Diagnostic Value Of Post Exercise Systolic Blood Pressure Response In Ischemic Heart Disease

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ABSTRACT

Background: The normal decline in systolic blood pressure during recovery phase of treadmill exercise dose not occur in most patients with coronary artery disease, in others recovery values systolic blood pressure may even exceed the peak exercise value.

Objectives: Treadmill exercise test parameters indicating the presence and extent of coronary artery disease have traditionally included such as exercise duration, blood pressure and ST-segment response to exercise. The three – minute systolic blood pressure ratio is another important indicator of presence and significance of coronary artery disease is useful and obtainable measure that can be applied in all patients who are undergoing stress testing for evaluation of suspected ischemic heart disease and this increase the sensitivity of exercise test .

Type of the study: A prospective study.

Methods: Between April 2011 and April 2012 ,all patients underwent treadmill exercise test , echocardiography coronary angiography in Ibn Ab-bitar Hospital Cardiac Surgery. Clinical and procedural data for patients undergoing treadmill and coronary angiography were prospectively collected and entered into database specially designed for the present study.To calculate mean systolic blood pressure ratio for each , Measurement of blood pressure in the 3rd minute of recovery time and divided by peak systolic blood pressure during exercise test ,after excluding patients . Coronary angiography was done for all patients who under went treadmill exercise test and multiple views were taken accordingly to clarify the lesion and critical lesion defined as >50% stenosis in LMS and >70% stenosis in LAD,LCX and RCA.

Results: We studied 100 patients In the period from April 2011 to April 2012, 78(78%) male and 22 (22%) a female with a mean age 55.49±7.60 who undergone treadmill exercise testing and coronary angiography to assess the chest pain, 32 patient had normal blood pressure 68 had hypertension and 24 patients had normal coronary angiography and 76 patients had abnormal coronary angiography. SBP/3 minute recovery blood pressure ratio was significantly higher in patient with coronary artery disease than patient without coronary artery disease (mean ±SD O.92±0.09 VS 0.81 SBP/3 minute recovery blood pressure ratio was significantly related with the severity of coronary artery disease its higher in three vessels than one vessel disease 0.95±0.10 vs0. 91 ±0.01 p-value 0.0001.

Conclusions: post exercise blood pressure response in patients with coronary artery diseaseis higher than patients with normal coronary artery .post exercise blood pressure is related to the severity of coronary artery disease.

Keywords: blood pressure, ischemia, exercise.

Al-Kindy College Medical Journal 2016: Vol.12 No.2 Page: 1-10

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Received 26th June 2014, accepted in final 13th June 2016

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Exercise is a common physiologic stress used to elicit cardiovascular abnormalities not present at rest and to determine the adequacy of cardiac function. Exercise electrocardiography is one of the most frequent noninvasive modalities used to assess patients with suspected or proven cardiovascular disease. The test is mainly used to estimate prognosis and determine functional capacity, the likelihood and extent of coronary artery disease (CAD), and the effects of therapy.[1-14]

Diagnostic Use of Exercise Testing

In patients selected for coronary angiography, the sensitivity of the exercise ECG in patients with CAD is approximately 68% and specificity is 77%. In patients with single-vessel disease, the sensitivity ranges from 25% to 71%, with exercise-induced ST displacement most frequent in patients with left anterior descending CAD, followed by those with right CAD and those with isolated left circumflex CAD. In patients with multivessel CAD, sensitivity is approximately 81% and specificity is 66%. The sensitivity and specificity for left main or three-vessel CAD are approximately 86% and 53%, respectively. The exercise ECG tends to be less sensitive in patients with extensive anterior wall myocardial infarction and when a limited exercise electrocardiographic lead set is used. Approximately 75% to 80% of the diagnostic information on exercise-induced ST-segment depression in patients with a normal resting ECG is contained in leads V_4 to V_6. The exercise ECG is less specific when patients in whom false-positive results are more common are included, such as those with valvular heart disease, left ventricular hypertrophy, marked resting ST segment depression, or digitalis therapy.

Exercise Physiology : Anticipation of dynamic exercise results in an acceleration of ventricular rate caused by vagal withdrawal, increase in alveolar ventilation, and increased venous return, primarily as a result of sympathetic vasoconstriction.[5] In normal persons, the net effect is to increase resting cardiac output before the start of exercise. The magnitude of hemodynamic response during exercise depends on the severity of the exercise and the amount of muscle mass involved. In the early phases of exercise in the upright position, cardiac output is increased by an augmentation in stroke volume mediated through the use of the Frank-Starling mechanism and heart rate; the increase in cardiac output in the later phases of exercise is primarily caused by a sympathetic-mediated increase in ventricular rate. At fixed submaximal workloads below anaerobic threshold, steady-state conditions are usually reached after the second minute of exercise, following which heart rate, cardiac output, blood pressure, and pulmonary ventilation are maintained at reasonably constant levels. During strenuous exertion, sympathetic discharge is maximal and parasympathetic stimulation is withdrawn, resulting in vasoconstriction of most circulatory body systems, except for that in exercising muscle and in the cerebral and coronary circulations. Venous and arterial norepinephrine release from sympathetic postganglionic nerve endings, as well as plasma renin levels are increased; the catecholamine release enhances ventricular contractility. As exercise progresses, skeletal muscle blood flow is increased, oxygen extraction increases by as much as threefold, total calculated peripheral resistance decreases, and systolic blood pressure, mean arterial pressure, and pulse pressure usually increase. Diastolic blood pressure does not change significantly. The pulmonary vascular bed can accommodate as much as a six fold increase in cardiac output with only modest increases in pulmonary artery pressure, pulmonary capillary wedge pressure, and right atrial pressure; in normal individuals, this is not a limiting determinant of peak exercise capacity. Cardiac output increases by four- to six fold above basal levels during strenuous exertion in the upright position, depending on genetic endowment and level of training.[5,6] The maximum heart rate and cardiac output are decreased in older persons, partly because of decreased beta-adrenergic responsivity.[15,16] Maximum heart rate (HR) can be estimated from the following formula: **Heart rate = 220 – age** (in years) with a standard deviation of 10 to 12 beats/min. This formula tends to overestimate maximum heart rate in a female population. The formula **HR = 200 − 0.88** (age in years) provides a more accurate estimate of maximum heart rate in women.[17] The age-predicted maximum heart rate is a useful measurement for safety reasons. However, the wide standard deviation in the various regression equations used and the impact of drug therapy limit the usefulness of this parameter in estimating the exact age-predicted maximum for an individual patient.[4]

In the post exercise phase, hemodynamics return to baseline within minutes of termination of exercise. Vagal reactivation is an important cardiac deceleration mechanism after exercise and is accelerated in well-trained athletes but blunted in patients with chronic heart failure. Intense physical work or significant cardiorespiratory impairment may interfere with achievement of a steady state, and an oxygen deficit occurs during exercis.[7, 8]

Hemodynamic Correlates of the Three-Minute SBPR

Studies evaluating intra cardiac hemodynamics and their relationship to the SBPR have been helpful in determining the mechanism of the abnormal three-minute SBPR.[20,21]In these studies, higher values for the calculated SBPR were associated with a significantly higher pulmonary capillary wedge pressure and a lower cardiac index at peak exercise.[22] By three minutes into the recovery phase, pulmonary capillary wedge pressure and cardiac index were similar in patients with either high or low SBPR values.[21,22] However, the patients with higher SBPR values had significantly greater systemic vascular resistance, elevated catecholamine levels and a pronounced delay in the return of stroke index to baseline .Study findings suggest that an abnormal SBPR is related to the following: (1) recovery from exercise-induced ischemia with ischemic left ventricular dysfunction, and (2) the effects of catecholamine-related enhanced peripheral vasomotor tone during recovery from exercise.

Aim of study:1-To study post exercise blood pressure response in patients with coronary artery disease to increase sensitivity of TMT result. 2-To study the relation between post exercise blood pressure response and severity of coronary artery disease and use it as a non invasive predictor of severity of coronary artery disease.

Method: A prospective study between April 2011 and April 2012 ,100 patients .Underwent treadmill exercise test, Coronary angiography and echocardiography in Ibn-Albitar Hospital for cardiac surgery in Baghdad. Clinical and procedural data for patient were collected and entered into database specially designed for the present study.

Excluding criteria

1. History of myocardial infarction
2. Valvular heart disease
3. Intraventricular conduction disturbance
4. High-risk unstable angina
5. Decompensated heart failure

6. Uncontrolled cardiac arrhythmias with symptoms or hemodynamic compromise
7. Acute myocarditis or pericarditis
8. Severe hypertrophic obstructive cardiomyopathy
9. Uncontrolled hypertension
10. Acute systemic illness (pulmonary embolism, aortic dissection)
11. Pre excitation syndrome
12. reports of TMT which not mention post exercise blood pressure in the recovery period .
13. Some reports although mention post exercise blood pressure in the recovery period but time of measurement not at the three minute of recovery time.
14. Patient or people who not reach 85% of maximum heart rate predicted during TMT.

Treadmill exercise testing: Multistage treadmill exercise testing were performed until patient reach target heart rate according to Bruce protocol. Some medication were withdrawn like beta blocker, nitrate and calcium channel at 24-72 hours while digoxin one week before the test. ECGs were monitored continuously and recorded at 2 minute intervals during the test. Blood pressure was measured by the arm cuff **.** Auscultation method standing during exercise and sitting after exercise.

The test discontinue if any of following occurred:

1. Angina pectoris of moderate severity
2. Exertional fatigue
3. Decrease in systolic blood pressure of >20mm Hg.
4. ≥3mV horizontal or down sloping ST – Segment depression measured 60msec after the J point. The usual clinical cutoff point of 0.1mV horizontal or down sloping ST-segment depression was adopted the standard criterion.
5. Increase systolic blood pressure > 250 mmHg.
6. Dizziness
7. Arrhythmia

The exercise ECGs were evaluated in blinded fashion by the observer who had no knowledge of the patient segment other clinical data. To estimate the post exercise systolic blood pressure response, ratio of systolic blood pressure measured at 3 minute of recovery to peak systolic blood pressure response obtained during exercise were calculated.

CARDIAC CATHETERIZATION: Coronary angiography done for the patient by Judkinse technique, multiple views of both the left and right coronary arteries were obtained, including cranial and caudal Projection as required. Coronary angiography was analyzed by senior operator. To classify the number of diseased coronary arteries, coronary obstruction was considered significant, if there was luminal narrowing of 70% or greater in left anterior descending artery, or in the left circumflex artery or right coronary artery. In the left main coronary artery stenosis of 50% or greater was considered significant and was analyzed separately.Sever coronary artery disease was defined as:[22]

1. Three -vessel disease with > 70% diameter stenosis in each major coronary artery system.
2. > 50%diameter stenosis of left main coronary artery.
3. Two-vessel disease with >70% diameter stenosis of the proximal left anterior descending coronary artery.

Data analysis: Data were analyzed using the computer software facilities of SPSS 16(Statisical package for social sciences version 16). Data were presented as mean, number and percentage. Chi -square, T- test and multivariate analysis for analysis of measured variable between groups, In each case p < .o5 was considered significant.

Sensitivity and specificity were defined as follows: [18]

Sensitivity= (true positive result ÷ total patient with disease) ×100%

Specificity= (true negative ÷ total patient without disease) ×100%

Systolic blood pressure recovery ratios were derived by dividing the blood pressure at three minute of recovery by the blood pressure at peak exercise.

Results: We studied 100 patients In the period from April 2011 to April 2012, 78(78%) male and 22 (22%) a female with a mean age 55.49±7.60 who underwent treadmill exercise testing and coronary angiography to assess the chest pain. Of these 32 patient had normal blood pressure 68 had hypertension and other baseline clinical characteristics are summarized in tables (1) and (2). TMT was positive in 76 patients (76%) and negative in 24 patients (24%). Fatigue was common cause of stopping TMT as shown in table (3) . 76(76%) patient had coronary artery disease (abnormal coronary angiography) , 24 (24%) had normal coronary angiography , LAD was most common artery involved in 66 (66%)patient as shown in table (4). Table (5) showing significant difference between normotensive with normal coronary angiography and normotensive with CAD in the duration of exercise (460±20 sec VS 345 sec respectively p-value <0.05) but not significant between hypertensive patients with and without CAD (364±12 sec VS 300±15 sec p-value <0.4), SBP was higher in the patient with hypertension than normotensive patients wither those with or without coronary artery disease. The distribution of SBP/3minute recovery blood pressure response in all patients in the study shown in Figure (1) and its range from 0.65 to 1.2 and SBPR which is equal to one was most frequent than other ratio systolic blood pressure / 3 minute recovery blood pressure ratio in patient with coronary artery disease and without coronary artery disease showing higher ratio more than (> 0.86) common in those with coronary artery disease and lesser ratio in those without coronary artery disease as shown in figure (2) and according to sensitivity and specificity of mean SBPR of 0.86 as shown in figure (3) and table (9). SBP/3 minute recovery blood pressure ratio was significantly higher in patient with coronary artery disease than patient without coronary artery disease (mean ±SD O.92±0.09 VS 0.81±0.09 respectively) with significant value p- value 0.0001 as shown in table (6). SBP/3 minute recovery blood pressure ratio was significant with severity of coronary artery disease as shown in table (7) its higher in three vessels than single vessel disease 0.91±0.06,0.95±0.07 The patients who had LMS involvement in coronary angiography had higher systolic blood pressure ratio 0.99±0.19 versus other arteries involve 0.92 ±0.09 and 0.81±0.09 for normal coronary angiography with significant p-value 0.001 as shown in table (8). Sensitivity and specificity of systolic blood pressure to 3minute recovery blood pressure ratio at 0.86 cutoff points are 75% and 83% respectively as Shown in ROC figure (3) and table (9).

Table (1) baseline clinical characteristics of cases included in our study

		Number of patients	%
Gender	Male	78	78.0
	Female	22	22.0
Age (years)	<50	16	16.0
	50–54	25	25.0
	55–59	33	33.0
	60–64	12	12.0
	=>65	14	14.0
	Mean±SD (Range)	55.49±7.60	(26-69)

TABLE (2) results of TMT

		No	%
Result of TMT	TMT negative	24	24
	TMT positive	76	76
Cause of stop TMT	Fatigue	60	60.0
	Pain	23	23.0
	Arrhythmia	0	0
	Dizziness	10	10
	SBP>250	7	7

TABLE (3) results ofTMT in hypertensive and normotensive patients with CAD and without CAD

GROUPS		NO.	Peak exercise blood pressure	P-value	Time of exercise	P-value	Mean SBPR	P-value
NORMOTENSIVE	without CAD	8	174±25mmhg	0.01	460±20 sec	0.05	0.81	0.001
	with CAD	14	150±20mmhg		345±175sec		0.91	
HYPERTENSIVE	Without CAD	16	200±50mmhg	0.2	364±12 sec	0.4	0.83	0.001
	with CAD	62	170±10mmhg		300±15 sec		0.93	

CAD : coronary artery disease SBPR: systolic blood pressure ratio

TABLE(4) mean SBPR in normal and abnormal coronary angiography

	Number		SBP/Recovery BP Ratio		P value
			Mean±SD	Range	
Coronary angiography	76	Abnormal	0.92±0.09	0.67-1.19	0.0001*
	24	Normal	0.81±0.09	0.65-1.00	

SBPR= systolic blood pressure ratio

Table(5) relation of SBPR and numbers of vessels involve

		SBP/Recovery BP Ratio		p value
			Mean±SD	
Coronary angiography	One	0.91±0.06	0.86-1.00	0.0001*
	Two	0.93±0.12	0.74-1.19	
	Three	0.95±0.10	0.67-1.00	
	Normal	0.81±0.09	0.65-1.0	

SBPR=systolic blood pressure ratio, SBP=systolic blood pressure

BP=blood pressure

Table(6) LMS involvement

	SBP/Recovary BP Ratio			p value
LMS involved	LMS	0.99±0.12	0.67-1.00	0.0001*
	Others	0.92±0.09	0.74-1.19	
	No	0.81±0.09	0.65-1.00	

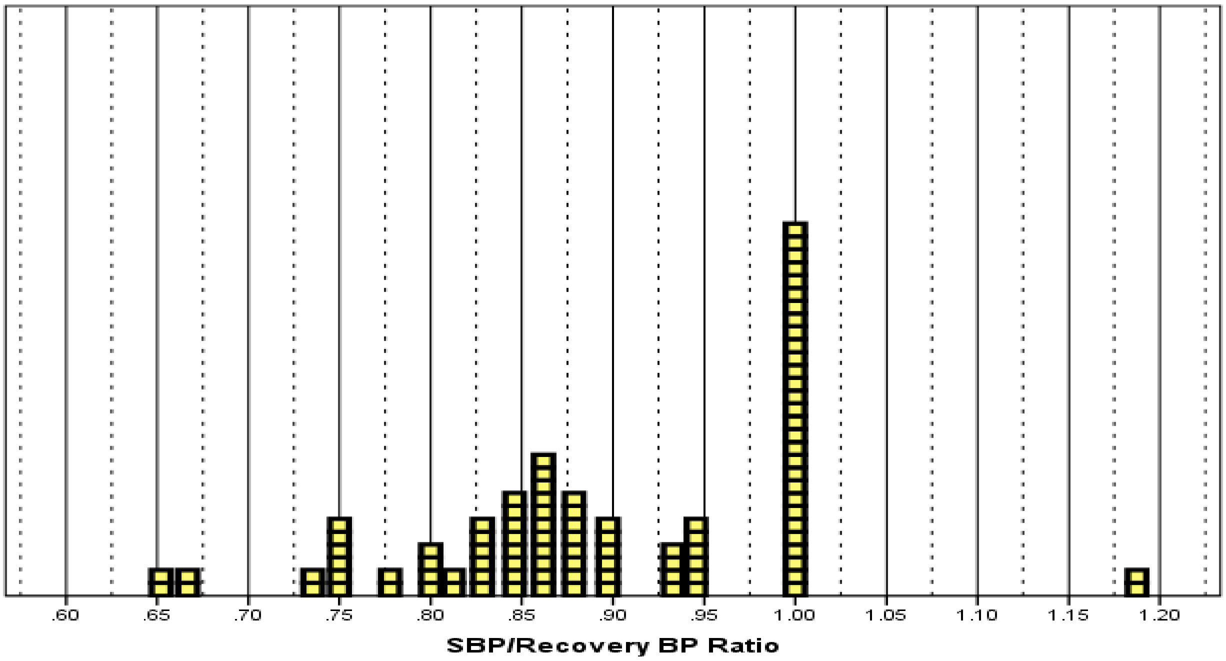
LMS=left main stem coronary artery

TABLE(7) Sensitivity and specificity of SBPR

Area Under the Curve	Std. Error	P-value	95% Confidence Interval	
			Lower Bound	Upper Bound
0.813	0.053	0.0001	0.709	0.916

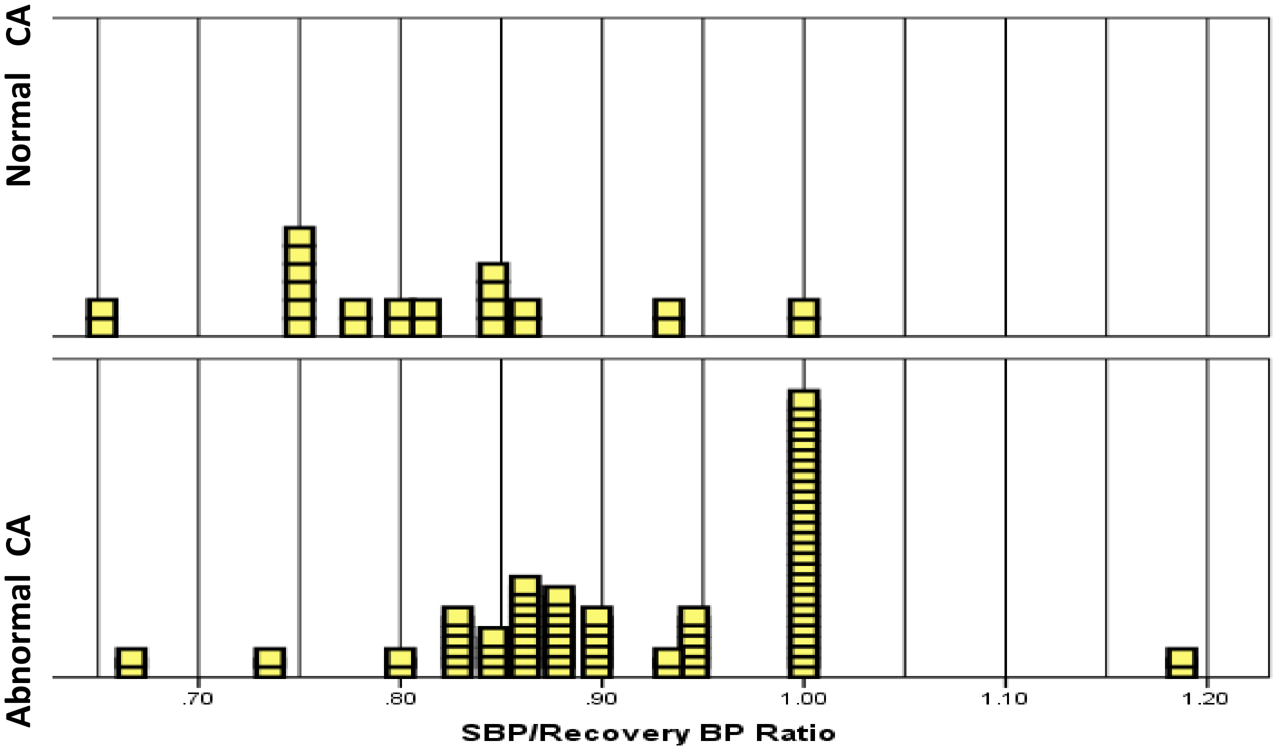
Test Result:SBP/Recovery BP Ratio Positive if Greater Than or Equal To	Sensitivity%	Specificity%
0.6594	100	8.3
0.7010	97.4	8.3
0.7426	94.7	8.3
0.7639	94.7	33.3
0.7889	94.7	41.7
0.8063	92.1	50.0
0.8180	92.1	58.3
0.8284	86.8	58.3
0.8377	84.2	58.3
0.8441	81.6	66.7
0.8481	81.6	75.0
0.8536	78.9	75.0
0.8619	75.0	83.3
0.8708	67.1	84.5
0.8787	61.8	86.4
0.8885	56.6	87.3

SBPR= systolic blood pressure ratio



Figure(1)Systolic blood pressure ratio (SBPR) distribution of the cases involved in our study

SBP=systolic blood pressure Bp=Blood pressure



Figure(2)

Distribution of SBP/recovery blood pressure ratio in normal and abnormal coronary angiography

CA=CORONARY ANGIOGRAPHY

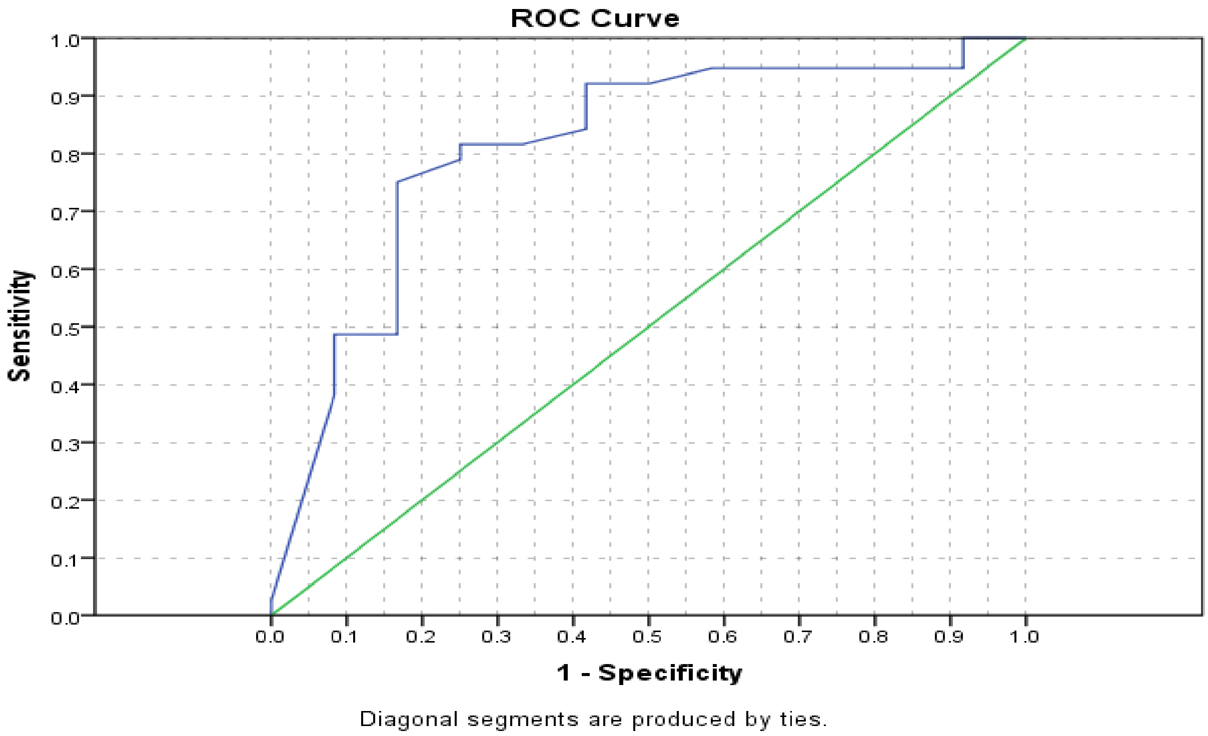


Figure (3)Receiver operating characteristic

ROC: Receiver operating characteristic used to find cut off value of mean SBPR of highest and sensitivity and specificity

Discussion: Mean age of patients is 55.49±7 years which is less than mean age 59±11 years of patients taken by McHam SA, Marwick TH, Pashkow FJ et al.[22] which may reflect that coronary artery disease occur earlier in our population this may be due to uncontrolled risk factors ,life style and dietary habits .The most common reason for terminating treadmill exercise test was fatigue which is similar to the result of McHam SA et al.[22] but higher percentage in their study 60% versus 81% which may be related to age of patients , 55.49±7 years in our study versus 59±11 in their study .Exercise duration during TMT of normotensive patient without coronary artery disease was significantly longer than normotensive with CAD 460±20 second versus 345±175 second with the significant p-value (patient<0.05) but it is not significant (p-value 0.4) in those with hypertension whether they have CAD or not 364±12second versus 300±15 second may be related to diastolic dysfunction which is present in most of hypertensive patients and usually presented with fatique. The peak systolic blood pressure in patients with coronary artery disease was less than peak systolic blood pressure in those with out coronary artery disease 174±25 mm Hg versus 150±20 mmgh respectively with significant (p-value 0.01) , while in hypertensive patients was not significant which is similar to the result of Tsuda et al.[21] But the peak systolic blood pressure in patient with coronary artery disease this study was less than their study 151.8±21 mm Hg which may be due to that coronary artery disease was more severe in patient included in our study and found that the 3-minute systolic blood pressure response was significantly greater in patient with coronary artery disease, irrespective of presence of hypertension and no significant differences in SBPR were detected in comparism between those with normal coronary angiography weither normotensive or hypertensive this is similar to the result of study done by Tsuda M, et al [21] , in normtensive with out coronary artery disease 0.84 versus 0.81 and those with coronary artery disease 0.99 versus 0.91 while in hypertensive patients in both groups without CAD and with CAD 0.86±0.11 versus 0.83 and 1.02 versus 0.93 respectively.Post exercise blood pressure ratio was related to the severity of coronary artery disease as appeared in our study. It is closely related to the number of vessels involved , the mean systolic blood pressure ratio in patients with single vessel disease and three vessel disease were0.91±0.06, 0.95±0.1 respectively while in those with normal coronary angiography was 0.81±0.9 with the significant p-value 0.0001 these results are compatible with that what is found by McHam SA et al[22] in their studies about (delayed systolic blood pressure recovery after graded exercise) which concluded that a delayed decline in SBP during recovery is associated with a greater liklihood of sever angiographic coronary artery disease and found that no patient with three vessel disease had SBP recovery ratio less than 0.9 . Blood pressure is directly proportional to cardiac output and systemic vascular resistance as in the equation {Blood pressure = cardiac output ×perepheral resistance}. The rise in blood pressure with exercise is predominantly caused by an increase in cardiac output, which is related to left ventricular systolic function and heart rate {Cardiac output = strok volume × heart rate} which are all influenced by the aforementioned mechanisms. During exercise, the increase in heart rate is a significant contributor to the increase in cardiac output. However, with recovery , heart rate decreases in virtually all patients , which translate into decrease in cardiac output and systolic blood pressure in these patients .This has not been the observation in many in many patients with coronary artery disease ,who frequently have exercise-induced impairment of left ventricular function, with a decline cardiac output. [20,23] After exercise, as myocardial oxygen demand decrease, left ventricular function rapidly improves, resulting in an elevation in systolic blood pressure during recovery as the heart rate decline. [24].The sensitivity and specificity of systolic blood pressure which is detected by using ROC curve for detecting CAD in our study, we found that the cutoff point with the highest sensitivity and specificity for detecting CAD was 0.86 which is lower than cutoff point (0.90)of the result of Tsuda M, Hatano K, Hayashi H, et al.[٢١] with sensitivity about 75 in our study versus74.4% but higher specificity (83%) than their result 77.1% these difference may be related to the number of patients taken in our study and their study 100patients versus 181 patients .

Limitation of the study: Limited number of the patients that full fill our criteria and relatively short period of thesis. Difficulty in the arrangement of the appointment for cardiac catheterization for the patients within short period from TMT .

Conclusions:1-Systolic blood pressure ratio in patients with ischemic heart disease disease is higher than normal population.2- Post exercise blood pressure response correlate with severity of coronary artery disease.

Recommendation: systolic blood pressure ratio is routinely documented in the reports of treadmill exercise test , which is simple and can be obtained in every patients doing treadmill exercise test and may reflect the presence and severity of coronary artery disease and increase the sensitivity of TMT .

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