The Relationship between Rate-Pressure Product and Coronary Artery Stenosis in Patients with Positive Exercise Stress Test

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Background: *Coronary artery disease (CAD) is known to be a leading cause of death. Although many studies have revealed a relationship between rate-pressure product and significant coronary artery stenosis in patients with a positive exercise stress test, there have been few studies on the subject in Thailand. Rate-pressure product results were reviewed of exercise stress tests performed at a single center in Thailand.*

Objective: *To determine a relationship between rate-pressure product and significant coronary artery stenosis in patients with positive exercise stress test.*

Material and Method: *A retrospective cross-sectional study was performed by collecting medical records of patients who had a positive exercise stress test confirmed by cardiac catheterization in Rajavithi Hospital between 1 January 2009 and 31 December 2014.*

Results: *A total of 126 patients were enrolled. Eighty-six patients (68.3%) were male, the mean age was 58.09±8.67 years and the mean body mass index was 25.60±3.55 kg/m^2. Although the study found that patients in the group with rate-pressure product ≥30,000 bpm·mmHg had more non-significant coronary artery stenosis (35.3%) than those in the group with rate-pressure product <30,000 bpm·mmHg (20.02%), the differences were not statistically significant (p-value = 0.163). The group without significant coronary artery stenosis had a higher mean rate-pressure product (27,370.75±5,190.89 bpm·mmHg) than the group with significant coronary artery stenosis (22,605.50±5,588.57 bpm·mmHg) (p-value <0.001).*

Conclusion: *A high rate-pressure product (≥30,000 bpm·mmHg) is not associated with coronary artery stenosis in patients with positive exercise stress test. Patients without significant coronary artery stenosis had a higher average rate-pressure product.*

Keywords: *Rate-pressure product, Double product, Coronary artery stenosis, Cardiac catheterization, Exercise stress test*

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Acute myocardial infarction is one of the major public health problems in Thailand, resulting in significant morbidity and mortality. Acute coronary syndrome can occur for a variety of reasons, but coronary artery disease (CAD) is the main cause of disease. The current screening technology for coronary artery disease includes stress tests, such as exercise or pharmacological stress tests, or anatomical study, such as Coronary Computed Tomography Angiography (CCTA). The most common screening test is still exercise electrocardiography (exercise ECG) because it is easy to perform and is widely available; however, its sensitivity and specificity for diagnosis of CAD can vary from 45% to 50% and 85% to 90%, respectively[1,2], and the severity of coronary artery stenosis cannot be accurately determined.

Rate-pressure product is the multiplied result of maximal heart rate and maximal systolic blood pressure at peak exercise. This product is correlated with maximum oxygen consumption[3-5] and cardiovascular risk[6], and it is a strong predictor of cardiovascular death[7]. Ansari M. et al demonstrated the correlation of rate-pressure product and abnormal myocardial perfusion imaging findings using gated SPECT imaging with dipyridamole stress[8]. Fornitano LD. et al showed that patients with rate-pressure product of over 30,000 beats per minute·mmHg (bpm·mmHg) had no significant obstructive coronary artery disease[9]. The authors of the present report studied the association between rate-pressure product

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and significant coronary artery stenosis in patients who had positive exercise ECG.

Objectives

The primary endpoint was to determine the relationship between the rate-pressure product and significant coronary artery stenosis in patients with positive exercise ECG. The secondary objective was to establish and compare the mean rate-pressure product of patients with significant and non-significant coronary artery stenosis.

Material and Method

Medical records were reviewed of patients who underwent both exercise ECG and cardiac catheterization between 1st January 2009 and 31st December 2014. All patients who had positive exercise ECG followed by coronary angiography were eligible for the present study. Patients were excluded if they did not successfully complete exercise ECG or did not have a coronary angiogram.

Baseline characteristics including age, sex, body mass index (BMI), and underlying disease were recorded. Maximum heart rate and systolic blood pressure at peak exercise were collected to calculate the rate-pressure product. The patients were divided into 2 groups, one with rate-pressure product <30,000 bpm·mmHg and the other with rate-pressure product ≥30,000 bpm·mmHg[9].

Positive exercise ECG[10] was defined as horizontal or down sloping ST-segment depression ≥1 mm, ST-segment elevation ≥1 mm, upsloping ST-segment depression ≥2 mm at 0.08 seconds after J-point or U wave inversion. Significant coronary artery disease was defined as angiographic stenosis of coronary artery ≥50%[11].

The protocol of this research was reviewed and approved by the ethics committee of Rajavithi Hospital No. 034/2558.

Statistical analysis

The estimated sample size was based on one used in a previous study[9]. Using 2-sided type I error of 5% and 90% power, the minimum required sample size was calculated at 124 patients.

Baseline characteristics were described using SPSS, Version 17.0 (IBM statistics) as number (percentage), median (range) and mean ± standard deviation (SD). Chi-square/Fisher's exact test was employed to compare proportions between the study groups while independent t-test was used to compare the means of the two groups. Mann Whitney U test was used for non-nominal distributions with significance set at a *p*-value <0.05.

Results

A total of 126 patients who met the inclusion criteria were enrolled. Baseline characteristics (Table 1) showed that the patients were mainly male with a mean age of 58.09±8.67 years, and mean BMI was 25.60±3.55 kg/m^2. The most common underlying diseases were hypertension, dyslipidemia and diabetes mellitus.

One hundred and nine patients had a rate-pressure product <30,000 bpm·mmHg, and the remaining 17 had a rate-pressure product ≥30,000 bpm·mmHg. The group of patients with a rate-pressure product <30,000 bpm·mmHg were older (58.70±8.54 vs. 54.18±8.71 years old, respectively, *p*-value = 0.045). There were no other significant differences in baseline characteristics.

In the present study, 77.8% of the patients had significant CAD consisting of left main artery disease 14.3%, left anterior descending artery disease (LAD) 83.7%, left circumflex artery disease (LCX) 63.3%, and right coronary artery disease (RCA) 64.3%, while triple vessel disease (TVD) was found in 35.7%. In patients without significant coronary artery stenosis, the coronary angiogram was normal in 57.1% of cases, and the remaining patients had coronary artery stenosis of less than 50%. In the group with a rate-pressure product <30,000 bpm·mmHg, LAD lesions were more common (86.2% compared to 63.6% in the other group, *p*-value = 0.026) but there was no significant difference in the number of patients with CAD and the severity of disease. There were more patients with significant CAD and more TVD in the group with lower rate-pressure product, but the results were not statistically significance (Table 2).

Mean rate-pressure product in the present study was 23,664.44±5,832.02 bpm·mmHg. In the group without significant CAD, it was 27,370.75±5,190.89 bpm·mmHg, while in the group with significant CAD the average rate-pressure product was only 22,605.50±5,588.57 bpm·mmHg with *p*-value <0.001 (Fig. 1).

Discussion

Bagali S et al[12] demonstrated that higher age is associated with a lower rate-pressure product, and this is in keeping with the results of the present study. Younger people can achieve a higher workload and have greater exercise capacity with a higher heart rate

Table 1. Baseline characteristic divided into 2 groups according to rate-pressure products

Baseline characteristic	Rate-pressure product			*p*-value
	Total (n = 126)	<30,000 (n = 109)	≥30,000 (n = 17)	
Sex				0.145
Male	86 (68.3)	77 (70.6)	9 (52.9)	
Female	40 (31.7)	32 (29.4)	8 (47.1)	
Age (years)				0.045*
Mean±SD	58.09±8.67	58.70±8.54	54.18±8.71	
Min-max	37 to 81	37 to 81	41 to 67	
BMI (kg/m^2)				0.098
Mean ± SD	25.60±3.55	25.39±3.61	26.93±2.90	
Min-max	18.37 to 34.33	18.37 to 34.33	22.66 to 32.89	
Underlying disease				
Hypertension	113 (89.7)	98 (89.9)	15 (88.2)	0.833
Dyslipidemia	85 (67.5)	75 (68.8)	11 (64.7)	0.735
Diabetes mellitus	41 (32.5)	35 (32.1)	6 (35.3)	0.794
Chronic kidney disease	3 (2.4)	3 (2.8)	0 (0.0)	
Cerebrovascular disease	2 (1.6)	2 (1.8)	0 (0.0)	

Values are represented as n (%), Mean ± SD, kg/m^2 = kilogram/square meter
* = Significant at $p<0.05$

Table 2. Relationship between rate-pressure product and coronary artery stenosis

Cardiac catheterization	Rate pressure product			*p*-value
	Total (n = 126)	<30,000 (n = 109)	≥30,000 (n = 17)	
Coronary artery stenosis				0.163
Significant	98 (77.8)	87 (79.8)	11 (64.7)	
Non-significant	28 (22.2)	22 (20.2)	6 (35.3)	
Significant (n = 98)				
LM	14 (14.3)	12 (13.8)	2 (18.2)	0.927
LAD	82 (83.7)	75 (86.2)	7 (63.6)	0.026*
LCX	62 (63.3)	55 (63.2)	7 (63.6)	0.476
RCA	63 (64.3)	57 (65.5)	6 (54.5)	0.192
Significant (n = 98)				0.407
SVD	26 (26.5)	21 (24.1)	5 (45.5)	
DVD	24 (24.5)	22 (25.3)	2 (18.2)	
TVD	35 (35.7)	33 (37.9)	2 (18.2)	
SVD + LM	2 (2.0)	2 (2.3)	0 (0.0)	
DVD + LM	5 (5.1)	4 (4.6)	1 (9.1)	
TVD + LM	6 (6.1)	5 (5.7)	1 (9.1)	
Non-significant (n = 28)				
Normal vessel	16 (57.1)	12 (54.5)	4 (66.7)	0.230
LAD	8 (28.6)	7 (31.8)	1 (16.7)	0.206
RCA	4 (14.3)	3 (13.6)	1 (16.7)	1.000

Values are represented as n (%), SVD = Single vessel disease, DVD = Double vessel disease, TVD = Triple vessel disease, LM = Left main artery disease, LAD = left anterior descending artery disease, LCX = left circumflex artery disease, RCA = right coronary artery disease
* = Significant at $p<0.05$

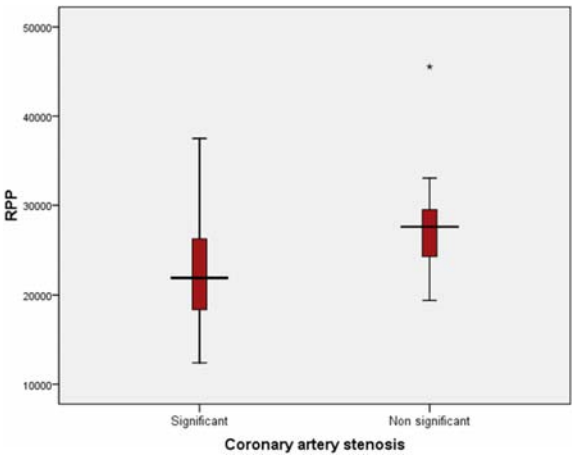

Fig. 1 Distribution of rate-pressure product divided during coronary artery stenosis.

and/or systolic blood pressure. Maximum heart rate during exercise depends on age, and older patients have lower maximum heart rates and lower rate-pressure product.

Fornitano LD, et al[9] showed that patients with rate-pressure product ≥30,000 bpm·mmHg did not have significant CAD after coronary angiography. In contrast, in the present study, 64.7% of the group with a higher rate-pressure product had significant CAD. This finding is probably due to the different prevalence rates of the disease and the characteristics of the patients enrolled. However, patients in the group with a high rate-pressure product ≥30,000 bpm·mmHg did show a tendency to have a lower incidence of significant CAD when compared with the other group. The positive exercise stress test results in patients with high workload are often false positives. Patients with high rate-pressure products were usually younger and had a lower prevalence of CAD.

Double product showed an inverse relationship with the degree of stenosis in both LAD and non-LAD lesion[13]. In the present study, double product also showed an inverse correlation with significant LAD lesion but not with other vessels. The cut-off point of the rate-pressure product in this study was different from that used in previous studies, and the sample size may have been too small to demonstrate any significant association with non-LAD lesion.

In the present study by Falcone C et al, rate-pressure product showed a correlation with silent myocardial infarction[14]. Other studies have shown that a lower rate-pressure product was associated with a higher degree of significant coronary artery stenosis while a higher rate-pressure product was associated with a lower incidence of significant CAD[9,15,16]. The present study had similar findings, showing that the group with significant CAD had a lower rate-pressure product. The group without significant CAD had a high rate-pressure product reflecting a higher workload capacity and high false positive stress test results. The older patients were often in the lower rate-pressure product group, and the incidence of CAD was also higher in older patients.

Limitations

This was a retrospective study and the prevalence of CAD was high, as patients were selected from a high-risk group. The sample size was not large, and patients who did not undergo coronary angiography were excluded.

Clinical implication

Patients with positive EST at a rate-pressure product ≤30,000 bpm·mmHg frequently had significant coronary artery disease; however further investigation is needed to confirm this finding.

Conclusion

Patients with positive exercise stress test and a rate-pressure product ≥30,000 bpm·mmHg group usually do not have significant coronary artery stenosis, but coronary angiography is still recommended to eliminate the possibility of coronary artery disease. Patients without significant coronary artery stenosis had a higher average rate-pressure product.

What is already known on this topic?

1) Coronary artery disease is one of the main causes of morbidity and mortality in Thailand.

2) Screening tests for CAD include stress testing or anatomical study.

3) Sensitivity and specificity of exercise ECG for diagnosis of CAD is inconsistent and cannot accurately determine the degree of coronary artery stenosis.

4) Rate-pressure product is related to cardiovascular risk and is a predictor of cardiovascular death.

What this study adds?

1) Patients with rate-pressure product ≥30,000 bpm·mmHg and positive exercise stress test are not associated with coronary artery stenosis.

2) Patients without significant coronary artery

stenosis generally have a higher rate-pressure product.

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Potential conflict of interest

None.

References

1. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013; 34: 2949-3003.
2. Morise AP, Diamond GA. Comparison of the sensitivity and specificity of exercise electrocardiography in biased and unbiased populations of men and women. Am Heart J 1995; 130: 741-7.
3. Mann DL, Zipes DP, Libby P, Bonow RO. Braunwald's heart disease: A textbook of cardiovascular medicine. 10th ed. Philadelphia: Saunders Elsevier; 2015.
4. Gobel FL, Norstrom LA, Nelson RR, Jorgensen CR, Wang Y. The rate-pressure product as an index of myocardial oxygen consumption during exercise in patients with angina pectoris. Circulation 1978; 57: 549-56.
5. Wilkinson PL, Moyers JR, Ports T, Chatterjee K, Ullyott D, Hamilton WK. Rate-pressure product and myocardial oxygen consumption during surgery for coronary artery bypass. Circulation 1979; 60: 170-3.
6. White WB. Heart rate and the rate-pressure product as determinants of cardiovascular risk in patients with hypertension. Am J Hypertens 1999; 12 (2 Pt 2): 50S-5S.
7. Sadrzadeh Rafie AH, Dewey FE, Sungar GW, Ashley EA, Hadley D, Myers J, et al. Age and double product (systolic blood pressure x heart rate) reserve-adjusted modification of the Duke Treadmill Score nomogram in men. Am J Cardiol 2008; 102: 1407-12.
8. Ansari M, Javadi H, Pourbehi M, Mogharrabi M, Rayzan M, Semnani S, et al. The association of rate pressure product (RPP) and myocardial perfusion imaging (MPI) findings: a preliminary study. Perfusion 2012; 27: 207-13.
9. Fornitano LD, Godoy MF. Increased rate-pressure product as predictor for the absence of significant obstructive coronary artery disease in patients with positive exercise test. Arq Bras Cardiol 2006; 86: 138-44.
10. Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, et al. ACC/AHA guidelines for exercise testing: executive summary. A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). Circulation 1997; 96: 345-54.
11. Harris PJ, Behar VS, Conley MJ, Harrell FEJr, Lee KL, Peter RH, et al. The prognostic significance of 50% coronary stenosis in medically treated patients with coronary artery disease. Circulation 1980; 62: 240-8.
12. Bagali S, Khodnapur J, Mullur L, Banu G, Aithala M. Aging and gender effects on rate-pressure product: an index of myocardial oxygen consumption. Int J Biomed Adv Res 2012; 3: 175-8.
13. Park TH, Tayan N, Takeda K, Jeon HK, Quinones MA, Zoghbi WA. Supine bicycle echocardiography improved diagnostic accuracy and physiologic assessment of coronary artery disease with the incorporation of intermediate stages of exercise. J Am CollCardiol 2007; 50: 1857-63.
14. Falcone C, Nespoli L, Geroldi D, Gazzaruso C, Buzzi MP, Auguadro C, et al. Silent myocardial ischemia in diabetic and nondiabetic patients with coronary artery disease. Int J Cardiol 2003; 90: 219-27.
15. Nagpal S, Walia L, Lata H, Sood N, Ahuja GK. Effect of exercise on rate pressure product in premenopausal and postmenopausal women with coronary artery disease. Indian J PhysiolPharmacol 2007; 51: 279-83.
16. Al Khalili F, Svane B, Wamala SP, Orth-Gomer K, Ryden L, Schenck-Gustafsson K. Clinical importance of risk factors and exercise testing for prediction of significant coronary artery stenosis in women recovering from unstable coronary artery disease: the Stockholm Female Coronary Risk Study. Am Heart J 2000; 139: 971-8.