Usefulness of the Duke Activity Status Index to Select an Optimal Cardiovascular Exercise Stress Test Protocol

Justin M. Canada, PhD[a,*], Mary Ann Reynolds, MS[a], Rachel Myers, MS[a], Josh West, MS[a], Katey Sweat, MS[a], Colton Powell, MS[a], Virginia McGhee, MSN[a], Michael C. Kontos, MD[a], Hem Bhardwaj, MD[a], Antonio Abbate, MD[a], Ross Arena, PhD[b], and W. Gregory Hundley, MD[a]

Exercise testing represents the preferred stress modality for individuals undergoing evaluation of suspected myocardial ischemia. Patients with limited functional status may be unable to achieve an adequate exercise stress, thus influencing the diagnostic sensitivity of the results. The Duke Activity Status Index (DASI) is a clinically applicable tool to estimate exercise capacity. The purpose of the current study was to assess the utility of the DASI to identify patients unable to achieve an adequate exercise stress result. Patients referred for exercise stress testing were administered the DASI pre-exercise. Baseline characteristics and exercise variables were evaluated including DASI-metabolic equivalents (DASI-METs), peak METs, exercise time (ET), and %-predicted maximal heart rate (%PMHR). Criteria for determining adequate exercise stress was defined as ≥85%PMHR or ≥ 5-METs at peak exercise. In 608 cardiovascular stress tests performed during the study period; 314 were exercise stress. The median DASI-METs (8.4 [interquartile range; 6.7 to 9.9]) was associated with estimated peak exercise METs (R=0.50, p <0.001), ET (R=0.29, p <0.001), and %PMHR (R=0.19, p = 0.003). DASI-METs were different between those with < or ≥85%PMHR (7.9 [6.6-9.0] vs. 8.9 [7.1-9.9], *P*=0.025) and those with < or ≥5-METs (5.8 [4.6 to 6.6] versus 8.9 [7.3-9.9], p <0.001). Receiver operating characteristic curve analysis identified a DASI-MET threshold of ≤/>7.4 to optimally predict adequate exercise stress (sensitivity=93%, specificity=71%). In conclusion, the DASI correlates with peak METs, ET, and %PMHR among patients referred for exercise testing and can be used to identify patients with an increased likelihood of an inadequate stress test result.
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Cardiac stress testing is the most common test used to diagnose ischemic heart disease and evaluate the extent and severity of inducible myocardial ischemia.[1] Exercise is the preferred stress modality due to the strong prognostic capability of exercise capacity, physiologic relevance, enhanced detection of ischemia, and capture of additional information (heart rate [HR], blood pressure [BP], symptoms), which are also predictors of adverse outcomes.[2] Adequate stress is typically defined as achieving ≥ 85% of age-predicted maximal heart rate (PMHR) during exercise despite its high variability between subjects and inability to accurately identify maximal effort.[3−5] However, patients referred for exercise testing with limited exercise capacity may be unable to achieve adequate levels of stress due to age, deconditioning, or co-morbidities. Use of the Bruce treadmill protocol (most common exercise protocol) may prevent patients from achieving adequate stress due to its relatively high starting workload (approximately 5 metabolic equivalents [METs]) and large incremental changes in speed/grade between stages (Figure 1).[4,6] The Duke Activity Status Index (DASI), a quick 12-item questionnaire using self-reported physical work capacity to estimate METs significantly correlates with peak oxygen consumption (VO_2).[7] In this context, the DASI may allow selection of an appropriate stress modality thus improving the likelihood of an adequate stress response, improved operational efficiencies, and clinical decision-making. The purpose of the study was to determine if DASI-METs were able to predict the achievement of adequate stress during exercise testing.

Methods

This was a prospective study of consecutive patients referred for clinical cardiovascular stress testing at our institution from January 1st through March 15th, 2019. Cardiac stress testing included patients referred for exercise and/or pharmacologic stress utilizing the following diagnostic modalities: (1) electrocardiography (ECG) exercise treadmill testing (ETT); (2) exercise or pharmacologic stress coupled with radionuclide myocardial perfusion imaging (MPI); (3) exercise or pharmacologic stress coupled with echocardiography (SECHO); and (4) cardiopulmonary exercise testing (CPET). All exercise tests were performed on a treadmill according to standard recommendations.[3] Treadmill protocols consisted of the standard Bruce, modified Bruce, or a conservative ramp protocol which consisted

[a]VCU Pauley Heart Center, Virginia Commonwealth University, Richmond, Virginia; and [b]Department of Physical Therapy, College of Applied Health Sciences, University of Illinois at Chicago, Chicago, Illinois. Manuscript received December 10, 2020; revised manuscript received and accepted January 19, 2021.

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*Corresponding Author: Tel.: (804) 628-6176; fax: (804) 628-6612.

E-mail address: Justin.M.Canada@vcuhealth.org (J.M. Canada).

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TIME	0.8 MET/Min Ramp Protocol					0.6 MET/Min Ramp Protocol					Modified Naughton Protocol					Modified Bruce Protocol					Standard Bruce Protocol				
	Stage	Stage Time	Speed (mph)	Grade (%)	METs	Stage	Stage Time	Speed (mph)	Grade (%)	METs	Stage	Stage Time	Speed (mph)	Grade (%)	METs	Stage	Stage Time	Speed (mph)	Grade (%)	METs	Stage	Stage Time	Speed (mph)	Grade (%)	METs
	1	00:30	1.5	1.5	2.5	1	00:30	1.0	0.0	1.8	1	2:00	1.5	0.0	2.1	0	3:00	1.7	0.0	2.4	1	3:00	1.7	10.0	4.7
1:00	2	00:30	1.6	2.0	2.7	2	00:30	1.1	0.5	1.9															
	3	00:30	1.7	2.5	2.9	3	00:30	1.2	1.0	2.1															
2:00	4	00:30	1.8	3.0	3.1	4	00:30	1.3	1.5	2.3			1.5	0.0	2.1			1.7	0.0	2.4			1.7	10.0	4.7
	5	00:30	1.9	3.5	3.4	5	00:30	1.4	2.0	2.5	2	2:00	2.0	3.5	3.5										
3:00	6	00:30	2.0	4.0	3.6	6	00:30	1.5	2.5	2.7															
	7	00:30	2.1	4.5	3.9	7	00:30	1.6	3.0	2.9						0.5	3:00	1.7	5.0	3.5	2	3:00	2.5	12.0	7.1
4:00	8	00:30	2.2	5.0	4.2	8	00:30	1.7	3.5	3.1			2.0	3.5	3.5			1.7	5.0	3.5			2.5	12.0	7.1
	9	00:30	2.3	5.5	4.5	9	00:30	1.8	4.0	3.4	3	2:00	2.0	7.0	4.5										
5:00	10	00:30	2.4	6.0	4.8	10	00:30	1.9	4.5	3.6															
	11	00:30	2.5	6.5	5.2	11	00:30	2.0	5.0	3.9															
6:00	12	00:30	2.6	7.0	5.5	12	00:30	2.1	5.5	4.2			2.0	7.0	4.5			1.7	5.0	3.5			2.5	12.0	7.1
	13	00:30	2.7	7.5	5.9	13	00:30	2.2	6.0	4.5	4	2:00	2.0	10.5	5.5	1	3:00	1.7	10.0	4.7	3	3:00	3.4	14.0	10.3
7:00	14	00:30	2.8	8.0	6.2	14	00:30	2.3	6.5	4.8															
	15	00:30	2.9	8.5	6.6	15	00:30	2.4	7.0	5.2															
8:00	16	00:30	3.0	9.0	7.0	16	00:30	2.5	7.5	5.5			2.0	10.5	5.5			1.7	10.0	4.7			3.4	14.0	10.3
	17	00:30	3.1	9.5	7.4	17	00:30	2.6	8.0	5.9	5	2:00	3.0	7.5	6.5										
9:00	18	00:30	3.2	10.0	7.9	18	00:30	2.7	8.5	6.2															
	19	00:30	3.3	10.5	8.3	19	00:30	2.8	9.0	6.6						2	3:00	2.5	12.0	7.1	4	3:00	4.2	16.0	13.5
10:00	20	00:30	3.4	11.0	8.8	20	00:30	2.9	9.5	7.0			3.0	7.5	6.5			2.5	12.0	7.1			4.2	16.0	13.5
	21	00:30	3.5	11.5	9.2	21	00:30	3.0	10.0	7.4	6	2:00	3.0	10.0	7.5										
	22	00:30	3.6	12.0	9.7	22	00:30	3.1	10.5	7.9															
	23	00:30	3.7	12.5	10.2	23	00:30	3.2	11.0	8.3															
12:00	24	00:30	3.8	13.0	10.7	24	00:30	3.3	11.5	8.8			3.0	10.0	7.5			2.5	12.0	7.1			4.2	16.0	13.5
	25	00:30	3.9	13.5	11.2	25	00:30	3.4	12.0	9.2	7	2:00	3.0	12.5	8.5	3	3:00	3.4	14.0	10.3	5	3:00	5.0	18.0	14.9
13:00	26	00:30	4.0	14.0	11.8	26	00:30	3.5	12.5	9.7															
	27	00:30	4.1	14.0	12.1	27	00:30	3.6	13.0	10.2															
14:00	28	00:30	4.2	14.5	12.6	28	00:30	3.7	13.5	10.7			3.0	12.5	8.5			3.4	14.0	10.3			5.0	18.0	14.9
	29	00:30	4.3	15.0	13.2	29	00:30	3.8	14.0	11.2	8	2:00	3.0	15.0	9.5										
15:00	30	00:30	4.4	15.5	13.8	30	00:30	3.9	14.5	11.8															
	31	00:30	4.5	16.0	14.4	31	00:30	4.0	15.0	12.3						4	3:00	4.2	16.0	13.5	6	3:00	5.5	20.0	17.1
16:00	32	00:30	4.6	16.5	15.0	32	00:30	4.1	15.5	12.9			3.0	15.0	9.5			4.2	16.0	13.5			5.5	20.0	17.1

Figure 1. Temporal relationship of exercise workload to stages of the standard Bruce protocol and other treadmill protocols.
Yellow bars indicate lower & upper range of preferred exercise test duration (8:00 − 12:00 minutes). Green bar indicates optimal exercise test duration (10:00 minutes).
Abbreviations: MET=metabolic equivalents; Min=minutes; mph=miles per hour.

of incremental workloads that increased approximately 0.3 METs every 30-seconds.[8] Radionuclide MPI stress was performed using single-photon emission computed tomography imaging coupled with exercise or pharmacologic vasodilator stress using regadenoson or dobutamine.[9] Exercise or dobutamine stress was utilized for echocardiography studies.[10] Patients were administered the DASI on the day of prior to testing as part of a quality control initiative to improve efficiency of noninvasive cardiology stress operations. There were no exclusion criteria. The local institutional review board approved conduction of this study.

Baseline patient characteristics were collected at the visit and/or from the medical record which included age, race, sex, height, weight, body mass index (BMI), indication for stress, referring provider type (cardiology versus non-cardiology), ordered stress modality (ETT, MPI, SECHO), ordered/performed stress type (pharmacologic or exercise), and the pre-stress DASI score. Indications for stress testing was grouped as follows: (1) chest pain/ coronary artery disease (CAD); (2) dyspnea; (3) pre-operative evaluation; (4) arrhythmias; (5) abnormal baseline ECG; (6) CAD risk factors; (7) valvular heart disease; and (8) research. Exercise test metrics evaluated included exercise protocol, peak METs, exercise time (ET), maximal HR, %PMHR, reason for test termination, interpretable baseline ECG (Yes/ No), and the Duke treadmill score (DTS). The maximal HR was recorded as the highest HR obtained before the termination of exercise from the 12-lead ECG. The PMHR was calculated using the standard equation where PMHR = 220 - age. Percent of PMHR was calculated as: max HR/PMHR x 100. Exercise time was calculated as the total duration of exercise in seconds. The baseline ECG of each patient was evaluated to be interpretable based on standard recommendations with stress ECGs evaluated as negative or positive for inducible myocardial ischemia.[3] Reasons for exercise test termination were grouped as: (1) chest pain; (2) dyspnea; (3) fatigue; (4) BP criteria; (5) arrhythmias; and (6) other (i.e., musculoskeletal reasons).

The total DASI score was converted into an estimated VO_2 using the equation: $VO_2 = 0.43$ x DASI score + 9.6.[7] The DASI VO_2 was then expressed in METs wherein 1-MET equals 3.5 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$. For those who underwent exercise stress, the peak MET level was derived from the exercise testing software (Welch Allen, Q-Stress Cardiac Stress Testing System, Milwaukee, WI) based on the peak treadmill speed and grade using the following vendor equations: (METS= $1.0+0.8 \times$ Speed $+0.1375 \times$ Speed $\times$ %Grade) for speeds ≤ 4 miles per hour (mph) and (METs = $1.0+1.54 \times$ Speed$+0.069 \times$ Speed $\times$ %Grade) for speeds >4mph. For staged protocols the MET calculations update every 10-seconds in a linear progression throughout the first 2-minutes of each stage after which the maximum MET levels are obtained and the value is maintained until stage completion.

Criteria for determining adequate exercise stress was defined in one of 2 ways: (1) obtaining ≥85% of PMHR during peak exercise; or (2) reaching ≥ 5 METs of exercise (approximately equivalent to completing Stage 1 on a Bruce protocol).

Data are presented as number (%) and mean (+/- standard deviation) or median [interquartile range] for variables with a non-Gaussian distribution. Normality was assessed using the Shapiro-Wilk test. Spearman rank correlation coefficients were used to assess associations between continuous variables and chi-square was performed to compare nominal variables. Patients who underwent exercise stress were dichotomized into groups based upon < or ≥85%PMHR and < or ≥5 peak METs and compared using the Mann-Whitney *U* test. Additionally, an independent samples t-test was also performed with bootstrapping (n=1000 samples) to evaluate the mean* DASI-METs for differences between these groups. Patients who underwent CPET were not included in the analysis as adequate stress was defined using the peak respiratory exchange ratio. Area under the curve (AUC) receiver operating characteristic (ROC) analysis was performed to determine the optimal DASI-METs that could predict a suboptimal exercise stress test result. Statistical analysis was performed using SPSS Statistics (IBM, Armonk, NY), version 25 software with significance set at $P<0.05$.

Results

During the study period 608 cardiovascular stress tests were performed. Radionuclide MPI was the most common stress procedure (n=282 [46%]) followed by SECHO (n=201 [33%]), ETT (n=85 [14%]), and CPET (n=40 [7%]). Exercise was the ordered stress type for 42% (n=117) of MPI and 81% (n=162) of SECHO patients, respectively. Including ETT and CPET, a total of 404 (66%) patients were referred for exercise stress. Exercise was performed in 354 (58%) as 50 (18%) patients were converted to a pharmacologic study. Evaluation for signs or symptoms suggestive of myocardial ischemia was the most common indication for cardiovascular stress test referral followed by dyspnea.

In general, patients who underwent exercise stress were younger, lighter (lower bodyweight), with a lower BMI, and scored higher on the DASI (Table 1). The indication for stress was significantly different between the exercise versus pharmacologic stress groups (χ^2_7 =29.0, p <0.001) where evaluation of the standardized residuals demonstrated patientspatients who underwent pre-operative evaluation were more likely to undergo pharmacologic stress while those who underwent evaluation for arrhythmias were more likely to undergo exercise stress. Sex, race, height, interpretable ECG, and ordering provider type were not significantly different between the groups.

The DASI-MET level demonstrated a significant positive relationship with the peak exercise MET level (Figure 2; R=0.50, p <0.001), ET (R=0.29, p <0.001), %PMHR (R=0.19, p = 0.003), max HR (R=0.26, p <0.001), and the DTS (R=0.39, p <0.001). The DASI-METs inversely correlated weakly with age (R=-0.18, p = 0.004), bodyweight (R=-0.13, p = 0.048), and BMI (R=-0.19, p = 0.003).

Treadmill ET (R=0.25, p <0.001), peak METs (R=0.26, p <0.001), and the DTS (R=0.30, p <0.001) positively correlated with %PMHR achieved during exercise. Bodyweight (R=-0.14, p = 0.01) and BMI (R=-0.30, p <0.001) were inversely associated with peak exercise %PMHR.

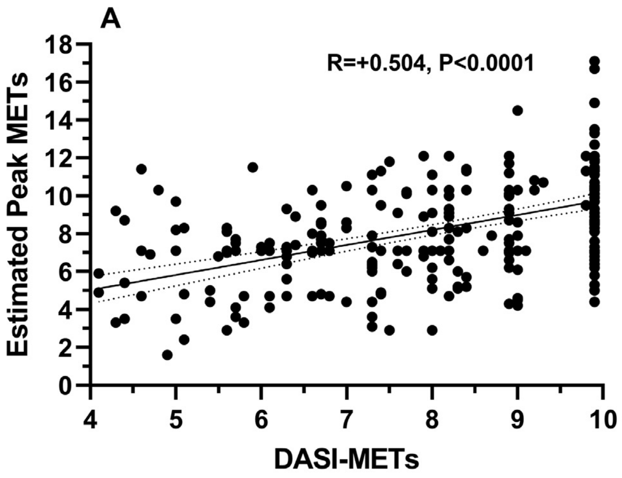
The peak METs achieved during exercise positively correlated with treadmill ET (R=0.86, p <0.001), %PMHR (R=0.26, p <0.001), and the DTS (R=0.77, p <0.001). Body mass index (R=-0.23, p <0.001) and age (R=-0.30, p

Table 1
Baseline demographics by stress type

Variable	Entire Cohort (N=608)	Pharmacologic Stress (n=254)	Exercise Stress (n=354)	p-value
Age (years)	57 ± 13.5	60 ± 12.5	55 ± 13.7	**<0.001**
Male	307 (51%)	128 (50%)	179 (51%)	1.000
Female	301 (49%)	126 (50%)	175 (49%)	
White	282 (46%)	110 (43%)	172 (49%)	0.08
Black	274 (45%)	128 (50%)	146 (41%)	
Other race	48 (8%)	16 (6%)	32 (9%)	
Height (cm)	170 ± 11	169 ± 13	170 ± 10	0.43
Weight (kg)	90.4 ± 24.7	96.2 ± 27.4	86.3 ± 21.7	**<0.001**
Body mass index (kg/m^2)	31.4 ± 8.1	33.6 ± 9.1	29.8 ± 6.8	**<0.001**
Test Indication				**<0.001**
Chest pain/CAD	280 (46%)	119 (47%)	161 (46%)	
Dyspnea	109 (18%)	45 (18%)	64 (18%)	
Pre-operative Eval	102 (17%)	58 (23%)	44 (12%)	
Arrhythmias	39 (6%)	5 (2%)	34 (10%)	
Heart Failure	46 (8%)	16 (6%)	30 (9%)	
Abnormal ECG	10 (1.5%)	2 (1%)	8 (2%)	
CAD risk factors	13 (2%)	7 (3%)	6 (2%)	
Valvular heart disease	6 (1%)	2 (1%)	4 (1%)	
Research	3 (0.5%)	0	3 (1%)	
Interpretable ECG	556 (91%)	229 (90%)	327 (92%)	0.34
Ordering Provider Type				0.46
Cardiology	315 (52%)	127 (50%)	188 (53%)	
Non-cardiology	293 (48%)	127 (50%)	166 (47%)	
DASI-METs	7.1 ± 2.2	5.4 ± 1.9	8.1 ± 1.7	**<0.001**

Data presented as mean ± SD or number (%). Abbreviations: CAD=coronary artery disease; DASI-METs=Duke activity status index-metabolic equivalents; ECG=electrocardiogram.

The bold p-values indicates significant differences (p<0.05) between the dichotomous groups excluding the entire cohort.



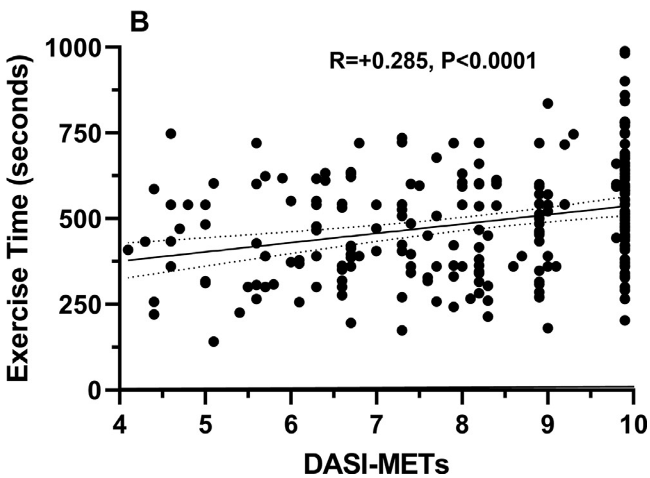


Figure 2. Comparison of DASI-METs and estimated peak METs and exercise time achieved during exercise stress.
Panel A: Correlation between DASI-METs and estimated peak MET levels achieved during exercise stress. Panel B: Correlation between DASI-METs and treadmill exercise time.
Abbreviations: DASI-METs=Duke activity status index-metabolic equivalents.

<0.001) were inversely associated with peak exercise METs.

Table 2 provides an analysis of groups dichotomized by < or ≥85%PMHR. Sixty-one (19%) patients who underwent physician-referred exercise stress did not achieve ≥85%PMHR. The median DASI-METs, peak exercise METs, ET, and max HR were significantly higher in those who reached ≥85%PMHR. Additionally, the mean* DASI-METs were significantly higher and different in those reaching ≥85%PMHR (8.3 [95%CI: 8.1 to 8.6] versus 7.7 [95%CI: 7.2 to 8.2]; p = 0.02). Exercise time was borderline significant (p = 0.05) for being higher in those who reached ≥85%PMHR. Chi-square analysis revealed a significant difference between groups (χ^2_1= 4.1, p = 0.04) for sex with males more likely not to achieve >85%PMHR than females and those with an interpretable ECG more likely to achieve >85%PMHR (χ^2_1= 5.4, p = 0.02). The Bruce protocol was the most common treadmill protocol (83%) followed by the ramp (11%) and modified Bruce protocols (6%). Age, race, anthropometrics, exercise modality/protocol, reason for termination, and ordering provider type were not significantly different between the %PMHR groups.

A ROC curve analysis was performed to evaluate whether DASI-METs had discriminative value to identify an adequate exercise stress response defined as ≥85%PMHR (Figure 3). For ≥85%PMHR, the AUC was 0.606 (standard error [SE=0.04]; 95%CI = 0.519 to 0.693, p = 0.02). Based on the coordinates of the ROC curve the optimal DASI-MET threshold to predict achieving ≥85%PMHR was >7.9 (sensitivity= 66%, specificity= 49%).

Table 3 illustrates the groups dichotomized by < or ≥5 METs during exercise testing. Twenty-four (8%) patients failed to reach ≥5 METs during exercise stress. Median age was higher while DASI-METs, peak METs, ET, and max HR were lower in those with <5 METs. Furthermore, the mean* DASI-METs were significantly higher and different in those reaching ≥5 METs (8.4 [95%CI: 8.1 to 8.6] versus 5.8 [95%CI: 5.2 to 6.5]; p <0.001). Treadmill protocol selection was significantly different (χ^2_2= 31.7, p <0.001) between groups with those who underwent Bruce or the ramp protocol being more likely to reach ≥5 METs compared with those who underwent a modified Bruce protocol. For ability to reach ≥5 METs during exercise stress, the AUC was 0.879 (SE=0.04, 95%CI = 0.801 to 0.957, p <0.001) (Figure 3). Based on the coordinates of the ROC curve, the optimal DASI-MET threshold to predict achieving ≥5 METs was >7.4 (sensitivity= 93%, specificity= 71%).

Discussion

The findings of the current study suggest that self-reported functional capacity derived from the DASI can assist in discerning the likelihood of a suboptimal effort level in patients referred for exercise stress testing. Baseline characteristics that are typically attributed to perceived poor exercise performance, including age and body habitus, were not able to predict a suboptimal exercise stress test in our population. If the primary intention of the exercise test is to evaluate for the presence of inducible myocardial ischemia, the use of DASI-METs may help identify those unlikely to achieve an adequate exercise stress response.

The results of the present study indicate individuals with a DASI-MET level <7.4 were less likely to achieve adequate exercise stress, defined as <85%PMHR or an inability to reach ≥5 METs. However, exercise testing provides a wealth of prognostic information, including exercise capacity, beyond that of ECG-derived ST segment changes indicative of myocardial ischemia.[11,12] Myers et al. demonstrated the relationship of VO_2 to work rate was more linear for ramp tests or tests with smaller workload changes compared with protocols employing larger increments between stages, thus improving the precision of estimating exercise capacity.[13] This has implications as the exercise capacity derived from Bruce protocol ET has been shown to overestimate METs and may lead to a less precise risk estimate in patients evaluated for suspected myocardial ischemia.[14] Pinkstaff et al. demonstrated a DTS including ET calculated from measured METs versus estimated

Table 2
Comparison of groups based on peak exercise heart rate response

Variable	Entire Cohort (N=314)	<85%PMHR (n=61)	≥85%PMHR (n=253)	p-value
Age (years)	56 [46-64]	57 [47-64]	56 [46-64]	0.59
Male	154 (49%)	37 (61%)	117 (46%)	**0.047**
Female	160 (51%)	24 (39%)	136 (54%)	
White	149 (48%)	33 (54%)	116 (46%)	0.49
Black	133 (42%)	22 (36%)	111 (44%)	
Other race	29 (9%)	5 (8%)	24 (10%)	
Weight (kg)	86.3 ± 21.7	89.7 ± 23.3	85.2 ± 21.0	0.39
Height (cm)	169 [163-178]	169 [162-178]	169 [163-178]	0.75
Body mass index (kg/m^2)	29.2 [24.9-33.5]	29.9 [25.7-33.2]	29.0 [24.8-33.6]	0.31
DASI-METs	8.4 [6.7-9.9]	7.9 [6.6-9.0]	8.9 [7.1-9.9]	**0.03**
Estimated peak METs	8.6 [7.1-10.3]	8.0 [7.1-10.3]	8.9 [7.1-11.1]	**0.02**
Exercise Time (seconds)	471 [360-601]	438 [353-541]	483 [362-604]	0.05
Max heart rate (bpm)	150 [138-165]	131 [121-138]	156 [143-169]	**<0.001**
%PMHR	91 [85-98]	80 [74-83]	94 [89-99]	**<0.001**
Duke treadmill score	7.0 [4.5-9.0]	6.5 [3.5-8.5]	7.0 [4.5-9.5]	0.16
Test Indication				0.27
Exercise Test Modality				0.61
SECHO	120 (38%)	26 (22%)	94 (78%)	
MPI	109 (35%)	18 (17%)	91 (84%)	
ETT	85 (27%)	17 (20%)	68 (80%)	
Interpretable ECG	297 (95%)	54 (18%)	243 (82%)	**0.02**
Exercise protocol				0.22
Bruce	260 (83%)	46 (54%)	217 (81%)	
Modified Bruce	20 (6%)	6 (7%)	14 (5%)	
Ramp	34 (11%)	33 (38%)	36 (13%)	
Ordering Provider Type				0.48
Cardiology	155 (49%)	33 (54%)	122 (48%)	
Non-cardiology	159 (51%)	28 (46%)	131 (52%)	
Reason for Termination				0.56
Chest pain	7 (2%)	2 (3%)	5 (2%)	
Dyspnea	117 (37%)	28 (46%)	89 (35%)	
Fatigue	163 (52%)	25 (41%)	138 (55%)	
Other	18 (6%)	4 (7%)	14 (6%)	
Blood pressure criteria	7 (2%)	2 (3%)	5 (2%)	
Arrhythmia	2 (1%)	0	2 (1%)	

Data presented as mean ± SD, median [interquartile range], or number (%). Abbreviations: DASI-METS=Duke activity status index-metabolic equivalents; ECG=electrocardiogram; ETT=exercise treadmill test; MPI=radionuclide myocardial perfusion imaging; %PMHR=percent-predicted maximal heart rate; SECHO=stress echocardiogram.

The bold p-values indicates significant differences ($p<0.05$) between the dichotomous groups excluding the entire cohort.

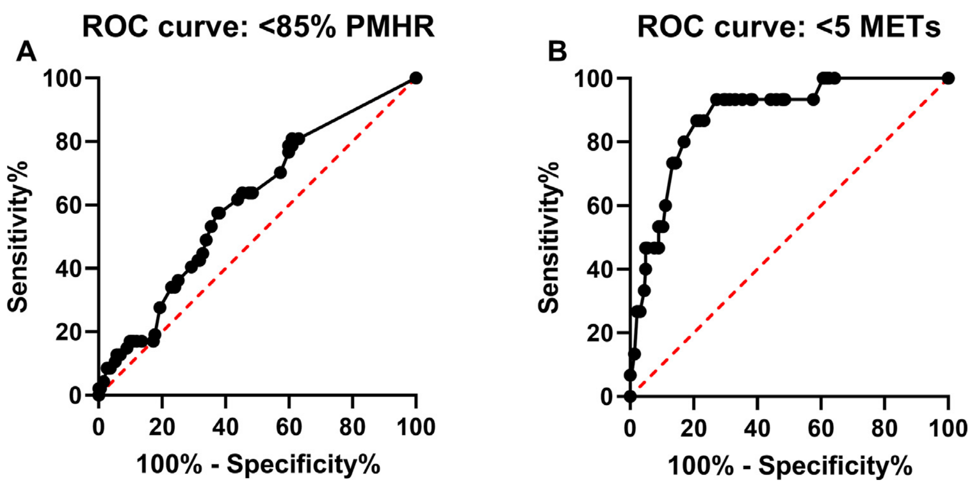


Figure 3. Receiver operating characteristic curves depicting the discriminative value of DASI-METs for identifying those with <85%PMHR (Panel A) or <5 METs (Panel B) at peak exercise. Abbreviations: METs=metabolic equivalents; PMHR=predicted maximal heart rate; ROC=receiver operating characteristic.

Table 3
Comparison of groups based on peak metabolic equivalents achieved during exercise.

Variable	Entire Cohort (N=314)	<5 METs (n=24)	≥5 METs (n=290)	p-value
Age (years)	56 [46-64]	65 [56-73]	55 [46-63]	**<0.001**
Male	154 (49%)	11 (46%)	143 (49%)	0.74
Female	160 (51%)	13 (54%)	147 (51%)	
Caucasian	149 (48%)	13 (54%)	136 (47%)	0.64
Black	133 (42%)	8 (33%)	125 (43%)	
Other race	32 (10%)	3 (13%)	29 (10%)	
Weight (kg)	85.8 ± 21.7	81.0 ± 21.8	86.7 ± 22.0	0.22
Height (cm)	169 [163-178]	166 [160-175]	169 [163-178]	0.10
Body mass index (kg/m^2)	29.2 [24.9-33.5]	28.8 [22.5-33.2]	29.3 [25.1-33.5]	0.64
DASI-METs	8.4 [6.7-9.9]	5.8 [4.6-6.6]	8.9 [7.3-9.9]	**<0.001**
Estimated peak METs	8.6 [7.1-10.3]	4.5 [3.7-4.7]	8.9 [7.1-10.7]	**<0.001**
Exercise time (seconds)	471 [360-601]	255 [180-315]	487 [378-606]	**<0.001**
Max heart rate (bpm)	150 [138-165]	134 [116-151]	151 [139-165]	**0.001**
%PMHR	91 [85-98]	87 [75-97]	91 [86-98]	0.05
Duke treadmill score	7.0 [4.5-9.0]	3.0 [2.0-4.0]	7.0 [5.0-9.5]	**<0.001**
Test Indication				0.59
Exercise Test Modality				0.32
SECHO	120 (38%)	6 (5%)	114 (95%)	
MPI	109 (35%)	9 (8%)	100 (92%)	
ETT	85 (27%)	9 (11%)	76 (89%)	
Interpretable ECG	297 (95%)	20 (83%)	277 (96%)	**0.02**
Exercise protocol				**<0.001**
Bruce	260 (83%)	14 (5%)	246 (95%)	
Modified Bruce	20 (6%)	8 (40%)	12 (60%)	
Ramp	34 (11%)	2 (6%)	32 (94%)	
Ordering Provider Type				0.48
Cardiology	155 (49%)	13 (54%)	142 (49%)	
Non-cardiology	159 (51%)	11 (46%)	148 (51%)	
Reason for Termination				0.37
Chest pain	7 (2%)	0	7 (2%)	
Dyspnea	117 (37%)	14 (58%)	103 (36%)	
Fatigue	163 (52%)	9 (38%)	154 (53%)	
Other	18 (6%)	0	17 (6%)	
Blood pressure criteria	7 (2%)	1 (4%)	6 (2%)	
Arrhythmia	2 (1%)	0	2 (1%)	

Data presented as mean ± SD, median [interquartile range], or number (%). Abbreviations: DASI-METS=Duke activity status index-metabolic equivalents; ECG=electrocardiogram; ETT=exercise treadmill test; MPI=radionuclide myocardial perfusion imaging; %PMHR=percent-predicted maximal heart rate; SECHO=stress echocardiogram.

The bold p-values indicates significant differences (p<0.05) between the dichotomous groups excluding the entire cohort.

METs provided more accuracy in predicting an abnormal MPI stress result.[14]

Based on the observed associations between peak METs achieved with %PMHR and ET, a protocol with smaller incremental changes in treadmill speed and grade (i.e., ramp protocol) tailored to the patients DASI-METs may allow a longer exercise duration, a higher likelihood of achieving adequate stress, and a more accurate assessment of exercise capacity.[15] Exercise test guidelines indicate an optimal exercise test duration to be between 8 and 12 minutes.[16,17] Individualized exercise protocols should be employed that permit this exercise duration to improve estimation of exercise capacity.[18] The initial stage of the Bruce protocol comprises a workload approaching maximal exercise tolerance in many older patients and those with chronic diseases, leading to early test termination.[19,20] The ETs observed in the current study (<85%PMHR= 7.3 minutes; <5 METs= 4.3 minutes) indicates a suboptimal exercise duration for those with an inadequate stress result. Kozlov et al. found that use of a ramp treadmill protocol allowed longer exercise duration, higher workloads achieved, and improved acceptability when compared with a modified Bruce protocol in elderly (≥70 years old) individuals.[21] These findings concur with the present study wherein the use of a ramp vs. a modified Bruce protocol was associated with achievement of an adequate stress result in patients not deemed appropriate for a standard Bruce protocol.

The DASI has previously been shown to predict exercise METs, survival, and likelihood of indeterminate exercise test results among patients who underwent clinical exercise testing.[19,22,23] Shaw et al. from the Women's Ischemia Syndrome Evaluation (WISE) study identified a DASI threshold of ≤ 4.7 METs for women who were at high risk of death or myocardial infarction irrespective of ability to undergo exercise testing. Furthermore, this threshold was able to identify those unlikely to achieve ≥85%PMHR who might benefit from pharmacologic stress to evaluate for myocardial ischemia.[19] However, it is important to note that exercise capacity is consistently among the most important prognostic indicators from the exercise test, highlighting assessment and amelioration of exercise intolerance as being of paramount importance regardless of obtaining an adequate stress result. [11,24,25]

In the context of clinical efficiency, simplified (4-5 vs. 12 questions) modified versions of the DASI have been developed for use in surgical evaluations that demonstrate equivalency to the original DASI for identifying high-risk CPET thresholds indicative of increased postoperative complications.[26] However, this modified version requires validation for use in other populations.

There were a number of limitations to the present study. This was a single-center analysis of patients referred for cardiovascular stress testing. The presence of potential contributing co-morbidities (i.e., pulmonary disease, CVD risk factors) and reasons for not who underwent exercise in the pharmacologic stress patients were not ascertained. Downstream patient management based on the results of testing and clinical outcomes were also not included. The DASI has an upper limit of 9.9 METS, thus will underestimate the exercise capacity of those with higher fitness.

In conclusion, in clinically referred patients, use of the DASI before exercise can detect patients with a higher likelihood of an inadequate exercise stress test result defined as <85%PMHR or <5 METs at peak exercise. Lower DASI-METs were significantly associated with achievement of lower peak exercise METS, reduced ET, lower peak HR, and a higher likelihood of an inadequate exercise stress result.

Credit Authorship Contribution Statement

J.M. Canada: conceptualization, methodology, investigation, resources, data curation, writing, review & editing, visualization, supervision, project administration. **M.A. Reynolds:** methodology, validation, formal analysis, data curation, investigation, writing, review & editing, visualization. **R. Myers:** methodology, validation, formal analysis, data curation, investigation, writing, review & editing, visualization. **J. West:** methodology, validation, formal analysis, data curation, investigation, writing, review & editing. **K. Sweat:** methodology, validation, formal analysis, data curation, investigation, writing, review & editing. **C. Powell:** investigation, data curation. **V. McGhee:** conceptualization, methodology, review & editing, visualization, supervision. **M.C. Kontos:** conceptualization, methodology, review & editing, visualization, supervision. **H. Bhardwaj:** conceptualization, methodology, review & editing, visualization, supervision. **A. Abbate:** review & editing, visualization, supervision. **R. Arena:** methodology, writing, review & editing, visualization, supervision. **G.W. Hundley:** conceptualization, resources, review & editing, visualization, supervision, project administration.

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