the procedure found a decrease in HF and increase in LF/HF ratio indicating an increase in the sympathetic tone and decrease in the balance between sympathetic and parasympathetic tone. They attributed this to changes induced by myocardial reperfusion which produced a pressure overload and strain on the myocardial fibers. Denervation of the myocardial nerve endings due to accumulation of potassium, adenosine, free radical and mitochondrial loading with calcium has also been hypothesized¹⁴.

Similar findings were reported in a study by Kanadasi et al. They assessed the HRV parameters 24h, 10 days and 30 days after PTCA and found a reduction in HRV 24 hafter PTCA which was more significant in patients with previous Myocardial infarction. Recovery was only observed 10th day post PTCA⁹.

Variable alterations in HRV have been observed in the above studies with some showing changes in the autonomic regulation as early as 24 h after the procedure. Our study has shown an increase in the HF nu one day post PTCA. However statistical significance has not been achieved. Ethnicity could be implicated for the delayed recovery as Indians are more prone to CAD and at an earlier age than the western population. Further research is needed in this direction.

Studies by Tseng et al, Sedziwy E et al, Wennerblom B et al have shown a more gradual recovery of the HRV. Tseng et al showed an improvement in the sympathovagal balance 1 month post PTCA. Sympathovagal imbalance did not correlate with the severity of the CAD score in this study¹⁵. Sedziwy E et al ¹⁶ showed increase in parasympathetic control of the heart rate two weeks after successful PTCA. Beneficial increase influenced both parts of the autonomic nervous system.

Wennerblom B et al¹⁰ studied the effect of complete revascularisation on the HRV parameters 1 month and 6 months after PTCA in patients with no previous myocardial infarction. They found partial normalization of vagal tone at 6 months post PTCA. Thus, concluding that ischemia may not be the only mechanism causing a reduction in HRV.

Incomplete restoration of the autonomic balance

could be due to still unrecognised factors influencing HRV other than the blood supply.

Location of the involved artery did not significantly alter the HRV parameters in our study. Similar results have been reported by Kanadasi et al⁹. However Agnieszka Janowska-Kulińska et al have reported statistically significant decrease of HF accompanied by an increase in LF/HF following angioplasty of the right coronary artery(RCA). PTCA of left anterior descending(LAD) caused no significant changes in the HRV indices and in circumflex artery there was significant decrease of time domain indices and a marked increase of the LF/HF ratio¹³.

Improvement in the autonomic balance in the above mentioned studies have occurred over varying time periods. Although the exact mechanism underlying these is not known, one can hypothesize these to be attributed to the differences in the selection of patient groups. Some studies included patients with previous MI and patients with complicated CAD while these being excluded in others. Presence or absence of diabetes mellitus which is known to modify autonomic function, could also have influenced the results. Presence of collateral circulation could be another factor influencing the results, as presence of collaterals would not cause a marked change in HRV parameters following restoration of blood flow. The reasons for these discrepancies could also be due to not completely understood underlying mechanism of HRV changes associated with myocardial ischemia and improved perfusion.

From this study we can conclude that myocardial ischemia is not the only mechanism altering the HRV since recovery of HRV does not take place immediately post PTCA. Delayed and incomplete restoration of HRV could explain prolongation in the recovery of the patients and susceptibility to arrhythmias post PTCA.

Conclusion

Revascularization with PTCA results in improvement of the autonomic tone. Improved autonomic modulation is seen as early as 3rd day post PTCA. It thus indicates that restoring the blood flow reverses to some extent the autonomic modulatory effect of coronary artery disease.

Limitations of the study – The present study is of a short duration. A longer follow up of the patients is required to study the recovery pattern of HRV following PTCA.

Ethical Clearance: Taken from institutional ethical committee in M S Ramaiah Medical College

Source of Funding: Nil

Conflict of Interest: Nil

Reference

1. Nikhil Singh, Kegan James Moneghetti, Jeffrey Wilcox Christle et al. Heart Rate Variability: An Old Metric with New Meaning in the Era of using mHealth Technologies for Health and Exercise Training Guidance. Part One: Physiology and Method. *Arrhythm Electrophysiol Rev* 2018 Aug; 7(3): 193–198.
2. Schwartz, Peter J and Levy, Matthew N. Vagal control of heart: experimental basis and clinical implications. Futura Pub. Co, Armonk, NY 1922-1994.
3. Rajeev Gupta, Indu Mohan, Jagat Narula. Trends in Coronary Heart Disease Epidemiology in India. *Annals of Global Health* 2016;82:307-315.
4. Hsin-Ru Li, Tse-Min Lu, Hao-Min Cheng et al. Additive Value of Heart Rate Variability in Predicting Obstructive Coronary Artery Disease Beyond Framingham Risk. *Circulation* 2016;80:494-50.
5. Evrengul H, Tanriverdi H, Kose S, et al. The relationship between heart rate recovery and heart rate variability in coronary artery disease. *Ann Non-invasive Electrocardiol*. 2006 Apr;11(2):154-62.
6. Maheshwari A, Norby FL, Soliman EZ, et al. Low Heart Rate Variability in a 2-Minute Electrocardiogram Recording Is Associated with an Increased Risk of Sudden Cardiac Death in the General Population: The Atherosclerosis Risk in Communities Study. *PLoS ONE*; 2016;11(8): e0161648.
7. Khan MF, Wendel CS, Thai HM, Movahed MR. Effects of percutaneous revascularization of chronic total occlusions on clinical outcomes: A metaanalysis comparing successful versus failed percutaneous intervention for chronic total occlusion. *Catheter Cardiovasc Interv*, 2013; 82: 95–107.
8. Olivari Z, Rubartelli P, Pisicone F et al. On behalf of TOAST-GISE Investigators: Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions, (TOAST-GISSE). *J Am Coll Cardiol*, 2003; 41: 1672–78.
9. Kanadasi M, Kudaiberdieva G, Birand A, et al. Effect of the final coronary arterial diameter after coronary angioplasty on heart rate variability responses. *Ann Noninvasive Electrocardiol* 2002;7:106-13.
10. Wennerblom B, Lurje L, Solem J, et al. Reduced heart rate variability in ischemic heart disease is only partially caused by ischemia: HRV study before and after PTCA. *Cardiology* 2000; 94: 146-51.
11. Heart Rate Variability. Standards of Measurement, Physiological Interpretation, and Clinical Use Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology. *European Heart Journal* 1996;17:354–381.
12. Fred Shaffer and J. P. Ginsberg. An Overview of Heart Rate Variability Metrics and Norms. *Front Public Health*. 2017; 5: 258.
13. Ali Aydinlar Tunay, Şentürk, Bülent Özdemir et al. Effect of percutaneous transluminal coronary angioplasty on QT dispersion and heart rate variability parameters. *Cardiovascular journal of Africa* 2009;20:240-244.
14. Agnieszka Janowska - Kulińska, Katarzyna Torzyńska. Changes in heart rate variability caused by coronary angioplasty depend on the localisation of coronary lesions. *Kardiologia Pol* 2009; 67: 130-138.
15. Tseng ChD, Wang TL, Lin JL, et al. The cause-effect relationship of sympathovagal activity and the outcome of percutaneous transluminal coronary angioplasty. *Jpn Heart J* 1996; 37: 455-62.
16. Sedziwy E, Olszowska M, Tracz W, Pieniazek P. Heart rate variability in patients treated with percutaneous transluminal coronary angioplasty. *Przeqł Lek*. 2002; 59(9):695-8.