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Original

The value of the Duke Activity Status Index (DASI) in predicting ischaemia in myocardial perfusion scintigraphy — a prospective study

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Abstract

BACKGROUND: Functional capacity assessment may be a useful tool to stratify patients according to risk of coronary artery disease (CAD). The Duke Activity Status Index (DASI) is a functional assessment based on activities of daily living and cardiovascular fitness, assessed using a self-administered questionnaire.

MATERIAL AND METHODS: We assessed the relationship between established clinical risk factors for CAD and the DASI with results of myocardial perfusion scintigraphy (MPS). The MPS results used in the analysis were the presence of reversible ischaemia and the resting left ventricular ejection fraction (LVEF). A DASI self-administered questionnaire was completed by 117 consecutive participants, and a patient history was taken to ascertain established risk factors. All participants underwent a stress test, and myocardial perfusion scintigraphy was performed. Statistical analysis consisted of logistic and linear regression using a statistical software package.

RESULTS: The DASI was the only factor that correlated significantly with reversible ischaemia on MPS. None of the previously established risk factors had a significant association with reversible ischaemia within the model. Our study found a potential relationship between the DASI score and the left ventricular ejection fraction (LVEF) although this was not statistically significant.

CONCLUSIONS: Our study findings suggest that the DASI may represent a powerful tool for risk stratification prior to investigation of CAD. A further study with a larger sample size will be required to investigate the predictive value of the DASI and the association with LVEF.

Key words: myocardial perfusion scintigraphy, Duke Activity Status Index, DASI, functional capacity, reversible ischaemia

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Introduction

Myocardial perfusion scintigraphy (MPS) is a widely utilised method of non-invasive cardiac imaging and is central to the diagnosis and management of coronary artery disease (CAD). The test detects the effect of fixed or dynamic flow limiting coronary stenosis. Gating also allows assessment of left ventricular ejection fraction (LEVF), wall motion, and wall thickening. Myocardial perfusion imaging is a particularly useful screening test for exercise intolerant patients and those who have inconclusive stress echocardiography. The test is an established and valuable screening test for CAD [1]. The current American guidelines state that the undertaking of a stress imaging test must be preceded by a pre-test likelihood assessment of CAD [2]. This is in keeping with the UK National Institute of Health and Clinical Effectiveness (NICE)

Table 1. The Duke Activity Status Index [7]

Activity	Weight (MET units)
Take care of yourself, that is, eating, dressing, bathing and using the toilet?	2.75
Walk indoors such as around your house?	1.75
Walk a block on level ground?	2.75
Climb a flight of stairs or walk up a hill?	5.50
Run a short distance?	8.0
Do light housework like dusting or washing dishes?	2.7
Do moderate housework like vacuuming, sweeping floors, carrying in groceries?	3.5
Do heavy housework like scrubbing floors, or lifting or moving heavy furniture?	8.0
Do gardening including such things as raking leaves, weeding, or pushing a lawn mower?	4.5
Have sexual relations?	5.25
Participate in moderate recreational activities, like golf, bowling, dancing, or throwing a ball?	6.0
Participate in strenuous sports like swimming, football, basketball, or skiing?	7.5

guidelines, which recommend pre-test likelihood of CAD should be based on age, gender, ethnicity, family history, associated co-morbidities, clinical presentation, physical examination, and results from other investigations [3]. National guidelines recommend MPS for the diagnosis of CAD in the following circumstances:

— as an initial tool for patients with suspected CAD in whom stress electrocardiography poses problems (e.g. females, left bundle branch block, mobility problems);
— for investigation of suspected CAD in patients with a lower likelihood of CAD;
— as part of the investigational strategy for established CAD in patients who remain symptomatic. Evidence suggests that major risk factors for CAD include "typical" chest pain, age, and male sex whereas factors such as smoking and hyperlipidaemia have been evaluated as minor factors [4–6].

Over the last decade the effectiveness of cardiovascular therapies and outcomes have been evaluated using health-related quality tools and functional capacity assessments. A well-recognised functional capacity tool is the Duke Activity Status Index (DASI), which is a self-administered questionnaire that measures the ability to perform a set of 12 common activities of daily living. It has been validated against the "gold standard" of functional capacity measurement: peak oxygen intake during exercise [7]. The non-weighted DASI is scored as 1 point for each activity whereas the weighted score is calculated by adding together the 'MET units' for each activity. MET units are a measure of the metabolic cost of the activity and were derived in the original study by Hlatky and colleagues (Table 1) [7].

DASI has been used to monitor progress in patients with coronary artery disease, has demonstrated prognostic value in patients with chronic heart failure, and can be used to identify those with reduced long-term survival following cardiac surgery [8–10]. The DASI has not as yet been investigated as a predictor of abnormal MPS. This study investigates the relationship between the DASI and established pre-test risk factors with the presence of reversible ischaemia and LVEF on myocardial perfusion scintigraphy.

Material and methods

Ethical approval was granted prior to the undertaking of this study. Prospectively, 117 consecutive eligible patients were recruited over a six-month period. All patients referred for investigation of chest pain according to the original request form were assessed for eligibility in the study. Exclusion criteria included inability to understand the questionnaire or give consent, incomplete forms, and immobility. All patients had their medical history taken by a doctor to establish risk factors prior to the test. Demographic data was also noted. Patients were requested to complete a self-administered questionnaire between their pharmacological stress and image acquisition. The questionnaire consisted of the 12-point abbreviated DASI and was scored as non-weighted and weighted results based on the original study by Hlatky et al. (Table 1).

Table 2. Prevalence of risk factors

Variable	Prevalence (%)
Hypercholesterolaemia	70
Hypertension	67
Known CAD	37
Smoking history	36
Family history	26
Diabetes	25
Obesity	23
PTCA [a]	16
CABG [b]	9
> 3 risk factors [c]	32

[a] PTCA — previous percutaneous transluminal coronary angioplasty; [b] CABG — previous coronary artery bypass graft; [c] >3 risk factors: includes those listed in this table only

The sample included 65 men (56%) and 52 women (44%). The mean age was 65 and the age range was 32 to 87. The risk factors that were assessed in the medical history and their prevalence among the sample population are displayed in Table 2. A positive family history was defined as one or more first degree relatives with coronary artery disease and obesity as a body mass index (BMI) greater than 30.

All patients were stressed with Adenosine or Dobutamine according to standard protocols of myocardial perfusion scintigraphy using a standard 2 day protocol. Stress and rest imaging were performed at least 48 hours apart using 500 MBq ^{99m}Tc tetrofosmin. The imaging was performed on a dedicated cardiac gamma

camera (Siemens C-Cam, Erlangen, Germany). A rest-gated acquisition was obtained. Images were reconstructed iteratively using a count optimised smoothing filter. Attenuation correction was not applied. For the purposes of analysis we recorded the left ventricular ejection fraction and the presence/absence of reversible ischaemia. Ischaemia was defined as a reduction of more than 50% of the maximum activity seen in the stress image which showed greater than 75% of the maximum activity in the rest image and covered > 10% of the myocardium. These outcomes were subsequently correlated with functional capacity assessed from the DASI (weighted and non-weighted scores), demographics, and established risk factors. Individual factors and their ability to predict changes on the myocardial scintigraphy were tested using statistical analysis performed using XLSTAT 2009 version 2.03. Statistical significance is regarded as $p < 0.05$.

Results

All questions were answered on the DASI questionnaire except the question on sexual relations, which was left blank by 17 (14.5%) participants. The left ventricular ejection fraction was reported on 92 MPS results as it was not possible to gate the study in 25 patients. Of the 117 participants 30.8% had demonstrable evidence of reversible ischaemia on MPS. 47.2% of all participants with reversible ischaemia had 3 or more risk factors, whereas 38.3% of all patients without evidence of reversible ischaemia had 3 or more risk factors.

Univariate and multivariate logistic regression was performed. The multivariate analysis consisted of 92 cases since those without a resting LEVF result were excluded (these were patients in which gating was not possible due to arrhythmia). Univariate and multivariate analysis revealed that only the DASI (both weighted and non-weighted) has a significant association with reversible ischaemia (Table 3).

The multivariate analysis revealed the following when modelled with the presence/absence of reversible ischaemia: non-weighted DASI odds ratio 0.325 (95% CI: 0.13–0.82) $p = 0.017$, weighted DASI odds ratio 0.838 (95% CI: 0.71–0.99) $p = 0.038$. The multivariate model overall did not achieve statistical significance according to the Fischer's F statistic; however, the DASI scores alone were significant predictors of reversible ischaemia.

The ROC (receiver operating characteristic) curve for the non-weighted DASI (univariate logistic regression) demonstrated that the DASI score has a statistically significant relationship with reversible ischaemia; however, this does not have a high sensitivity or specificity (Figure 1). The ROC curve for the weighted DASI is similar (area under curve = 0.661, $p < 0.001$). Each of the remaining risk factors did not have a statistically significant independent relationship to reversible ischaemia in univariate or multivariate analyses.

As 14.5% of the participants did not respond to a question on sexual relations in the questionnaire, a second analysis was performed in which this particular question was removed to produce "adjusted" DASI scores. Therefore, the adjusted non-weighted

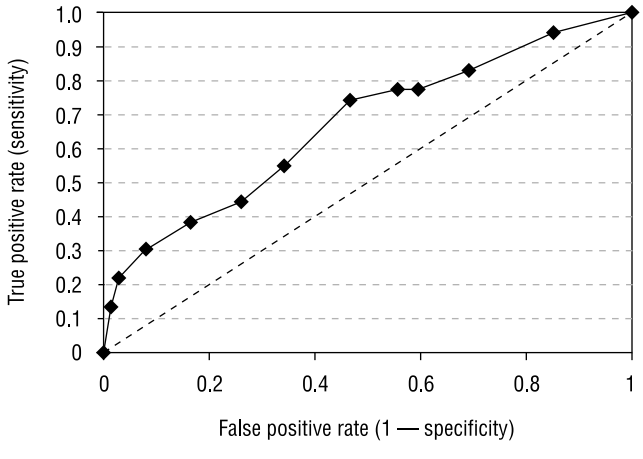

Figure 1. The area under the curve above is 0.672. The ROC curve corresponds to the logistic regression statistics for the non-weighted DASI in Table 3.

Table 3. Univariate logistic regression

Variable	Odds Ratio (CI 95%)	P value
DASI score (non-weighted)	*0.820 (0.72–0.93)*	*0.002**
DASI score (weighted)	*0.967 (0.95–0.99)*	*0.006**
LVEF	0.990 (0.96–1.03)	0.591
Age	1.026 (0.99–1.06)	0.135
Male sex	0.723 (0.33–1.59)	0.432
Hypercholesterolaemia	0.957 (0.40–2.22)	0.92
Hypertension	1.20 (0.52–2.79)	0.67
Known CAD	1.060 (0.72–3.57)	0.252
Smoking history	1.425 (0.62–3.28)	0.405
Family history	0.952 (0.39–2.35)	0.916
Diabetes	1.255 (0.51–3.06)	0.618
Obesity	1.789 (0.73–4.34)	0.20
PTCA	0.772 (0.26–2.33)	0.646
CABG	2.016 (0.57–7.10)	0.275
> 3 risk factors	1.835 (0.76–4.45)	0.179

*The DASI is statistically significant on the basis of the probability of χ^2 test in logistic regression, and the validity of the overall model is confirmed by the Fischer's F Test, which showed the following when modelled for reversible ischaemia: non-weighted DASI: $p = 0.001$, weighted DASI: $p = 0.004$

Table 4. Characteristics of participants according to DASI score

DASI score	Reversible ischaemia (n)	N	Males	3 or more risk factors (n)
0 to 2	80% (8)	10	60%	(2) 20%
3 or 4	35% (6)	17	29.40%	(9) 52.9%
5 or 6	28.60% (6)	21	52.40%	(14) 67%
7 or 8	32% (8)	25	52%	(7) 28%
9 or 10	15.40% (2)	13	76.90%	(5) 38.5%
11 or 12	19.40% (6)	31	64.50%	(15) 48.4%

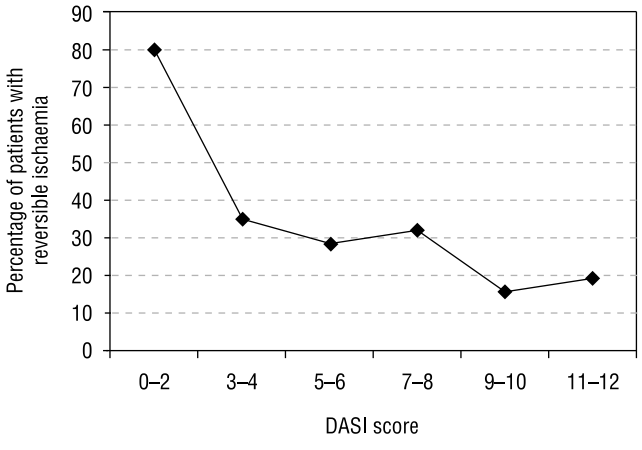

Figure 2. The relationship of DASI score to incidence of ischaemia as seen on MPS.

score was out of a maximum possible score of 11 and the adjusted weighted DASI assessed as a maximum score of 52.95. In this second analysis, the odds ratio for the adjusted weighted DASI score and reversible ischaemia was 0.981 (CI: 0.968–0.994), p = 0.006, Fischer's F test 0.004, area under ROC = 0.662, and the odds ratio for the adjusted non-weighted DASI score and reversible ischaemia was 0.976 (95% CI: 0.962–0.991), p = 0.002, Fishers F Test p = 0.001, area under ROC = 0.653.

The relationship between the non-weighted DASI score was further analysed with respect to the presence of reversible ischaemia (Table 4, Figure 2). This demonstrates the inverse trend between an increasing DASI score and the rates of demonstrable reversible ischaemia. It reveals, however, that 20% of those with a DASI score between 0 and 2 inclusive did not have reversible ischaemia and 19.4% of those with DASI scores or 11 or 12 did.

Through linear regression, the left ventricular fraction was correlated against the weighted DASI (Spearman's rho = –0.1855; 95% CI: –0.3773–0.02167, p = 0.0705) and non-weighted DASI scores (Spearman's rho = –0.15; 95% CI: –0.3773–0.02167, p = 0.14). Although no statistically significant results were found, left ventricular ejection fraction is close to statistical significance when correlated against the weighted DASI score.

Discussion

Investigation and treatment of CAD has evolved rapidly over the past decade. The overall goal of MPS is to increase detection of patients in whom there may be a significant survival advantage of coronary intervention, and to identify those who do not have CAD. Broad clinical guidelines have been developed for the investigative pathway for patients with suspected coronary artery disease, which state that a stress imaging study must be preceded by a pre-test likelihood of CAD [2–3, 11]. Consensus regarding the quantification of risk, however, is lacking and must be determined by the clinician based on a Bayesian analysis of risk factors, clinical history, and non-invasive tests such as echocardiography. It is suggested that patients with high risk of CAD may be appropriate referrals for angiography where benefits outweigh the risks of the procedure. In contrast, patients of intermediate and low risk are appropriate referrals for MPS. MPS has a good safety profile and there is evidence to demonstrate its strength in correctly identifying those at very low risk of cardiac events [12, 13]. Furthermore, MPS has also been correlated with angiographic findings, which demonstrate increasing likelihood of benefit from revascularisation with greater perfusion defects on MPS [14].

Nelson and colleagues studied associations between the DASI and clinical risk factors to angiographic evidence of CAD [15]. The authors validated the DASI as a functional outcome measure and demonstrated significant measurable differences in DASI scores between groups of patients with varying severity of CAD [15]. Furthermore, in their study, functional capacity was not associated with any combination of clinical factors (e.g. diabetes, smoking, and angina) [15]. These findings are in keeping with our study, which also found that, although not highly sensitive or specific, the DASI is the only pre-test variable which has a statistically significant association with reversible ischaemia. It is thus a more powerful pre-test predictor of reversible ischaemia on MPS than any of the established risk factors included in the study. Further investigation is required to assess the positive predictive value of this test and the realistic trade offs between sensitivity and specificity. The DASI has potential for use in cases where a low DASI score (i.e. 0–2) indicates patients at high risk of reversible ischaemia who warrant expedited investigation and treatment. The DASI is a short, 12-point questionnaire, which is easy to administer making it a feasible and low-cost tool for use in a clinical setting.

The DASI has been used as an estimate of functional capacity in patients with heart failure and can also provide prognostic information in patients with chronic heart failure [10]. Nelson and colleagues, however, did not find that the ejection fraction was predictive of functional capacity, and this has also been observed by other investigators [15–17]. Similarly, our study did not confirm a significant relationship; however, the result for the weighted DASI score was close to statistical significance, indicating that a relationship may exist. Further investigation with a larger

sample size will be required to determine the precise value of the DASI in this context.

There were poor responses rates for a question on sexual relations in the DASI questionnaire (14.5% of participants left this question blank), which therefore had an effect on the overall DASI scores. To ensure validity the scores for the weighted and non-weighted DASI were adjusted for this omission and re-analysed. The adjusted models have no change in the p value or Fischer's F test. This demonstrates that our results were not significantly affected by this factor. We must also take into account that bias may be introduced through patient responses by the education background and health awareness of participants. Definitions of chest pain were taken from the referral forms from the requesting clinician, which may also represent a potential source of bias. The investigators of the CASS study demonstrated high prevalence of coronary and multi-vessel disease in specific groups according to gender and definitions of chest pain [4].

Conclusions

The DASI is potentially a powerful tool to establish the likelihood of reversible ischaemia on MPS in patients with chest pain. This study demonstrates that the DASI is more reliable than previously established pre-test risk factors in predicting CAD in this cohort. It highlights that functional capacity in terms of cardiovascular ability is a valid measure of CAD risk. An important use of the DASI may be to identify patients with a low score in whom expedited investigation and treatment may confer a survival benefit. Further research in a bigger patient group is required to investigate the strength of the association between resting LVEF and weighted DASI score.

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