A Noninvasive Measure to Quantify Cardiovascular Risk in Cases with Concomitant Diabetes Mellitus and Cardiac Autonomic Neuropathy: A Case-Control Study

Rishu Segan[1] Lily Walia[2] Naveen Mittal[3] Aditi Rana[1]

[1] Baba Jaswant Singh Dental College, Hospital and Research Institute, Ludhiana, Punjab, India
[2] Department of Physiology, Dayanand Medical College and Hospital, Ludhiana, Punjab
[3] Department of Endocrinology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Address for correspondence Rishu Segan, MBBS, MD, Department of Physiology, Baba Jaswant Singh Dental College Hospital and Research Institute, Sector 40, Ludhiana 141010, Punjab, India (e-mail: seganldh@gmail.com).

Int J Health Environ Res 2024;2:52–54.

Abstract

Introduction Patients with diabetes mellitus (type 2 diabetes) possess higher risk of developing cardiovascular complications, which is further increased with cardiac autonomic neuropathy (AN). Knowing the condition of myocardial blood flow in individuals with diabetic cardiac AN might help explain unfavorable cardiovascular events in such patients.

Materials and Methods Based on predetermined inclusion and exclusion criteria, 100 patients from a tertiary health care hospital were included in this study. Patients were divided into two groups (A and B) of 50 each. Group A and group B included diabetic patients with (case) and without (control) cardiac AN, respectively. Rate pressure product (RPP), also known as double product, was used as a parameter to assess the myocardial blood flow as it is the major determinant of cardiac oxygen demand. Statistical analysis was performed using one way analysis of variance (ANOVA) with SPSS software.

Results Patients in group A had a significantly higher resting RPP ($p < 0.1$) as compared with patients in group B. No significant difference in age and gender distribution between two groups was evident.

Conclusion RPP at rest was higher in diabetic cardiac AN patients as during stress events the body's ability to raise RPP and enhance myocardial perfusion was either minimal or nonexistent. Higher RPP values above the normative range suggests high myocardial oxygen demand, potentially contributing to adverse cardiovascular events.

Keywords
- rate pressure product
- diabetes
- cardiac autonomic neuropathy
- myocardial flow
- oxygen consumption

Introduction

Cardiac autonomic neuropathy (AN) is a serious complication of diabetes mellitus that affects the autonomic nervous system's ability to regulate cardiac function. It occurs when the nerves that control the heart's autonomic functions are damaged, disrupting the normal communication between the heart and the nervous system. Most common symptoms include abnormal heart rate variability, orthostatic hypotension, exercise intolerance, syncope (fainting), and

DOI https://doi.org/10.1055/s-0044-1793848.
ISSN XXXX-XXXX.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

sudden cardiac death. Cardiac AN is associated with silent, inexplicable, abrupt death in type 2 diabetes. An understanding of the condition of myocardial blood flow in individuals with diabetic cardiac AN can give a clue about the adverse cardiovascular events occurring in such patients.

Myocardial oxygen consumption is altered in cardiac AN, leading to impaired cardiac function and increased risk of cardiac events. Thus, measuring myocardial consumption in cardiac AN is crucial to assess cardiac function and energy expenditure. Given that myocardial consumption is difficult to quantify directly, this study used a noninvasive and cost-effective parameter known as double product or rate pressure product (RPP) to assess the myocardial blood flow in diabetic cardiac AN patient. As systolic pressure and ventricular wall tension are correlated, the product of heart rate and systolic pressure becomes a readily computed measure of myocardial oxygen consumption[1] and thus an effective indicator of myocardial blood flow.[2]

Materials and Methods

The current study was approved by the institutional review board in accordance with the Helsinki Declaration (1964). Informed written consent was obtained from each patient before conducting the study.

One hundred diabetic patients who were receiving treatment in a tertiary hospital in North India participated in the study. A glucometer was used to record fasting and random blood sugar test, while a sphygmomanometer was used to measure blood pressure (BP). Heart rate was calculated using lead II of Medicaid Cardiofax electrocardiogram machine. Patients included in the study were categorized into two groups. Group A included 50 patients aged 40 to 60 years with diabetes mellitus and cardiac AN. The postural decrease in BP of these cases was greater than 30 mm Hg. Group B included 50 patients aged 40 to 60 years with diabetes mellitus but without cardiac AN. No postural fall in blood pressure was observed in these patients. Comprehensive history of all the patients on a special proforma was recorded. Ischemic heart disease, cardiac dysrhythmia, and congestive heart failure cases were excluded.

The product of heart rate and systolic blood pressure was used to determine RPP[3] and the resultant value was stated as mm Hg beats/min $\times 10^{-2}$. Statistical analysis was performed using one way analysis of variance (ANOVA) with SPSS software. Values were recorded as mean $\pm$ standard deviation. Probability value less than 0.1 was considered statistically significant.

Result

The demographic characteristics of the patients is shown in ►**Table 1**. The mean age of the patients in groups A and B did not show any statistical difference. Gender-based statistical difference was also not observed.

RPP was substantially higher in group A cases as compared with group B and the results were statistically significant ($p < 0.1$; ►**Table 2**). The mean RPP was also higher in group A cases (>12; ►**Fig. 1**).

Table 1 Demographic characteristic of patients included in the study

Characteristic	Group A	Group B
Gender (number)		
Male Female	27 23	26 24
Age (mean $\pm$ SD)	51.02 $\pm$ 6.154	51.40 $\pm$ 6.212

Abbreviation: SD, standard deviation.

Discussion

RPP is an index of myocardial oxygen consumption that is closely correlated with myocardial hemodynamics. It is a useful noninvasive measure to assess cardiac AN in diabetes. RPP reflects the balance between sympathetic and parasympathetic nervous system activity, which is often disrupted in diabetic cardiac AN. Elevated RPP values indicate sympathetic dominance, while lower values suggest parasympathetic dominance.[4,5] The result of current study indicates significantly higher resting RPP in diabetic cardiac AN patients secondary to relatively increased sympathetic tone. This is because the earliest signs of AN in diabetes are typically linked to parasympathetic denervation as neuropathy initially manifests in the longest nerve fibers. Therefore, early enhancement of sympathetic tone characterizes the cardiac AN development in diabetes.[6]

A low value of RPP is an indicator of more parasympathetic nerve activity and parasympathetic tone, which is believed to be cardioprotective.[7] A persistent increase in RPP could indicate continued cardiac stress that could result in cardiac dysfunction.[8] In a previous study, it was reported that in comparison to individuals with a lower resting RPP, healthy adult participants with a higher resting RPP had more than 60% higher risk of all-cause mortality.[9] Diabetic cardiac AN patients typically have higher RPP at rest such that the body's ability to raise RPP further and enhance myocardial perfusion is limited or nonexistent in stress episodes. As a result, RPP is frequently recommended as an extra useful marker for predicting morbidity and death in AN patients, particularly during periods of elevated cardiac demand such as physical activity, mental or emotional stress, or exposure to cold.

Table 2 Rate pressure product (RPP) in patients with and without cardiac autonomic neuropathy suffering from diabetes

Groups	RPP (mean $\pm$ SD)	*F*-ratio	*p*-value
Group A	12.65 + 1.75	2.579	0.096
Group B	11.25 + 1.14		

Abbreviation: SD, standard deviation.

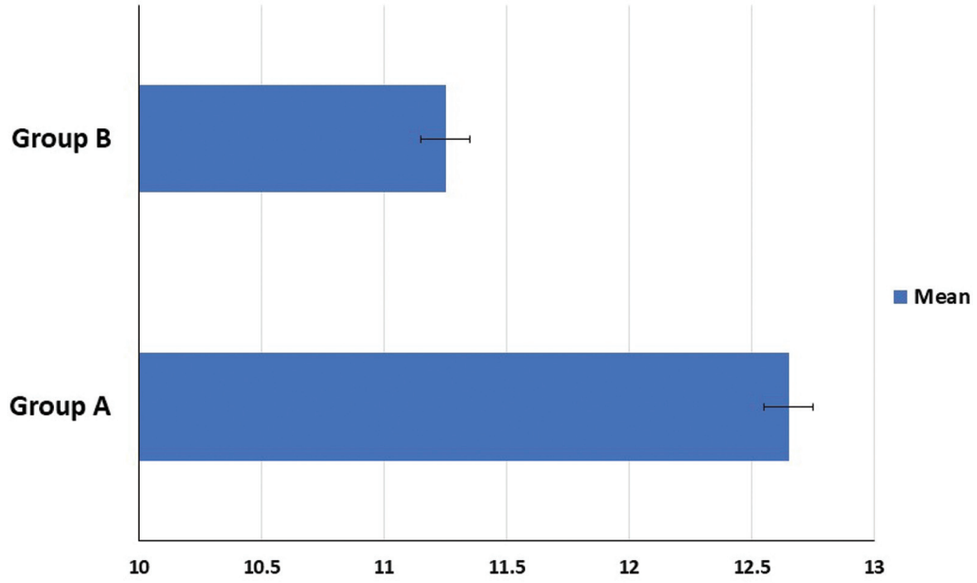

Fig. 1 Comparison of mean rate pressure product in group A and B patients.

Conclusion

The RPP is a noninvasive measure that can be used to estimate the cardiovascular risk of patients with diabetic cardiac AN. Both resting RPP and changes in RPP can provide information about the state of coronary perfusion. Subsequent research with a larger patient population will contribute to elucidating the significance of the RPP in forecasting the degree of cardiac risk in these individuals.

Conflict of Interest

None declared.

References

1 Zhou J, Li YJ, Zhou XD, Wang LJ. Rate-pressure product is a novel predictor for short- and long-term mortality in patients with acute coronary syndrome undergoing primary PCI/immediate invasive strategy. Clin Interv Aging 2024;19:571–579
2 Center HC. Circadian variability of rate-pressure product in essential hypertension with enalapril therapy. Scr Med (Brno) 2000;73(02):67–75
3 Madanmohan,Udupa K, Bhavanani AB, Vijayalakshmi P, Surendiran A. Effect of slow and fast pranayams on reaction time and cardiorespiratory variables. Indian J Physiol Pharmacol 2005; 49(03):313–318
4 Ebihara S, Otsuki H, Arashi H, Yamaguchi J, Hagiwara N. Rate pressure products affect the relationship between the fractional flow reserve and instantaneous wave-free ratio. J Interv Cardiol 2020;2020(01):6230153
5 Cockcroft JR, Wilkinson IB, Evans M, et al. Pulse pressure predicts cardiovascular risk in patients with type 2 diabetes mellitus. Am J Hypertens 2005;18(11):1463–1467, discussion 1468–1469
6 Foo K, Sekhri N, Knight C, et al. The effect of diabetes on heart rate and other determinants of myocardial oxygen demand in acute coronary syndromes. Diabet Med 2004;21(09):1025–1031
7 Sembulingam P, Sembulingam K, Ilango S, Sridevi G. Rate pressure product as a determinant of physical fitness in normal young adults. IOSR J Dent Med Sci 2015;14(04):8–12
8 Raut RA, Mehta A. Comparison of resting rate pressure product in obese and non-obese women. Int J Health Sci Res 2020;10(05): 29–33
9 Visaria A, Moon SJ, Panahon P. Association between resting rate pressure product and all-cause mortality among United States adults. Circulation 2023;147(Suppl 1):AP512

