The value of exercise stress testing in prediction of angiography amongst South African patients using quantitative scoring systems

Preesha Premsagar, Colleen Aldous# and Tonya Esterhuizen†*

*Department of Internal Medicine, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa
#Department of Clinical Medicine, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa
†Division of Epidemiology/Biostatistics, Department of Global Health, Faculty of Medical and Health Sciences, Stellenbosch University and Tygerberg Hospital, Bellville, South Africa

Address for correspondence:
Dr Preesha Premsagar
Department of Internal Medicine
Nelson R Mandela School of Medicine
University of KwaZulu-Natal
Durban
4001
South Africa

Email:
preesha1@yahoo.com

ABSTRACT

Background: Accurate pre-test assessment of high risk patients may increase positive yield on angiography. Exercise stress testing (EST) prediction of angiography, may be evaluated by Duke Treadmill Score (DTS), and Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score, respectively.

Aim: To investigate the value of EST in prediction of angiography amongst South African patients using quantitative scoring systems.

Methods: The DTS and SYNTAX score were compared in patients with high risk pre-test assessments selected for angiography. Logistic regression modelling determined the odds ratio of abnormal angiograms using EST as a predictor.

Results: Pre-test assessment of 525 suspected coronary artery disease patients, indicated angiography in 131 high risk individuals. The positive yield of abnormal angiograms was 58.0%, with no correlation between DTS and SYNTAX scores (Pearson's correlation coefficient = 0.113, p=0.200). There was low predictive probability on receiver-operator-curve for DTS when compared to angiogram results (area under curve (AUC)=0.529, p=0.574), and SYNTAX categories (AUC=0.432, p=0.378). Chi-square tests had no significance between angiography and EST (all p-values >0.05). However DTS predicted abnormal angiograms with odds ratio of 1.92 when relevant cardiovascular risk factors (smoking, BMI, age) were added.

Conclusion: Pre-test assessment of high risk patients represented a homogenous group with prevalent cardiovascular risk factors. However, the high risk group had no relationship between DTS and SYNTAX scores, indicating DTS alone discounts risk factors. Modelling accounted for DTS limitation by demonstrating an obese, elderly smoker with high risk category DTS is 1.92 times more likely to have an abnormal angiogram.

SAHeart 2021;18:96-106

INTRODUCTION

Exercise stress testing is often performed on patients with suspected coronary artery disease (CAD). It is used as a standard for comparison with other clinical tests and risk markers. It is also the least costly of all provocative non-invasive tests. Results are reported as positive, negative and in some cases, inconclusive. However, further diagnostic and prognostic predictive accuracy may be extracted from the exercise stress test when multiple pieces of information from the patient's clinical history and the treadmill test are integrated.(1) This integration was achieved in 1987 when Mark and colleagues described a prognostic exercise treadmill score that was based on the duration of exercise, ST-segment deviation (depression or elevation), and the presence and severity of angina during exercise. Known as The Duke Treadmill Score, this treadmill score has been shown to stratify prognosis accurately for both inpatient and outpatient coronary artery disease populations. The Duke Treadmill Score functions as a method to quantitatively measure outcomes on exercise stress test and select the high risk patient for angiography and possible revascularisation.(2) The Duke Treadmill score has been shown to be better than ST depression alone for diagnosing angiographic coronary artery disease.(3)

The 2002 joint report from the American College of Cardiology and the American Heart Association Task Force on exercise testing (ACC/AHA) declared that an exercise stress test is most useful as a diagnostic test in patients with an intermediate (25% - 75%) pre-test assessment of CAD. Abnormal exercise stress test results in these patients are more likely to be true positives than in patients with lower pre-test assessments.[3] However, the gold standard for diagnostic testing for coronary artery disease is coronary angiography. Outcomes on angiography can also be quantitatively measured with a scoring system. The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score, developed from the SYNTAX trial, characterise coronary anatomy based on nine anatomic criteria. Following this trial, the European Society of Cardiology and The Japanese Circulation Society had produced guidelines forming an integral part in the decision making for coronary revascularisation.[4,5]

Although invasive coronary angiography is the gold standard for diagnosis of CAD, the diagnostic yield is reported to be approximately 41%. This implies the need for better screening and risk stratification tools in order to make more accurate decisions on patients selected for angiography.[6] Our study aimed to evaluate the relationship between exercise stress testing and coronary angiography amongst South African participants, using quantitative scoring systems.

AIM

To investigate the value of exercise stress testing in prediction of angiography amongst South African patients using quantitatively scoring systems.

METHOD

Patient selection

We retrospectively studied 525 consecutive participants with suspected CAD, from January 2002 - December 2008 at Inkosi Albert Luthuli Hospital, Durban, South Africa. CAD was suspected based on demographic information, chest pain, medical comorbid risks, electrocardiographic findings, echocardiography results and exercise stress test results. Patients with known CAD were excluded. After screening of the 525 subjects, 173 subjects were selected for coronary angiography. Written informed consent for investigation was obtained from patients. The study was approved by the Biomedical Research Ethics Committee of University of KwaZulu-Natal Nelson R Mandela School of Medicine. There was no conflict of interest.

Exercise stress

Angina indicates coronary artery disease and is therefore caused by a demand-supply mismatch as a consequence of coronary stenosis. The exercise stress test screens for angina by using effort (exercise stress) to measure the heart's ability to increase blood supply in response to a demand increase during workload. Bruce Protocol treadmill testing was performed. Stress-test results were reported as negative, positive or inconclusive in some cases.

In addition to results, the Duke Treadmill Score (DTS), an objective scoring system was applied. DTS is used to measure and risk-stratify exercise time measurements, ECG changes and symptoms. DTS equation = Exercise time (minutes) – (5 x maximum ST deviation in mm) – (4 x treadmill angina index). The ST deviation is the measurement of ST change from baseline for both ST elevation and horizontal or down-sloping ST depression. The angina index is the score representative of the patient's symptoms on effort. For no angina, the score is 0, for angina induced by effort but relieved with rest, the score is 1, and for angina that does not decrease with rest, the score is 2. Once calculated, the Duke Treadmill Score is categorised into a Duke Risk Category which reflects the predictive likelihood of having coronary artery disease, as well as the 4 year predicted survival rate (measured as a percentage). A score above 5 is low and associated with a 4 year survival rate of 79%. If the score is in the range between +4 and -10, it is a moderate risk and predicts a 4 year survival rate of 85%. However, a score below -10 is high risk and indicates a survival rate of 99% only.[2,3]

The online calculator was used for the measurement key, available at http://www.cardiology.org/tools/medcalc/duke/. Scores were captured in Microsoft Excel and risk-stratified.

Angiography

Angiography results were reported as normal or abnormal. Angiograms reported as normal had no atheroma or non-occlusive atheroma. Angiograms with single, double or triple vessel disease with >50% luminal stenosis were reported as abnormal. Angiography was also scored with the SYNTAX score. SYNTAX score was calculated using 2 factors: the segment weighing factors and the lesions adverse characteristics. The coronary arteries were divided into 16 segments representing the coronary tree. Left and right dominance had different trees. In the right dominated system, the RCA and LMS supply 16% and 84% of the blood to the left ventricle, respectively. From the 84%, two thirds and one third flowed through the LAD and circumflex, respectively. In the left dominated system, there was no RCA supply; therefore, the LMS supply was 100%, and the RCA share of blood to the LV was through the circumflex. A weighting factor was given for each segment of the vessel, representing the portion of blood supply through each vessel to the LV for the left or right dominant system of normal coronary vessels.[7]. The degree of stenosis and the other adverse characteristics were visually assessed on angiography. A lesion above 50% stenosis was considered significant. Subtotal stenosis (50% - 99%) and total occlusions (100%) were assigned a diameter reduction value of 2 and 5, respectively. The weighting factor for each vessel in the arterial tree was multiplied by the appropriate diameter reduction value. The points were then added for all the tree segments. Further points were added for other adverse characteristics. The total was the SYNTAX score. The total SYNTAX score was assigned to a risk category. A score from ≤22 was low risk, 23 - 32 was intermediate risk, and ≥33 was high risk.[4,5] The online calculator was used for the measurement key, available at http://www.syntaxscore.com. Scores were captured in Microsoft Excel and risk-stratified. The LV function category was also captured.

Statistical analysis

The study data were analysed with Stata version 16.0. Descriptive analysis was done to evaluate the demographics, DST and SYNTAX scores. Relationships were first tested between 2 patient groups: those not selected for angiography and those selected for angiography. Thereafter, amongst those selected for angiography, EST was compared between those with normal angiograms and those with abnormal angiograms. Chi-squared tests were used for categorical data, and t-tests were used to compare means between the groups. DTS and SYNTAX scores were correlated. Receiver operator curve (ROC) analysis was used to compare the DTS with angiogram outcomes (normal and abnormal) and to compare DTS with the Duke Risk Category (low and medium-high). Logistic regression analysis was used to measure the prediction of DTS on an abnormal angiogram result, after adjustment of the relevant predictors (demographics and medical comorbidities).

RESULTS

Demographics and risk factors for cohort of 525 patients

The cohort consisted of 525 participants who were screened for CAD. Thereafter 173 participants underwent coronary angiography, and 352 did not. Of the 173 patients, 131 underwent exercise stress testing prior to angiography. Of the 352 subjects without angiography 319 underwent exercise stress testing. EST was contra-indicated or not available for the remainder (Figure I). Descriptive statistics for demographics and CAD risk factors are tabulated (Table I).

Differences between the patients selected for angiography (n=173) and those not selected for angiography (n=352)

The differences between those patients selected for angiography and those not selected were demographic and medical risk

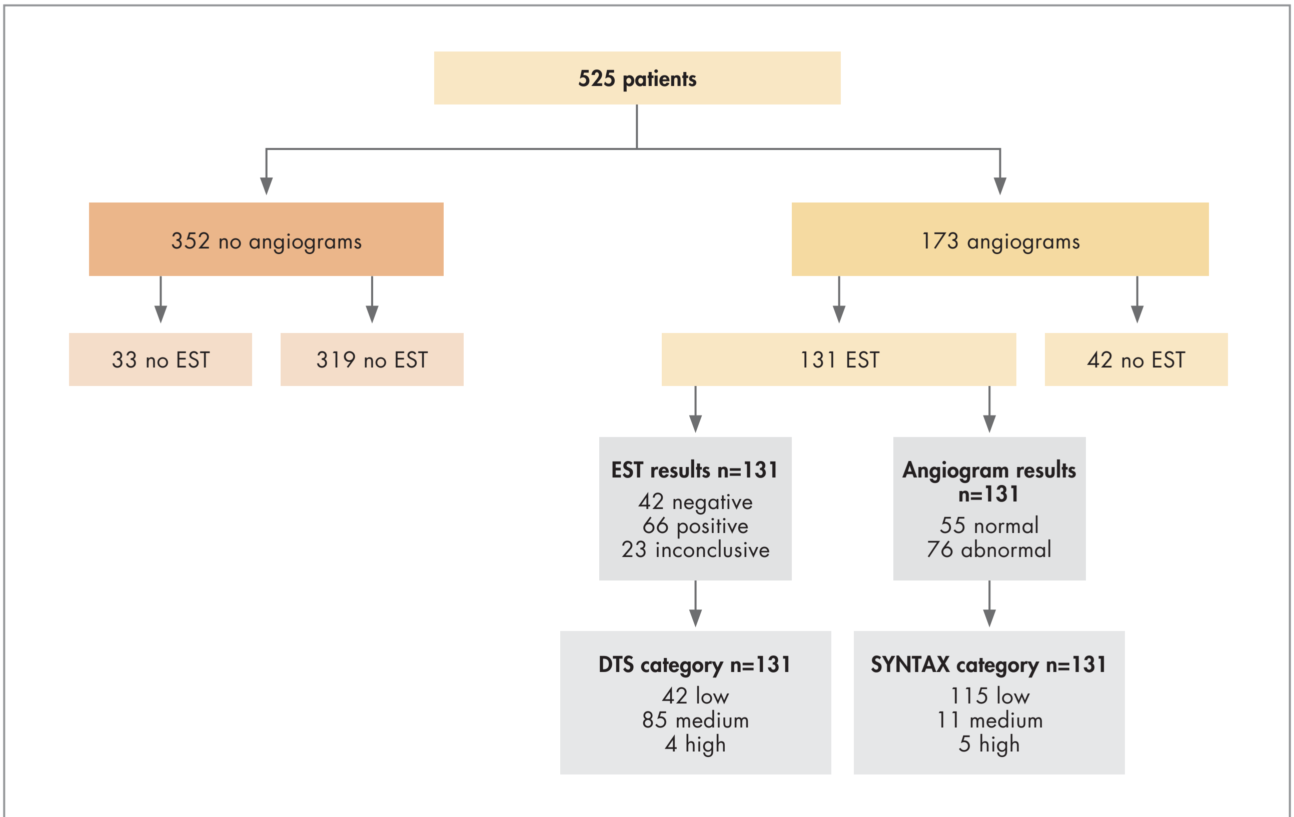

FIGURE I: Cohort, investigations, results, score categories.
EST = exercise stress test , DTS = duke treadmill score, SYNTAX = synergy between percutaneous coronary intervention with taxus and cardiac surgery.

TABLE I: Baseline characteristics (n=525).

Demographics				
Gender	Female		Male	
	299 (57%)		226 (43%)	
Race	Black	Coloured	White	South-East Asian descent
	33 (6.3%)	9 (1.7%)	82 (15.6%)	401 (76.4%)
Presentation age	Minimum-maximum	Mean	Std. error	Std. dev.
	24.33 - 81.75	53.4062	0.45051	10.32258
Medical Comorbidities				
	No		Yes	
Diabetes	358 (68.2%)		167 (31.8%)	
Hypertension	186 (35.4%)		339 (64.6%)	
Dyslipidaemia	250 (47.6%)		275 (52.4%)	
Family history of CAD	289 (55.0%)		236 (45%)	
Smoking	338 (64.4%)		187 (35.6%)	
	Minimum-maximum	Mean	Std. error	Std. dev.
BMI score kg/m^2	16 - 50	29.22	0.262	6.001
WC (cm) (n=524) 1 missing (0.2%)	74 - 150	97.07	0.501	11.459
Duke Score (n=450) 75 missing (14.3%)	-22.51 - 35.00	3.1588	0.25232	5.34664
	Normal/underweight	Overweight		Obese I II III
BMI category	132 (25.1%)	173 (33.0%)		220 (71.9%)
WC category (n=524) 1 missing (0.2%)	Normal		Increased	
	211 (40.2%)		313 (59.6%)	
Duke risk category (n=450) 75 missing (14.3%)	Low risk	Medium risk		High risk
	209 (39.8%)	233 (44.4%)		8 (1.5%)
EST and angiography done (n=525)				
	EST done			
	No	Yes		Total
Angiogram done No	33	319		352
Yes	42	131		173
Total	75	450		525

BMI = body mass index, CAD = coronary artery disease, EST = exercise stress test, Std. dev. = standard deviation, Std. error = standard error, WC = waist circumference.

factors, as well as screening test results. Chi-squared tests and t-tests showed that patients selected for angiography were more likely male gender (p=0.001), presented at an older age (p=0.011, mean age selected 51-years), South-East Asian descent (p=0.013), diabetics (p=0.047), dyslipidaemia (p<0.001), had positive family history of CAD (p=0.002) and increased BMI (p=0.042). Although 99 out of 525 (18.9%) patients had inconclusive EST, the EST results influenced the decision to proceed to angiogram (p=0.002). The Duke Treadmill Score was higher in patients who were selected for angiography (p<0.001). The Duke Risk category was higher amongst patients selected for angiography (p<0.001). Overall, the high risk patient likely to have CAD based on risk factors and screening was appropriately selected to undergo diagnostic testing with angiography (Table II).

Differences in EST results for patients with normal angiography and abnormal angiography (n=131):

After the 525 patients' risk factors and screening tests were considered, 173 patients were selected for angiography. Out of this 173, 131 had undergone exercise stress testing prior to selection, but 42 did not have exercise stress testing. The reasons for these 42 patients were: grade IV dyspnoea = 16, fast atrial fibrillation = 2, fixed outflow tract obstruction = 5, hypertensive urgency = 2, lower limb pathology = 5, systolic dysfunction = 4, unknown/unavailable = 8 (Figure 1). Baseline characteristics of the 131 patients with angiography are described (Table III).

The results, scoring systems and risk categories were determined from the stress tests and angiograms in the n=131 patients: Out of 131 stress tests, 23 results were inconclusive (2 = variable baseline, 2 = had bundle branch blocks at baseline, 19 had early fatigue), 42 results negative, and 66 results were positive. Out of 131 angiograms, 55 results were normal, and 76 results were abnormal (Figure 1).

The SYNTAX score increases as disease severity and risk increase; in contrast, the DTS decreases as disease severity and risk increase; therefore a negative correlation between the 2 quantitative scores was expected. Pearson's correlation demonstrated that there was no correlation between DTS and SYNTAX scores (Pearson's correlation coefficient = 0.113, p=0.200) (Figure 2). Receiver-operator-curve (ROC) curve analysis was performed with exercise stress testing as the screening test and angiography as the gold standard. The ROC analysis for DTS and angiogram results (normal and abnormal) had an area under the curve of 0.529 (p=0.574) (Figure 3A). The ROC analysis for DTS and SYNTAX categories (low and medium-high) had an area under the curve of 0.432 (p=0.378) (Figure 3B).

The angiogram was tested with results (normal and abnormal) and SYNTAX risk categories (low and intermediate-high) against exercise stress testing results (positive, negative and inconclusive) and Duke Risk Categories (low and intermediate-high) using chi-squared tests. There was no significance detected. (Table IV).

Logistic regression analysis for angiogram results (normal and abnormal) (n=131)

An analysis with contributing risk factors was done using the DTS and the contributing variables extracted from the crude analysis (smoking, BMI, age). The final odds ratio of having an abnormal angiogram result based on DTS categories with added factors of the presence of smoking, increased BMI, increased age, was 1.92 (Table V).

DISCUSSION

Suspected CAD and the pre-test probability from 525 patients

The initial evaluation of a patient having suspected stable coronary artery disease involves the pre-test assessment for CAD. This is an important stage of the investigation process because it directs further diagnostic management with invasive coronary angiography, which is the gold standard for diagnosis of CAD.[6,8] The pre-test assessment includes demographics, medical comorbidities and screening tests. Amongst the 525 patients who underwent pre-test assessment in our study, male gender, older presentation age, South-East Asian descent, diabetes, dyslipidaemia, positive family history of CAD, increased BMI, and increased WC were noted in the patients selected for angiography compared to those not selected. The EST in the patients selected for angiography also showed a higher risk compared to those not selected. Overall, it appears that the 131 high risk patients likely to have CAD based on pre-test assessment were appropriately selected for angiography.

Patients selected for diagnostic testing after screening from 131 patients

Out of 131 patients who underwent angiography, abnormal angiogram yield was 76 patients (58.0%). However, it may be noted that there was no correlation between the DTS on EST and the SYNTAX scores on angiography. It is further observed that ROC curve analysis testing EST against angiography as the gold standard has a small area under the ROC curve indicating low sensitivity and specificity for EST as a pre-test for CAD. The categorical tests for outcomes further support the absence of a relationship. It may be considered that the 131 patients selected for angiography had an inherent bias as they had a high risk pre-test assessment based on demographics, medical comorbidities and EST. The American College of Cardiology and the American Heart Association Task Force on exercise testing (ACC/AHA) describes work-up bias which refers to the fact that most reported studies were affected by clinical practice where pre-test results were used to determine who should be included for further testing.[3]

Advantages and limitations to DTS

In 1998 Shaw had assessed the utility of the DTS for risk-stratifying high risk outcomes of tight stenosis and multi-vessel disease on angiography. Patients with low risk DTS had no CAD, while high-risk DTS patients had extensive or multivessel CAD. The study demonstrated that DTS provided accurate prognostic estimates with independent predictive information, concluding that DTS was useful for risk-stratifying diagnostic and prognostic categories.[1]

TABLE II: Differences between the patients selected for angiography (n=173) and those not selected for angiography (n=352).

		Angiogram done			Cross-tabulation	
		No	Yes	Total	Pearson's x2	P-value
Gender	Female	219 (73.2%)	80 (26.8%)	299 (100%)	12.071	0.001
	Male	133 (58.8%)	93 (41.2%)	226 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Race	Black	26 (78.7%)	7 (21.3%)	33 (100%)	10.840	0.013
	Coloured	2 (22.2%)	7 (77.8%)	9 (100%)		
	White	58 (42.9%)	24 (57.1%)	82 (100%)		
	South-East Asian descent	266 (66.3%)	135 (33.7%)	401 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Diabetes	No	250 (69.8%)	108 (30.2%)	358 (100%)	3.950	0.047
	Yes	102 (60.0%)	65 (40.0%)	167 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Hypertension	No	129 (69.3%)	57 (30.7%)	186 (100%)	0.694	0.405
	Yes	233 (68.7%)	116 (31.3%)	339 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Dyslipidaemia	No	193 (77.2%)	57 (22.8%)	250 (100%)	22.265	<0.001
	Yes	159 (57.8%)	116 (42.2%)	275 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Family history of CAD	No	210 (72.6%)	79 (27.4%)	289 (100%)	9.180	0.002
	Yes	142 (60.1%)	94 (39.9%)	236 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Smoking	No	245 (72.4%)	93 (27.6%)	338 (100%)	12.699	<0.001
	Yes	107 (57.2%)	80 (42.7%)	187 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
BMI category	Underweight/ Normal	91 (68.9%)	41 (31.1%)	132 (100%)	5.831	0.054
	Overweight	104 (60.1%)	69 (39.9%)	173 (100%)		
	Obese I, II, III	157 (71.3%)	63 (28.7%)	220 (100%)		
	Total	**352 (67.0%)**	**173 (33.0%)**	**525 (100%)**		
Waist circumference category	Normal	139 (65.8%)	72 (34.2%)	211 (100%)	0.270	0.270
	Increased	213 (68.1%)	100 (31.9%)	313 (100%)		
	Total	**352 (67.1%)**	**172 (32.9%)**	**524 (100%)**		
EST result	Negative	139 (76.9%)	42 (23.1%)	181 (100%)	12.489	0.002
	Positive	104 (61.7%)	66 (38.3%)	170 (100%)		
	Inconclusive	76 (76.7%)	23 (23.3%)	99 (100%)		
	Total	**319 (70.8%)**	**131 (29.2%)**	**450 (100%)**		
Duke category	Low	167 (79.9%)	42 (20.1%)	209 (100%)	16.055	<0.001
	Medium	148 (63.5%)	85 (36.5%)	233 (100%)		
	High	4 (50.0%)	4 (50.0%)	8 (100%)		
	Total	**319 (70.8%)**	**131 (29.2%)**	**450 (100%)**		

Independent samples t-test for patients selected for angiography (n=173) and those not selected for angiography (n=352)						
	t	Mean diff.	Std. error diff.	95%CI lower	95%CI upper	P-value
Age	-2.561	2.41758	.94382	.56133	4.27383	0.011
WC (cm)	-2.102	-2.233	.961	-4.122	-.344	0.021
BMI (kg/m^2)	2.044	1.063	.520	.041	2.086	0.042
Duke score	4.960	2.83797	.57223	1.71006	3.96588	<0.001

BMI = body mass index, CAD = coronary artery disease, EST = exercise stress test.

TABLE III: Baseline characteristics of n=131 patients.

Demographics					
Gender	Female		Male		
	57 (43.5%)		74 (56.4%)		
Race	Black	Coloured		White	South-East Asian descent
	5 (3.8%)	5 (3.8%)		18 (13.7%)	103 (78.6%)
Presentation age	Minimum-maximum	Mean	Std. error	Std. dev.	Variance
	2.50 - 74.17	51.0231	0.96059	10.99442	120.877
Medical Co-morbidities and screening tests					
	No			Yes	
Diabetes	358 (68.2%)			167 (31.8%)	
Hypertension	186 (35.4%)			339 (64.6%)	
Dyslipidaemia	250 (47.6%)			275 (52.4%)	
Family history of CAD	289 (55.0%)			236 (45%)	
Smoking	338 (64.4%)			187 (35.6%)	
	Minimum-maximum	Mean	Std. error	Std. dev.	Variance
BMI score kg/m^2	17.6 - 41.9	27.659	0.4158	4.7591	22.649
WC (cm)	75 - 141	98.28	0.841	9.584	91.849
Duke Score	-22.51 - 10.00	1.1489	0.50006	5.72339	32.757
SYNTAX Score	0.00 - 43.50	8.0382	0.88803	10.16397	103.306
	Normal/ underweight	Overweight/Increased WC			Obese I II III
BMI category	37 (28.2%)	53 (40.5%)			41 (31.3%)
WC category	56 (42.7%)	74 (56.5%)			
EST result	Negative	Inconclusive			Positive
	42 (32.1%)	23 (17.6%)*			66 (50.4%)
Duke category	Low risk category	Medium risk category			High risk category
	42 (32.1%)	85 (64.9%)			4 (3.1%)
Angiogram result	Normal		Abormal		
	55 (42.0%)		76 (58.0%)		
SYNTAX category	Low risk category	Medium risk category			High risk category
	115 (87.7%)	11 (8.4%)			5 (3.8%)

BMI = body mass index, CAD = coronary artery disease, EST = exercise stress test, Std. dev. = standard deviation, Std. error = standard error, WC = waist circumference.
**Reasons for 23 inconclusive exercise stress tests: 2=variable baseline, 2=bundle branch block, 2=early fatigue*

The SYNTAX score takes into account different parameters such as lesion location, bifurcation, angulation, diameters and calcification, and it is widely accepted and used as a CAD complexity marker. There is however, little information about the relationship between DTS and coronary artery lesion properties. Acar found a significant association between DTS and coronary artery lesion complexity. Acar compared DTS and SYNTAX scores and observed that patients with low risk DTS had normal coronary arteries, and patients with high risk DTS had higher SYNTAX scores, with higher rate of long term cardiac events.[9]

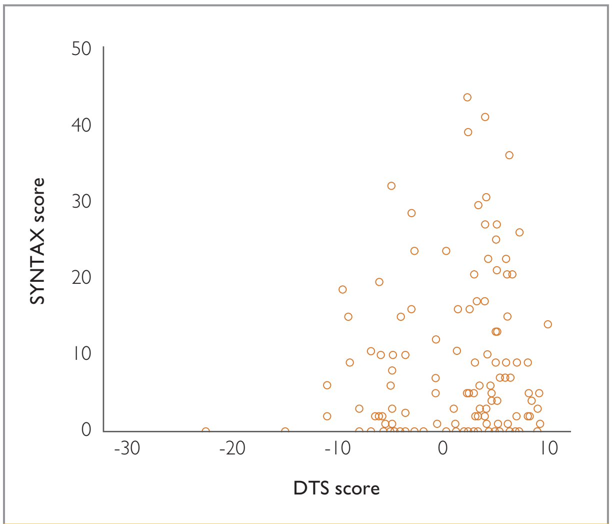

FIGURE 2: Scatter plot demonstrating DTS (independent) and SYNTAX score (dependant).

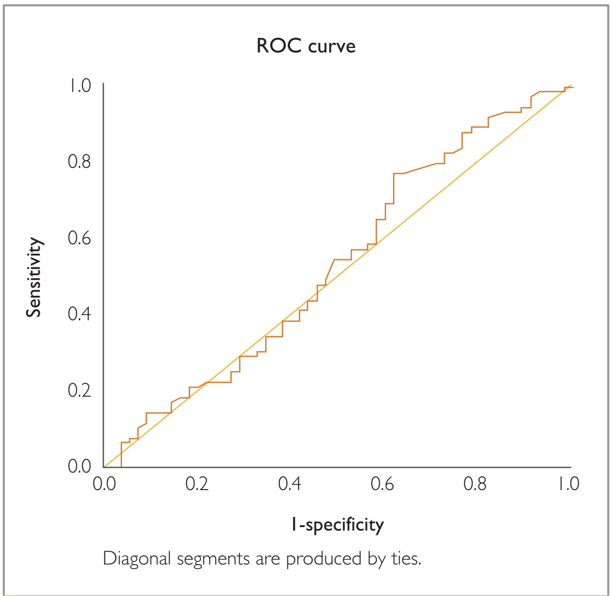

FIGURE 3A: ROC curve analysis of DTS and angiogram outcome.

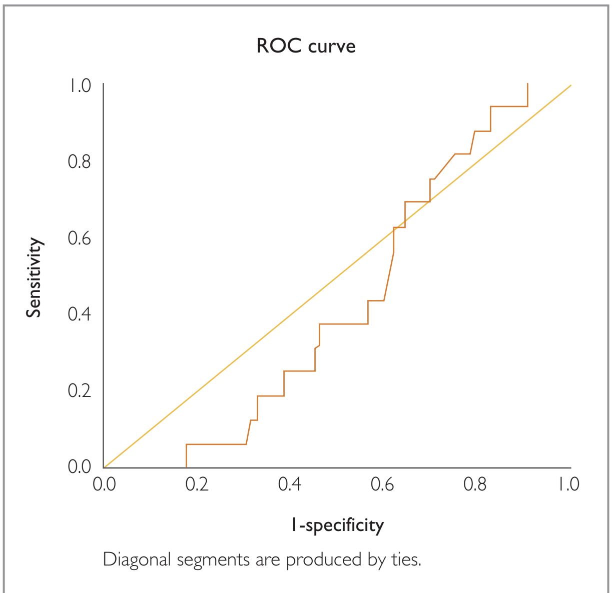

FIGURE 3B: ROC curve analysis of DTS and SYNTAX categories

Asad demonstrated that the analysis of variance between DTS and SYNTAX score has a strong association (p=0.04). Therefore Duke Treadmill score is a significant prognostic tool for coronary artery disease. Chi-square test between Duke Treadmill Score and coronary arteries involvement showed a strong significance (p=0.001); therefore it was concluded that DTS might predict artery lesions and be used as a tool guiding management strategy.[10]

While the DTS may be found to correlate with the SYNTAX score, the cut-off points may not always align, indicating that further information may be needed to make the DTS correspond better with the SYNTAX score. In a study by Gunayadin, a strong negative correlation between DTS and SYNTAX score (r=-072, p<0.001) was found. The AUC of DTS was 0.83 (0.77 - 0.88, p<0.001) for predicting the significant presence of CAD, with optimal DTS cut-off value calculated at -3.7 (sensitivity of 74%, a specificity of 73%). The AUC of DTS was 0.84 (0.78 - 0.90, p<0.001) for predicting high risk SYNTAX category, with optimal DTS cut-off value calculated at -11.2 (sensitivity of 81%, a specificity of 80%).[11]

Shaw, Acar and Asad effectively demonstrated that DTS is useful in stratifying important diagnostic and prognostic patient risk categories.[1,9,10] Gunaydin DTS was an independent predictor of the high SYNTAX score in multivariate analysis once the cut-off points were adjusted.[11] A limitation, however, that did not affect these studies is that DTS, does not describe the role of modifiable cardiovascular risk factors for complexity of coronary artery disease.[6,12] Our research found no data assessing the addition of cardiovascular risk factors in DTS diagnostic values to predicting the complexity of coronary artery lesions assessed based on SYNTAX, both in South African publications and others. Notably, our patient selection to undergo coronary angiography was also dependent upon cardiovascular risk factors (demographic and medical comorbidities) and not based on DTS alone. While the homogeneity of the angiography group may influence the results found, other studies have identified a relationship with lesion complexity. The answer, therefore, may lie in the combination of the cardiovascular risk factors with the DTS to predict the angiogram.

TABLE IV: Differences in EST results for patients with normal angiography and abnormal angiography (n=131).

Correlation between DTS and SYNTAX scores							
Score	Mean		Std. deviation		Pearson's correlation		P-value
DTS	1.1489		5.72339		0.113		0.200
SYNTAX	8.0382		10.16397				
ROC curve analysis							
Predictor	Gold standard		Area under the curve	Standard error	95% confidence interval		P-value
					Lower	Upper	
DTS	Angiogram outcome		0.529	0.052	0.427	0.631	0.574
	Normal	Abnormal					
	55 (41.9%)	76 (58.1%)					
DTS	SYNTAX category		0.432	0.060	0.314	0.550	0.378
	Low	Medium high					
	115 (87.7%)	16 (12.3%)					
Comparisons of outcomes							
		SYNTAX risk category			Cross tabulation		
		Low	Intermediate-high	Total	Pearson chi x^2		P-value
EST result	Negative	36 (85.7%)	6 (14.3%)	42 (100%)	3.439		0.179
	Positive	61 (92.4%)	5 (7.6%)	66 (100%)			
	Inconclusive	18 (78.2%)	5 (21.8%)	23 (100%)			
	Total	**115 (87.7%)**	**16 (12.3%)**	**131 (100%)**			
DST category	Low	37 (88.0%)	5 (12.0%)	42 (100%)	0.941		0.593
	Medium-high	78 (87.6%)	11 (12.4%)	89 (100%)			
	Total	**115 (87.7%)**	**16 (12.3%)**	**131 (100%)**			
		Angiogram result			Cross tabulation		
		Normal	Abnormal	Total	Pearson chi x^2		P-value
EST result	Negative	20 (47.6%)	22 (52.2%)	42 (100%)	1.025		0.599
	Positive	25 (37.8%)	41 (62.2%)	66 (100%)			
	Inconclusive	10 (43.4%)	13 (56.6%)	23 (100%)			
	Total	**55 (41.9%)**	**76 (58.1%)**	**131 (100%)**			
DST category	Low	21 (50.0%)	21 (50.0%)	42 (100%)	1.631		0.202
	Medium-high	34 (38.2%)	55 (61.8%)	89 (100%)			
	Total	**55 (41.9%)**	**76 (58.1%)**	**131 (100%)**			

DTS = duke treadmill score, EST = exercise stress test,

Combining cardiovascular risk factors to the DTS

Almeida calculated the pre-test assessment of CAD using 3 scoring systems: Coronary Artery Disease Consortium 1 (age, gender, type of chest pain), Duke Clinical Score (age, gender, smoking, diabetes, previous myocardial infarction, type of chest pain, dyslipidaemia, electrocardiogram changes) and Coronary Artery Disease Consortium 2 (age, gender, type of chest pain, diabetes, hypertension, dyslipidemia, smoking). The population was classified according to the risk of having CAD: low (<15%), intermediate (15% - 85%), and high (>85%), in line with the ESC guidelines. Almeida noted that combined risk factors improve accuracy, especially, with Duke Clinical Score identified the higher risk patients and CAD consortia identified the lower risk patients.[6] Although this study did not take into account the DTS as part of the predictive model, it did demonstrate that considering combining risk factors improves predictive accuracy.

Dzenkeviciute used DTS and SYNTAX score to determine subjects for coronary revascularisation. Calculated DTS and SYNTAX scores were categorised into Duke Risk Categories

TABLE V: Logistic regression analysis for angiogram results (normal and abnormal) with contributing risk factors.

Angiogram outcome (normal or abnormal)		Odds ratio	Std. error	z	p	95% CI lower	95% CI upper
Duke score and angiogram							
Duke categories (medium-high versus low)		**1.617647**	**0.6113586**	**1.27**	**0.203**	**0.7712382**	**3.392962**
Constant estimate of baseline odds		0.6181818	0.404683	-0.73	0.463	0.1713525	2.23019
Adding age							
Age		1.046973	0.0190822	2.52	0.012	1.010233	1.08505
Duke categories (low and medium-high)		**1.761847**	**0.6928714**	**1.44**	**0.150**	**0.8151194**	**3.808161**
Constant estimate of baseline odds		0.0520526	0.0633293	-2.43	0.015	0.0047955	0.5649999
Adding BMI							
BMI category with reference to underweight/normal	Overweight	2.591298	1.187303	2.08	0.038	1.055617	6.361041
	Obese 123	1.656249	0.7952467	1.05	0.293	0.6462816	4.244528
Age		1.04661	0.0193041	2.47	0.014	1.00945	1.085137
Duke categories (low and medium-high)		**1.856917**	**0.7518504**	**1.53**	**0.126**	**0.8397462**	**4.10617**
Constant estimate of baseline odds		0.0284333	0.0368762	-2.75	0.006	0.0022381	0.3612291
Adding smoking							
Smoking		1.810475	0.688102	1.56	0.118	0.8595654	3.813347
BMI category with reference to underweight/normal	Overweight	2.503456	1.160481	1.98	0.048	1.009169	6.210346
	Obese 123	1.598307	0.7765616	0.97	0.334	0.6167241	4.142183
Age		1.04811	0.0196299	2.51	0.012	1.010334	1.087299
Duke categories (low and medium-high)		**1.918149**	**0.7835452**	**1.59**	**0.111**	**0.8613404**	**4.271593**
Constant estimate of baseline odds		0.01949	0.0262483	-2.92	0.003	0.0013914	0.273007

Std. error = Standard error, z = z-value, p = p-value, CI = confidence interval, BMI = body mass index.

and SYNTAX Risk Categories. A negative correlation between DTS and significant coronary artery stenosis (r=-0.181, p=0.005), SYNTAX score (r=-0.173; p=0.007), and cardiac revascularisations (r=-0.213; p=0.001) was found. Significant coronary artery stenosis was observed more often in patients of the high-risk group (85.7%) and more often in the moderate-risk group (71%) than in the low-risk group (50.7%; p=0.005). However, when multiple linear regression was used to predict coronary revascularisation from both the scores and previous myocardial infarction; a significant positive correlation was found. Dzenkeviciute demonstrated that DTS alone is a useful tool in suspecting significant coronary artery stenosis, but it is not accurate enough for revascularisation. Thus, by adding clinical information, its value may be maximised.[13]

While Shaw, Acar and Asad[1,9,10] found DTS alone to be a strong predictor for CAD, Almeida used combined risk factors (excluding DTS) to predict angiography,[6] and Dzenkeviciute used combined risk factors including DTS and SYNTAX score to predict revascularisation.[13] Our study also demonstrated appropriate patients were selected for angiography from the 525 patients who underwent pre-test assessment. However amongst that 131 identified high risk patients who underwent angiography, DTS alone did not reliably predict angiography. We therefore used a combination of risk factors, including DTS, to predict angiography, by applying logistic regression analysis. When the contributing risk factors (smoking, BMI, age) were added to DTS categories, the odds ratio of having an abnormal angiogram result was 1.92.

LIMITATIONS

Our study only consisted of patients who were able to complete exercise stress testing as of the pre-test assessment criteria. There were many patients whose pre-test assessment indicated angiography without exercise stress testing being performed, because EST was contraindicated. These patients had conditions such as claudication, osteoarthritis, fixed aortic valve output defects (aortic sclerosis). These patients were excluded from the study.

Some patients who were selected for angiography after EST was performed never underwent angiography. They were lost to follow up or declined invasive testing. These patients were also excluded from the study.

CONCLUSION

Suspected stable coronary artery disease requires a pre-test assessment to direct further diagnostic management. Coronary angiography remains the gold standard to diagnose CAD, but has a diagnostic yield of only 41%. This yield indicates the need for more precise pre-test assessment with comprehensive interpretation.[6]

Our study shows that the high risk patient likely to have CAD based on pre-test assessment was appropriately selected to undergo diagnostic testing with angiography. The patients selected for angiography further represent a homogenous group in whom risk factors are already identified as being significant.[3]

Our study had a positive yield of 58.0% abnormal angiograms, higher than other reports,[6] indicating the better pre-test assessment in our cohort. However, amongst these patients, it was found that EST and angiography alone had no relationship in any test performed. Despite our finding, it has previously been demonstrated that DTS is useful in stratifying patient risk categories.[1,11,12] A noted limitation of DTS is the exclusion of modifiable cardiovascular risk factors. This is significant because the pre-test assessment for CAD is based on cardiovascular risk factors (demographic and medical comorbidities) and not on DTS alone. A model was therefore created to combine the cardiovascular risk factors and DTS to predict the angiogram.

We created a logistic regression model using DTS as a predictor, with added cardiovascular risk factors to predict abnormal angiography outcomes. DTS categories predicted an odds ratio of having an abnormal angiogram of 1.92 once contributing risk factors (smoking, BMI, age) were added. Our study indicated that although DTS alone is an unreliable predictor of angiography, its reliability improves substantially when the cardiovascular risk factors that used in the pre-test assessment were added.

ACKNOWLEDGEMENTS

Prof Naresh Ranjith
Professor of Cardiology at Nelson R Mandela School of Medicine University at University of KwaZulu-Natal; and Coronary Care Unit RK Khan Hospital, Durban.

Prof Mariam Adhikari
Emeritus Professor of Paediatric Neonatology at Nelson R Mandela School of Medicine KwaZulu-Natal and Neonatology King Edward VIII Hospital, Durban.

Prof Datshana Prakash Naidoo
Professor of Cardiology at Nelson R Mandela School of Medicine KwaZulu-Natal and Coronary Care Inkosi Albert Luthuli Central Hospital, Durban.

Conflict of interest: none declared.

REFERENCES

1. Shaw LJ, Peterson ED, Shaw LK, et al. Use of a prognostic treadmill score in identifying diagnostic coronary disease subgroups. Circulation. 1998; 98:1622-1630.
2. Mark BD, Hlatky MA, Harrell FE Jr, et al. Exercise treadmill score for predicting prognosis in coronary artery disease. Clinical Trial Ann Intern Med. 1987;106(6):793-800.
3. Gibbons RJ, Balady GJ, Bricker TJ, et al. ACC/AHA 2002 Guideline update for exercise testing: A report of the American College of Cardiology/ American Heart Association task force on practice guidelines (Committee on exercise testing). American College of Cardiology Foundation and the American Heart Association, Inc. 2002.
4. Serruys PW, Morice M, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961-72.
5. Serruys PW, Onuma Y, Garg S, et al. Assessment of the SYNTAX score in the SYNTAX study. EuroIntervention, 2009;5:50-6.
6. Almeida J, Fonseca P, Dias T, et al. Comparison of coronary artery disease consortium 1 and 2 scores and Duke clinical score to pPredict obstructive coronary disease by invasive coronary angiography. Clin. Cardiol. 2016; 39(4):223-228.
7. Sianos G, Morel M, Kappetein AP, et al. The SYNTAX Score: An angiographic tool grading the complexity of coronary artery disease. EuroInterv. 2005;1:219-227.
8. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease – addenda. The European Society of Cardiology 2013.
9. Acar Z, Korkmaz L, Agac TC, et al. Relationship between Duke treadmill score and coronary artery lesion complexity. Clin Invest Med. 2012; 35(6):E365-E369
10. Asad M, Khadim R, Iqbal T, et al. Role of Duke treadmill score in assessing the severity of coronary artery disease in patients presenting with angina. Pak Armed Forces Med J. 2018;68 (Suppl-1):S147-S52.
11. Günaydın ZY, Bektaş 0, Gürel YE, et al. Value of Duke treadmill score in predicting presence and severity of coronary artery disease. Kardiologia Polska. 2016;74(2):127-134.
12. Nasution MKS, Siregar AA, Hasan H, et al. Addition of risk factors of coronary heart disease in diagnostic value of treadmill score for detecting complexity of coronary arterial lesions. ACI (Acta Cardiologia Indonesiana). 2018;4(2):88-94.
13. Dzenkeviciute V, Sapoka V, Kasiulevicius1 V, et al. Value of Duke treadmill score in predicting coronary artery lesion and the need for revascularisation. Kardiologia Polska, 2017;75(5):439-444.