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Integration of the Duke Activity Status Index into preoperative risk evaluation: a multicentre prospective cohort study

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Abstract

Background: The Duke Activity Status Index (DASI) questionnaire might help incorporate self-reported functional capacity into preoperative risk assessment. Nonetheless, prognostically important thresholds in DASI scores remain unclear. We conducted a nested cohort analysis of the Measurement of Exercise Tolerance before Surgery (METS) study to characterise the association of preoperative DASI scores with postoperative death or complications.

Methods: The analysis included 1546 participants (≥40 yr of age) at an elevated cardiac risk who had inpatient noncardiac surgery. The primary outcome was 30-day death or myocardial injury. The secondary outcomes were 30-day death or myocardial infarction, in-hospital moderate-to-severe complications, and 1 yr death or new disability. Multivariable logistic regression modelling was used to characterise the adjusted association of preoperative DASI scores with outcomes.

Results: The DASI score had non-linear associations with outcomes. Self-reported functional capacity better than a DASI score of 34 was associated with reduced odds of 30-day death or myocardial injury (odds ratio: 0.97 per 1 point increase above 34; 95% confidence interval [CI]: 0.96–0.99) and 1 yr death or new disability (odds ratio: 0.96 per 1 point increase above 34; 95% CI: 0.92–0.99). Self-reported functional capacity worse than a DASI score of 34 was associated with increased odds of 30-day death or myocardial infarction (odds ratio: 1.05 per 1 point decrease below 34; 95% CI: 1.00–1.09), and moderate-to-severe complications (odds ratio: 1.03 per 1 point decrease below 34; 95% CI: 1.01–1.05).

Conclusions: A DASI score of 34 represents a threshold for identifying patients at risk for myocardial injury, myocardial infarction, moderate-to-severe complications, and new disability.

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Keywords: cardiopulmonary fitness; Duke Activity Status Index; functional capacity; perioperative risk; postoperative complications; preoperative evaluation; surgery

Editor's key points

- The Duke Activity Status Index (DASI) questionnaire is a valid measure of preoperative cardiopulmonary fitness, but it is unclear what threshold scores define an elevated perioperative risk.
- A nested cohort analysis of the Measurement of Exercise Tolerance before Surgery study sample was conducted to characterise the association of preoperative DASI scores with postoperative cardiac complications and moderate-to-severe complications.
- A DASI score of 34 was identified as a threshold for identifying patients at risk for myocardial injury, myocardial infarction, moderate-to-severe complications, and new disability in surgical patients.
- The use of the DASI should help the preoperative identification of patients at an elevated risk of postoperative morbidity.

Evaluation of functional capacity or cardiopulmonary fitness is considered integral to preoperative risk assessment for major inpatient noncardiac surgery.[1] This evaluation typically involves a doctor making a subjective estimate of the patient's functional capacity (i.e. 'subjective assessment') after a standard preoperative interview. Whilst subjective assessment is ubiquitous to clinical practice in the perioperative setting, several single-centre studies have raised questions about its validity as a measure of cardiopulmonary fitness and perioperative risk.[2–4] The recent multicentre Measurement of Exercise Tolerance before Surgery (METS) prospective cohort study found that subjective assessment did not accurately identify patients who performed poorly on formal preoperative exercise testing, and did not correctly identify which patients are at an elevated risk for postoperative morbidity.[5] Instead, the Duke Activity Status Index (DASI),[6] a 12-item self-reported questionnaire about usual physical activities, improved the identification of patients at an elevated risk for postoperative myocardial infarction and myocardial injury, even when used in combination with clinical risk indices, such as the Revised Cardiac Risk Index (RCRI).[7]

The DASI questionnaire (Supplementary Table 1) was developed in a sample of English-speaking adults undergoing exercise testing in the USA,[6] and has a score ranging from 0 to 58.2, with higher scores indicating greater levels of fitness. The questionnaire is a valid measure of preoperative cardiopulmonary fitness,[5,8,9] but there is a disagreement as to how best to convert DASI scores to estimated metabolic equivalents.[10,11] It is also unclear what specific thresholds in DASI scores define an elevated perioperative risk, and whether the DASI questionnaire provides additional prognostic information when used in combination with preoperative biomarkers, such as brain natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT pro-BNP).[12,13] Whilst prognostically important DASI thresholds have been determined in non-surgical populations,[10,14,15] their generalisability to surgical patients has yet to be evaluated. Overall, the lack of clear DASI score cut-offs that identify patients at risk has limited the ability of perioperative clinicians to incorporate the questionnaire into preoperative assessment practice.

We therefore conducted a nested cohort analysis of the METS study sample to characterise the adjusted association of preoperative DASI scores with postoperative cardiac and moderate-to-severe complications. Our primary objective was to identify thresholds in the DASI score that clinicians can use in routine practice to better identify patients at an elevated risk of postoperative morbidity.

Methods

Design

This report adhered to the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology criteria.[16] We performed a nested cohort analysis of the METS study, which was a prospective cohort study conducted at 25 hospitals in Canada, New Zealand, Australia, and the UK. Participants provided written informed consent, and each centre obtained research ethics board approval before commencing recruitment. The objectives, design, methods, and primary results of the METS study have been reported.[5,17] This analysis included all eligible participants who underwent surgery, regardless of whether they underwent preoperative cardiopulmonary exercise testing. Therefore, this nested cohort analysis included more participants than the primary METS study analysis,[5] which was restricted to participants who underwent both surgery and preoperative exercise testing.

Participants and study procedures

Eligible patients had to be aged 40 yr or older, scheduled for elective inpatient noncardiac surgery under general or regional anaesthesia, and deemed to have one or more risk factors for cardiac complications or coronary artery disease (Supplementary Table 2). Of the 1741 individuals who consented to participate in the METS study, 1546 were included in this nested cohort analysis (Fig. 1). The participants completed the DASI questionnaire on the date of recruitment, and underwent blood sampling to measure serum NT pro-BNP concentrations at any point between recruitment and surgery. The blood samples were stored at −70 to −80°C in each study site, and analysed at the Aberdeen Royal Infirmary (Aberdeen, UK) using the Siemens Vista™ immunoassay analyser (Siemens Healthcare Diagnostics Ltd, Frimley, UK). The participants, healthcare providers, and outcome

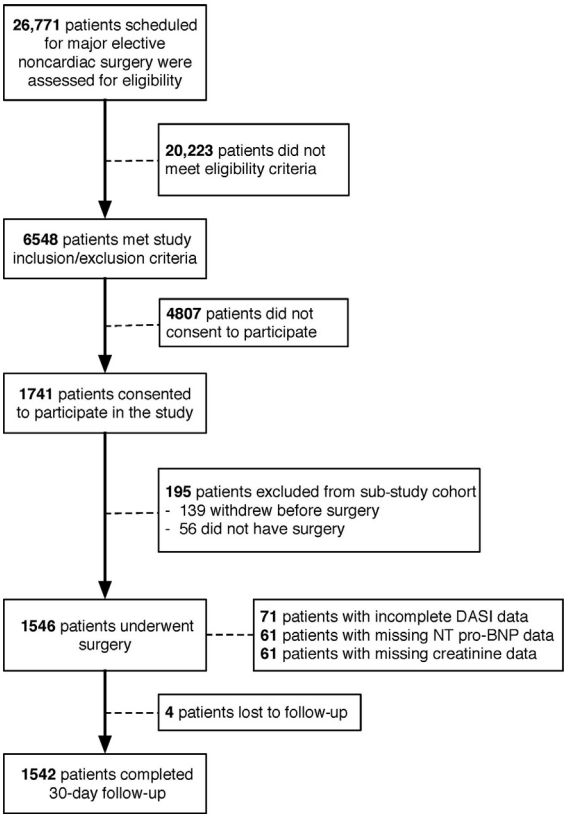

Fig 1. Participant screening, recruitment, and follow-up in the primary nested cohort analysis of the Measurement of Exercise Tolerance before Surgery study cohort. DASI, Duke Activity Status Index; NT pro-BNP, N-terminal pro-B-type natriuretic peptide.

adjudicators were blinded to DASI scores and NT pro-BNP results. Additionally, anaesthesiologists in the preoperative evaluation clinic or operating theatre subjectively rated the participants' functional capacity based on their usual preoperative history. Subjectively assessed functional capacity was categorised as 'poor' (<4 metabolic equivalents), 'moderate' (4–10 metabolic equivalents), or 'good' (>10 metabolic equivalents). After surgery, the participants underwent daily electrocardiograms and blood sampling to measure troponin concentrations until the third postoperative day or hospital discharge (whichever came first). The participants were also followed daily whilst in hospital to ascertain the presence of other complications, the severity of which were classified as mild, moderate, severe, or fatal using a modified Clavien–Dindo scheme (Supplementary Table 3).[18–20] After hospital discharge, the participants were contacted at 30 days after surgery to ascertain vital status.

Outcomes

Death or myocardial injury within 30 days after surgery was selected as the primary outcome because it is a prognostically important postoperative cardiac complication and it occurred with sufficient frequency in the METS study sample to allow unbiased multivariable logistic regression analyses to identify any relevant thresholds in the DASI score.[21] The secondary outcomes were (i) death or myocardial infarction within 30 days after surgery, and (ii) moderate-to-severe postoperative complications during the index hospitalisation. Myocardial injury was defined as postoperative troponin concentrations exceeding both the 99th percentile upper reference limit and the threshold at which the assay coefficient of variation was 10%.[22] Myocardial infarction was diagnosed by an adjudication committee that used the Third Universal Definition of Myocardial Infarction whilst remaining blinded to DASI and NT pro-BNP results.[23] The endpoint of moderate-to-severe complications included fatal events.

Statistical analysis

Descriptive statistics were initially used to characterise the sample, both overall and across strata defined by the presence or absence of the study outcomes. Categorical data were compared using the χ^2 or Fisher's exact test, whilst continuous variables were compared using the two-sample *t*-test. Multivariable logistic regression models were then used to separately evaluate the adjusted association of preoperative DASI scores with the primary and secondary outcomes. Covariates in these models were selected *a priori* based on prior evidence, their inclusion in guideline-recommended assessment algorithms (i.e. RCRI and natriuretic peptides for cardiac risk stratification),[1,12] need to prevent model overfitting,[21] and consistency with typical clinical practice during preoperative evaluation. For the models predicting (i) 30-day death or myocardial injury and (ii) 30-day death or myocardial infarction, co-variates were the validated RCRI and preoperative NT pro-BNP concentrations.[7,12,24] As recommended by the Canadian Cardiovascular Society guidelines, NT pro-BNP concentration was dichotomised based on a 300 ng L^{-1} threshold.[12] In the model predicting moderate-to-severe complications, the co-variates were age, sex, and high-risk surgery, which was defined as intra-peritoneal, -thoracic, or supra-inguinal vascular procedures.[7] To account for non-linear relationships between continuous predictor variables (i.e. DASI and age) and the study outcomes, we used restricted cubic spline plots to determine which transformation or categorisation, if any, was necessary. Adjusted associations were expressed as odds ratios with 95% confidence intervals. Model discrimination was characterised by the c-index, whilst calibration was assessed using the Hosmer–Lemeshow statistic.

We conducted a complete case analysis, and assumed that the six participants lost to follow-up between hospital discharge and the 30th postoperative day remained alive during this follow-up window. Several sensitivity analyses were performed to evaluate the robustness of our primary analysis. Firstly, analyses were repeated after multiple imputation to account for missing baseline data (i.e. DASI score, creatinine concentration, and NT pro-BNP concentration) that occurred in 8% of the study sample. Twenty imputed data sets were calculated using chained predictive mean matching. Secondly, we used bootstrap resampling (1000 samples) to internally validate the multivariable logistic regression models predicting the three study outcomes. Thirdly, age and sex (which are not considered in the current guideline-recommended assessment algorithms)[1,12] were included as

Table 1 Characteristics of the study sample. eGFR, estimated glomerular filtration rate; IQR, inter-quartile range; NT pro-BNP, N-terminal pro-B-type natriuretic peptide; SD, standard deviation. *Current smoker or quit within previous 1 yr. †Prior diagnosis of asthma, reactive airway disease, chronic obstructive lung disease, chronic bronchitis, or emphysema. ‡Estimated glomerular filtration rate was calculated using the preoperative serum creatinine concentration and Chronic Kidney Disease Epidemiology Collaboration equation. ¶Revised Cardiac Risk Index scores were calculated using a modified definition of diabetes mellitus (i.e. any known diagnosis *vs* requirement for insulin). All missing Revised Cardiac Risk Index scores were related to missing preoperative creatinine concentration data.

	Overall cohort (n=1546)	Missing data (n)
Patient characteristics		
Age (yr)		
Median (IQR)	65 (57–72)	
Mean (SD)	64 (10)	
Female sex, n (%)	629 (41)	
Preoperative characteristics, n (%)		
Coronary artery disease	210 (14)	
Heart failure	26 (2)	
Cerebrovascular disease	64 (4)	
Peripheral arterial disease	49 (3)	
Diabetes mellitus	301 (19)	
Hypertension	865 (56)	
Atrial fibrillation	58 (4)	
Current or recent smoker*	255 (16)	
Obstructive lung disease†	200 (13)	
Subjective assessment of functional capacity		52
Poor (<4 metabolic equivalents)	109 (7)	
Moderate (4–10 metabolic equivalents)	848 (57)	
Good (>10 metabolic equivalents)	537 (36)	
Duke Activity Status Index, points		71
Median (IQR)	42.7 (28.7–53.0)	
Mean (SD)	40.5 (15.2)	
Preoperative renal function, n (%)‡		58
eGFR ≥60 ml min^{-1} (1.73 m)$^{-2}$	1311 (88)	
eGFR 30–59 ml min^{-1} (1.73 m)$^{-2}$	144 (9)	
eGFR <30 ml min^{-1} (1.73 m)$^{-2}$ or dialysis	33 (2)	
Preoperative natriuretic peptide concentration, n (%)		61
NT pro-BNP <100 ng L^{-1}	826 (56)	
NT pro-BNP 100 to <300 ng L^{-1}	470 (32)	
NT pro-BNP ng L^{-1} ≥300 ng L^{-1}	189 (13)	
Revised Cardiac Risk Index, n (%)¶		58
Class 1	557 (37)	
Class 2	677 (46)	
Class 3	204 (14)	
Class 4	50 (3)	
Operative characteristics		
Procedure type, n (%)		
Vascular	29 (2)	
Intra-thoracic	35 (2)	
Intra-peritoneal or retro-peritoneal	489 (32)	
Urological or gynaecological	457 (30)	
Head and neck	109 (7)	
Orthopaedic	388 (25)	
Other	39 (3)	

additional co-variates in the multiple variable logistic regression model predicting 30-day death or myocardial injury. Fourthly, the models predicting (i) 30-day death or myocardial injury and (ii) 30-day death or myocardial infarction were re-estimated with the RCRI as the only co-variate, because preoperative NT pro-BNP concentrations are not routinely measured in many perioperative settings.

Analyses were conducted using the R statistical language (version 3.5.1) and Stata version 14.2 (StataCorp, College Station, TX, USA). Statistical significance was defined as a two-tailed P<0.05, and no adjustment was made for multiple comparisons. The number of participants available for this sub-study was determined by the sample size calculation for the METS study as described.[5,17]

Subset analysis on new postoperative disability

To understand whether DASI scores also predicted functional recovery at 1 yr after surgery, we conducted a subset analysis of METS study participants in whom self-reported disability status was prospectively measured using the validated 12-item WHO Disability Assessment Schedule (WHODAS) 2.0 instrument.[25,26] As part of a pre-specified sub-study on the prognostic performance of the 6 min walk test, the WHODAS questionnaire was administered before surgery and subsequently at 1 yr post-surgery.[27] The questionnaire consists of 12 items, each of which is scored 0–4. The sum of all item responses is the WHODAS disability score, which ranges from 0 to 40 and can be expressed as a

Table 2 Bivariate comparisons between patients who did *vs* did not suffer 30-day postoperative death or myocardial injury. eGFR, estimated glomerular filtration rate; NT pro-BNP, N-terminal pro-B-type natriuretic peptide; SD, standard deviation. *Current smoker or quit within previous 1 yr. †Prior diagnosis of asthma, reactive airway disease, chronic obstructive lung disease, chronic bronchitis, or emphysema. ‡Estimated glomerular filtration rate was calculated using the preoperative serum creatinine concentration and Chronic Kidney Disease Epidemiology Collaboration equation. ¶Revised Cardiac Risk Index scores were calculated using a modified definition of diabetes mellitus (i.e. any prior diagnosis of diabetes mellitus, as opposed to requirement for insulin therapy).

	Alive at 30 days without myocardial injury (*n*=1359)	30-Day death or myocardial injury (*n*=187)	P-value
Patient characteristics			
Age (yr), mean (SD)	63 (10)	70 (10)	<0.001
Female sex, *n* (%)	554 (41)	75 (40)	0.86
Preoperative characteristics, *n* (%)			
Coronary artery disease	162 (12)	48 (26)	<0.001
Heart failure	21 (2)	5 (3)	0.23
Cerebrovascular disease	50 (4)	14 (7)	0.01
Peripheral arterial disease	40 (3)	9 (5)	0.17
Diabetes mellitus	258 (19)	43 (23)	0.19
Hypertension	743 (55)	122 (65)	0.006
Atrial fibrillation	46 (3)	12 (6)	0.04
Current or recent smoker*	231 (17)	24 (13)	0.15
Obstructive lung disease†	182 (13)	18 (10)	0.15
Duke Activity Status Index (points), mean (SD)	41 (15)	36 (15)	<0.001
Preoperative renal function, *n* (%)‡			
eGFR ≥60 ml min^{-1} (1.73 m)$^{-2}$	1165 (89)	146 (80)	0.002
eGFR 30–59 ml min^{-1} (1.73 m)$^{-2}$	114 (8)	30 (16)	
eGFR <30 ml min^{-1} (1.73 m)$^{-2}$ or dialysis	27 (2)	6 (3)	
Preoperative natriuretic peptide concentration, *n* (%)			
NT pro-BNP <100 ng L^{-1}	763 (59)	63 (35)	<0.001
NT pro-BNP 100 to <300 ng L^{-1}	403 (31)	67 (37)	
NT pro-BNP ng L^{-1} ≥300 ng L^{-1}	138 (11)	51 (28)	
Revised Cardiac Risk Index, *n* (%)¶			
Class 1	501 (38)	56 (30)	<0.001
Class 2	602 (46)	75 (41)	
Class 3	166 (13)	38 (21)	
Class 4	37 (3)	13 (7)	
Operative characteristics			
Procedure type, *n* (%)			
Vascular	20 (2)	9 (5)	<0.001
Intra-thoracic	28 (2)	7 (4)	
Intra-peritoneal or retro-peritoneal	435 (32)	54 (29)	
Urological or gynaecological	415 (31)	42 (22)	
Head and neck	102 (8)	7 (4)	
Orthopaedic	320 (24)	68 (37)	
Other	39 (3)	0 (0)	

percentage of the maximum possible score. Moderate, severe, or complete disability is defined as a WHODAS disability score exceeding 25%, and an 8% absolute difference in scores is considered meaningful.[28] The outcome for this subset analysis was new disability or death within 1 yr after surgery, where new disability was defined as a postoperative WHODAS disability score that exceeded 25% and represented an 8% or greater absolute increase from the preoperative measurement.[27] Multivariable logistic regression modelling was used to estimate the adjusted association of preoperative DASI scores with new disability or death within 1 yr after surgery. The co-variates in the model were age; sex; preoperative moderate, severe, or fatal disability; and high-risk surgery. We conducted a complete case analysis and used restricted cubic spline plots to determine the need for transformation or categorisation of continuous variables.

Results

Participant characteristics

From March 2013 to March 2016, 1741 patients were recruited for the METS study at 25 hospitals in Canada, Australia, New Zealand, and the UK. From this sample, 1546 participants were included in this sub-study, of whom 1540 (99.7%) completed the 30-day follow-up. The characteristics of the sub-study cohort are presented in Table 1. Their median age was 65 yr (inter-quartile range [IQR]: 57–62), 41% (*n*=629) were females, 61% (*n*=946) underwent major abdominal or pelvic procedures, 59% (*n*=881) were classified as RCRI Class 2 or 3, and 13% (*n*=189) had preoperative NT pro-BNP concentrations greater than the high-risk threshold of 300 ng L^{-1}.[12] Whilst only seven participants completely missed their DASI questionnaires, 64 had one or more missing responses to individual items in the questionnaire (Supplementary Table 1).

Table 3 Adjusted association of DASI score and other clinical risk factors with 30-day postoperative death or myocardial injury. Model was fit using 1417 observations with complete data. The multivariable regression model had a c-index of 0.66 and Hosmer–Lemeshow goodness-of-fit statistic P-value of 0.12. Revised Cardiac Risk Index scores were calculated using a modified definition of diabetes mellitus (i.e. any known diagnosis *vs* requirement for insulin). CI, confidence interval; DASI, Duke Activity Status Index; NT pro-BNP, N-terminal pro-B-type natriuretic peptide.

Preoperative risk factor	Odds ratio (95% CI) for 30-day death or myocardial injury	P-value
DASI score		
Expressed as transformed continuous variable		
Per 1 point increase above 34 points	0.97 (0.96–0.99)	0.002
Thresholds extrapolated from transformed variable		
≤34 points	1.97 (1.28–3.04)	
35 points	1.92 (1.26–2.90)	
40 points	1.67 (1.20–2.31)	
45 points	1.44 (1.14–1.83)	
50 points	1.26 (1.09–1.46)	
55 points	1.09 (1.03–1.16)	
58.2 points (maximum score)	Reference	
Revised Cardiac Risk Index		
Class 1	Reference	0.07
Class 2	1.08 (0.74–1.59)	
Class 3	1.65 (1.02–2.68)	
Class 4	2.05 (0.97–4.35)	
Preoperative NT pro-BNP concentration		
<300 ng L^{-1}	Reference	
≥300 ng L^{-1}	2.43 (1.60–3.69)	<0.001

The item with the highest frequency of missing responses (n=45) was the question, 'Can you have sexual relations?' Amongst the 1475 participants (95%) who responded to all questionnaire items, the median DASI score was 42.7 (IQR: 28.7–53.0).

Postoperative outcomes

By 30 days after surgery, 187 (12.1%) participants experienced the primary outcome of death or myocardial injury, and 26 (1.7%) experienced the secondary outcome of death or myocardial infarction. During their postoperative hospitalisation, 210 (13.6%) participants experienced the secondary outcome of in-hospital moderate-to-severe complications. The specific types of complications associated with postoperative myocardial injury are presented in Supplementary Table 4.

Prediction of 30-day postoperative death or myocardial injury

In unadjusted comparisons, the participants who did or did not experience 30-day death or myocardial injury differed with respect to age, cardiovascular comorbidities (i.e. coronary artery disease, cerebrovascular disease, hypertension, and atrial fibrillation), renal function, RCRI score, NT pro-BNP concentration, surgery, and DASI score (Table 2). After adjustment for RCRI score and NT pro-BNP concentration, restricted cubic spline analyses demonstrated a non-linear association between the DASI score and 30-day death or myocardial injury (Supplementary Fig. 1). Based on visual inspection of this plot, there was maximum at a score of about 34; ~32% of participants (n=494) had DASI scores of 34 or less. In multivariable logistic regression analyses, the DASI score was therefore modelled as a transformed continuous variable, where values below 34 were treated as 34. The transformed score had a linear and statistically significant adjusted association with 30-day death or myocardial injury (Table 3).

Prediction of 30-day postoperative death or myocardial infarction

The restricted cubic spline analyses showed a non-linear unadjusted association between DASI scores and 30-day death or myocardial infarction (Supplementary Fig. 2). Visual inspection of this plot suggested a minimum at a DASI score of 34. We therefore modelled the DASI score as a transformed continuous variable, where values above 34 were treated as 34. This transformed DASI score had a statistically significant adjusted association with 30-day postoperative death or myocardial infarction (Table 4).

Prediction of postoperative moderate-to-severe complications

In unadjusted comparisons, the participants who did or did not experience moderate-to-severe complications differed with respect to sex, cardiovascular comorbidities (i.e. cerebrovascular disease and atrial fibrillation), NT pro-BNP concentration, and surgery, but not DASI score (Supplementary Table 5). The restricted cubic spline analyses showed a non-linear adjusted association between the DASI score and postoperative complications (Supplementary Fig. 3), with suggestion of a minimum at a DASI score of 34. In multivariable logistic regression analyses, the DASI score was therefore modelled as a transformed continuous variable, where values above 34 were treated as 34. The transformed score had a linear and statistically significant adjusted association

with moderate-to-severe complications (Supplementary Table 6).

Sensitivity analyses

The adjusted association of the DASI score with the primary and secondary outcomes was qualitatively unchanged in sensitivity analyses that incorporated multiple imputation, bootstrap internal validation, and different model co-variates (Supplementary Table 7).

Subset analysis on new postoperative disability

About 35% (n=546) of patients in the primary analysis cohort completed the preoperative WHODAS questionnaires, of whom 17% (n=95) had preoperative moderate, severe, or complete disability, and 95% (n=517) completed 1 yr follow-up (Supplementary Fig. 4). The subset cohort (Supplementary Table 8) was qualitatively similar to the primary cohort (Table 1), aside from a lower prevalence of orthopaedic surgical procedures (16% in the subset cohort *vs* 25% in the primary cohort). By 1 yr after surgery, 14 participants (2.6%) had died, 46 (8.4%) had new disability, and 60 (11.6%) had either died or developed new disability.

In unadjusted comparisons, the participants who did or did not experience new disability or death within 1 yr after surgery differed with respect to some cardiovascular comorbidities (i.e. heart failure and atrial fibrillation), smoking status, and possibly preoperative disability status (Supplementary Table 9). The restricted cubic spline analyses suggested a non-linear adjusted association between the DASI score and new disability or death within 1 yr after surgery (Supplementary Fig. 5). Based on visual inspection of this plot, we modelled the DASI score as a transformed continuous variable, where values below 34 were treated as 34. The transformed score had a statistically significant adjusted association with new disability or death within 1 yr after surgery (Supplementary Table 10).

Post hoc comparison of DASI thresholds *vs* subjective assessment

As a DASI score of 34 was a consistent prognostically important threshold across the different study outcomes, we performed a *post hoc* analysis comparison between this DASI score threshold and anaesthesiologists' subjective assessment of functional capacity. Whilst 97% of participants with DASI scores of 35 or more were deemed to have moderate or good functional capacity, only 15% of individuals with DASI scores of 34 or lower were judged as having poor functional capacity (Supplementary Table 11).

Discussion

In this nested cohort analysis of the METS study, a preoperative DASI score threshold of 34 improved the identification of patients at risk for cardiac complications, moderate-to-severe complications, and new disability after major elective noncardiac surgery. After adjustment for clinical risk factors, the patients with self-reported functional capacity better than a DASI score of 34 had a lower risk of 30-day myocardial injury and 1 yr new disability, whilst individuals with self-reported functional capacity worse than a DASI score of 34 experienced greater risks of 30-day myocardial infarction and in-hospital moderate-to-severe complications. This threshold retained prognostic importance for identifying patients at an elevated cardiac risk even after accounting for preoperative plasma natriuretic peptide concentrations. The findings were also consistent across sensitivity analyses that accounted for other preoperative risk factors, missing data, and internal validation using bootstrap resampling. Importantly, fewer than 20% of individuals with concerning DASI scores were

Table 4 Adjusted association of DASI score and other clinical risk factors with 30-day postoperative death or myocardial infarction. Model was fit using 1417 observations with complete data. The multivariable regression model had a c-index of 0.67 and Hosmer–Lemeshow goodness-of-fit statistic *P*-value of 0.66. Revised Cardiac Risk Index scores were calculated using a modified definition of diabetes mellitus (i.e. any known diagnosis *vs* requirement for insulin). CI, confidence interval; DASI, Duke Activity Status Index; NT pro-BNP, N-terminal pro-B-type natriuretic peptide.

Preoperative risk factor	Odds ratio (95% CI) for 30-day death or myocardial infarction	*P*-value
DASI score		
Expressed as transformed continuous variable		
Per 1 point decrease below 34 points	1.05 (1.00–1.09)	0.04
Thresholds extrapolated from transformed variable		
5 points	3.63 (1.05–12.61)	
10 points	2.90 (1.04–8.15)	
15 points	2.32 (1.03–5.26)	
20 points	1.86 (1.02–3.40)	
25 points	1.49 (1.01–2.20)	
30 points	1.19 (1.01–1.42)	
≥34 points	Reference	
Revised Cardiac Risk Index		
Class 1 or 2	Reference	
Class 3 or 4	2.22 (0.93–4.35)	0.07
Preoperative NT pro-BNP concentration		
<300 ng L^{-1}	Reference	
≥300 ng L^{-1}	1.55 (0.58–4.19)	0.38

subjectively assessed as having poor functional capacity by their responsible anaesthesiologists. Overall, the results help inform clinicians seeking practical approaches to better incorporate the evaluation of functional capacity into usual preoperative risk assessment.

Notably, when considering outcomes ascertained during the same short-term postoperative time frame (≤30 days after surgery), the adjusted association of the DASI score with biochemically determined (albeit prognostically important) myocardial injury differed qualitatively from its association with clinical events, such as myocardial infarction and moderate-to-severe complications.[29,30] Whilst DASI scores *below* 34 demarcated a high-risk plateau for experiencing myocardial injury, scores *above* 34 instead demarcated a low-risk plateau for experiencing myocardial infarction and moderate-to-severe complications. The basis for these differences warrants further research, but there are at least two possible explanations. Myocardial injury episodes occurring in individuals with DASI scores above 34 may have been more likely to represent biochemical elevations not associated with overt clinical manifestations. Whilst the risk of any myocardial injury may have reached a local maximum at DASI scores of 34 or less, the magnitude of such injury may have been greater in individuals with DASI scores further below this threshold. Importantly, the practical implications for clinicians are largely straightforward. When using the DASI questionnaire to assess self-reported functional capacity during preoperative evaluation, DASI scores lower than 34 are associated with greater risks of myocardial injury, myocardial infarction, and moderate-to-severe complications, whilst scores greater than 34 are associated with lower risks of these same events.

Whilst it is tempting to interpret the clinical relevance of a DASI score by converting it to estimated metabolic equivalents, the results of our study would caution against such an approach. Instead, clinicians should focus on prognostically important thresholds based on the DASI score itself. Prior publications highlight uncertainty as to how best to convert DASI scores to estimated metabolic equivalents.[10,11] The METS study confirmed this uncertainty: a DASI score of 34 corresponded to a peak oxygen consumption of 17–18 ml kg^{-1} min^{-1} (or five metabolic equivalents) in the METS study sample,[5] as opposed to seven metabolic equivalents based on the recommended conversion formula.[6] Furthermore, the association of DASI scores with outcomes might have largely been explained by prognostically important factors aside from cardiopulmonary fitness (e.g. frailty),[31] especially as peak oxygen consumption was correlated with DASI scores, but not postoperative cardiac complications in the METS study.[5]

An increasing body of literature shows that the use of preoperative BNP or NT pro-BNP concentrations improves the accuracy of preoperative cardiac risk assessment, even when used in combination with clinical risk factors.[13,32] Whilst our analysis confirms these prior findings, it highlights that natriuretic peptides do not substitute for the evaluation of preoperative functional capacity. In adjusted regression models, both NT pro-BNP concentrations and DASI scores were independently associated with postoperative cardiac complications. Notably, NT pro-BNP concentrations and DASI scores have a relatively low correlation (Spearman's coefficient: −0.21; $P<0.001$), suggesting that they measure related but different prognostically important constructs.[5]

Our study has several important limitations. *First*, whilst the METS study was a relatively large multicentre prospective cohort study, it was likely biased towards excluding very high-risk patients, largely because of the selection bias associated with the study's requirement for strenuous preoperative exercise testing. Consistent with this possibility, the observed rate for myocardial infarction was lower than originally anticipated.[5,17] Importantly, our findings, with respect to the prognostic accuracy of DASI scores, remained consistent in analyses focused on the more frequent, but related, outcome of prognostically important myocardial injury.[29,33] Nonetheless, our analyses should be validated in other large surgical cohorts to ensure that the identified DASI score thresholds are generalisable to other intermediate-to-high-risk surgical patients.

Second, whilst we selected the DASI questionnaire *a priori* as the standardised instrument for assessing preoperative functional capacity in the METS study,[17] our results do not rule out a potential prognostic role of other questionnaires that provide similar information.[34]

Third, there remain opportunities to update and improve the DASI questionnaire. For example, to improve interpretability outside North America, the wording of some items (e.g. question pertaining to 'yard work') could be modified,[35] and the entire questionnaire could undergo a more extensive validated translation to other languages.[36] In addition, the questionnaire item pertaining to sexual relations may be prone to missing responses.[35] In our present study, this specific question was responsible for the vast majority of missing responses. Further methodological research is needed to determine whether the item pertaining to sexual relations can be feasibly omitted, such that the overall response rates are improved whilst the overall questionnaire validity is preserved.

Fourth, efficacious interventions for reducing perioperative risk in patients with low DASI scores remain to be identified. Possible approaches that merit evaluation in future studies include pre-habilitation (i.e. multimodal preoperative exercise training and nutritional supplementation), intensive perioperative haemodynamic management to minimise hypotension, and enhanced postoperative monitoring.

Finally, this present study was a *post hoc*, albeit methodologically robust, secondary analysis of a multicentre prospective cohort study that was designed primarily to compare the prognostic accuracy of several different preoperative measures of functional capacity (i.e. physicians' subjective assessment, DASI scores, cardiopulmonary exercise testing, and natriuretic peptides).[5,17] Therefore, further studies are needed to confirm the findings of this study.

Conclusions

In this nested cohort analysis of a multicentre prospective cohort study, preoperative scores on the 12-item DASI questionnaire were predictive of 30-day death or myocardial injury, 30-day death or myocardial infarction, in-hospital moderate-to-severe complications, and 1 yr new disability or death after major inpatient noncardiac surgery. In general, those patients with DASI scores lower than 34 experienced elevated risks of these complications, even after accounting for clinical risk factors. These findings suggest that incorporation of DASI scores into preoperative evaluation will help improve the accurate identification of intermediate-to-high-risk patients who warrant modifications in perioperative care or recruitment into targeted clinical research studies.

Authors' contributions

Study conception/design: all authors
Data acquisition/analysis/interpretation: all authors
Writing of first draft: DNW
Revising manuscript for important intellectual content: all authors
Approving final version: all authors

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2019.11.025.

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